Index of Disease Management Guidelines

The disease management guidelines (DMGs) were developed by the CMC Pharmacy and Therapeutics Committee through review of the medical literature, review of national treatment guidelines, and evaluation of population-specific treatment data. The goal was to develop tools that would assist practitioners in making treatment decisions regarding commonly encountered disease states found within the health care system that would result in improved outcomes and consistent and cost-effective care. Complimentary written patient education leaflets in English and Spanish are also available for providers and nursing staff. The DMGs should not replace sound clinical judgment, nor are they intended to strictly apply to all patients. The DMGs are reviewed and/or revised every five years or when new national treatment guidelines, landmark clinical studies, and/or new drug entities become available, whichever is sooner.

Disease Management Guideline

Disease Management Guidelines for Youth

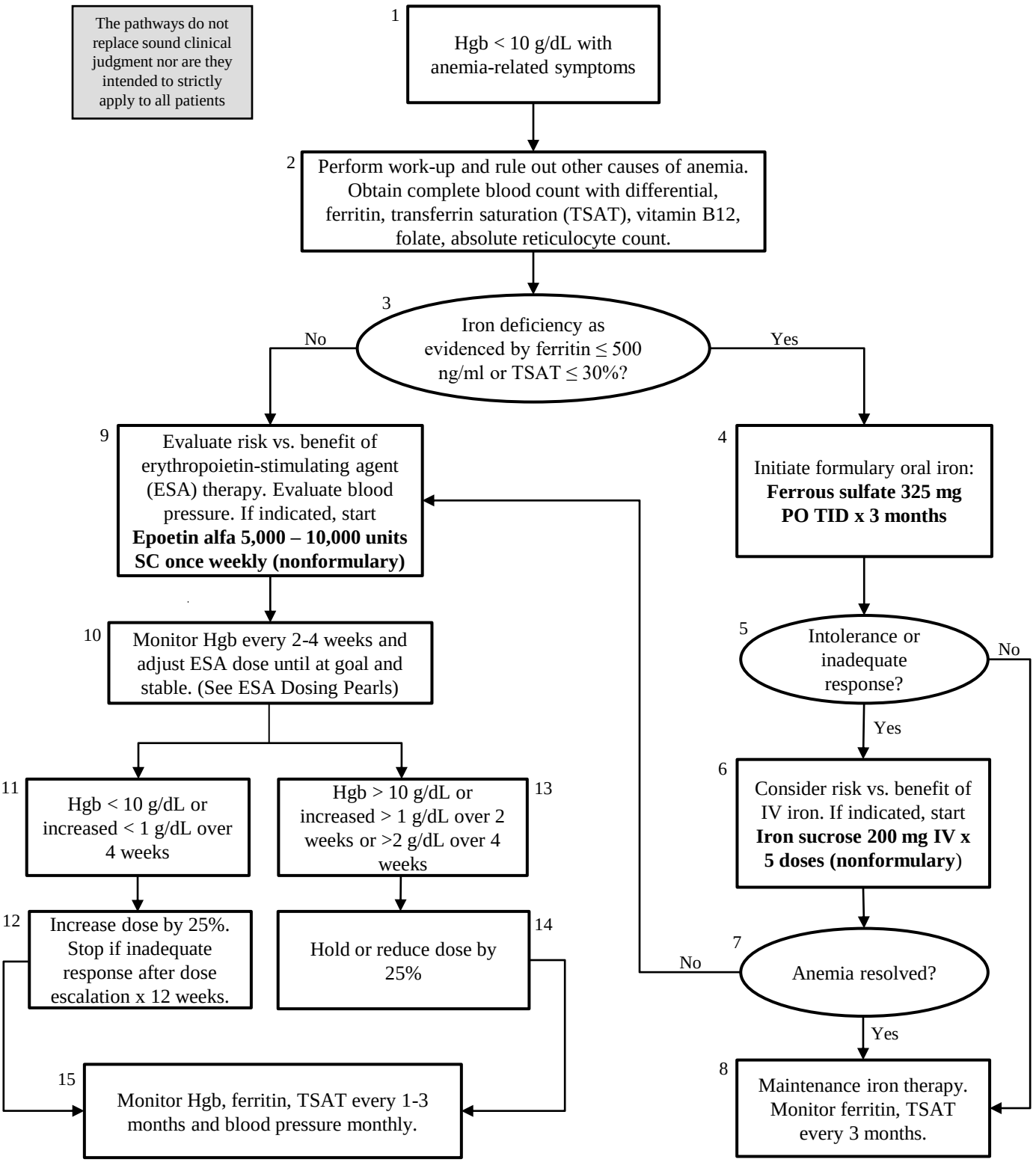
The youth psychiatric disease management guidelines were prepared by the Youth Services Pharmacy and Therapeutics Committee.

Disease Management Guideline

1. Acne Vulgaris Adolescents
2. Anxiety and Panic Disorder Adolescents
3. Asthma, Adults and Adolescents (see adult listing)
4. Attention Deficit Hyperactivity Disorder Adolescents
5. Bipolar Disorder Adolescents
6. Depressive Disorders Adolescents
7. Diabetes Mellitus Children & Adolescents
8. Hypertension Adolescents
9. Insomnia Adolescents
10. Post Traumatic Stress Disorder Adolescents
11. Psychosis Adolescents
12. Seizures Acute and Chronic Adolescents

Anemia in Non-Dialysis Dependent Chronic Kidney Disease

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients



Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.

Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee;
Approved July 2009; Revised 7/2011, 3/2021; Reviewed 1/2012, 05/2016.

Provider Education

I. Treatment Principles
   A. Treat CKD patients with anemia-related symptoms and Hgb < 10 g/dL.
   B. Monitor and correct iron deficiency before considering erythropoietin-stimulating agent (ESA) treatment and during ESA treatment. Correcting iron deficiency can lower ESA requirements.
   C. Use the lowest ESA dose sufficient to improve anemia-related symptoms, reduce the need for blood transfusions, and minimize the risk for cardiovascular adverse events.
   D. In general, target a Hgb goal of 10-11 g/dL. However, Hgb goal may need to be individualized based on response to treatment.

II. Other Causes of Anemia
   A. Aluminum toxicity
   B. Bleeding or occult blood loss
   C. Bone marrow disorders
   D. Folate or vitamin B12 deficiency
   E. Hemolysis
   F. Hyperparathyroidism
   G. Hypothyroidism
   H. Infection or inflammation
   I. Iron deficiency
   J. Malignancy
   K. Malnutrition
   L. Pure red cell aplasia

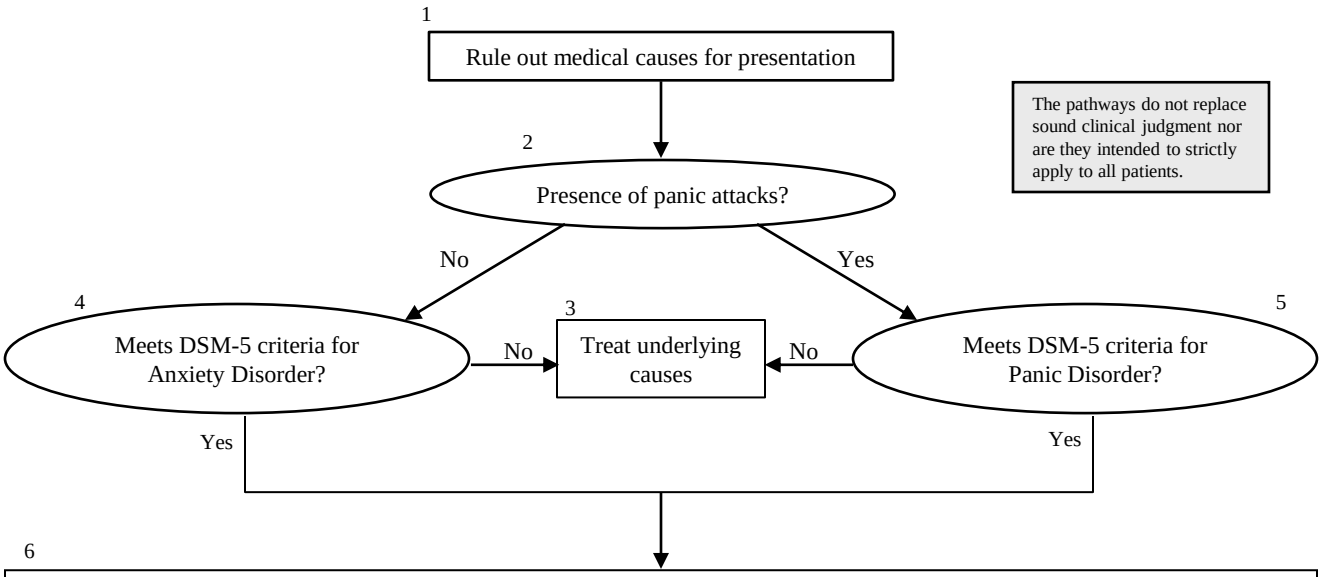
III. Intravenous Iron Warnings and Precautions
   I. Hypersensitivity Reactions. Monitor for signs and symptoms of hypersensitivity for at least 30 minutes after administration. (Requires ACLS-trained staff)
   II. Hypotension
   III. Iron Overload

IV. ESA Warnings and Precautions
   A. Increased risk of death, myocardial infarction, stroke, congestive heart failure, and other thromboembolic events
   B. Increased risk of tumor progression or recurrence in patients with cancer
   C. Increased risk of seizures in CKD patients

V. ESA Contraindications
   A. Uncontrolled hypertension
   B. Pure red cell aplasia secondary to ESA treatment
   C. Pregnant and lactating women with use of multi-dose vials containing benzyl alcohol
   D. Serious allergic reaction to ESA product

VI. ESA Dosing Pearls
   A. Dose adjustments should generally not exceed 25%. Round calculated dose to nearest 1,000 units.
   B. Do not increase dose more often than every 4 weeks. Dose may be reduced more frequently.
   C. Avoid Hgb levels > 11 g/dL. In particular, Hgb > 13 g/dL is associated with increased risk for cardiovascular adverse events.
   D. Stop ESA treatment if inadequate Hgb response after 12 weeks of dose escalation. Consider if patient is iron deficient or if there are other causes of anemia.

ANXIETY and PANIC DISORDER



The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

6

- Obtain baseline BPRS
- Psychotherapy should be initial treatment of choice and should be continued throughout treatment, even if drug therapy is started
- Initiate formulary SSRI antidepressant
  - Start at lower end of dosing range and titrate gradually upward to decrease potential for activating side effects
  - Continue for 4-6 weeks at a therapeutic dose and assess response*

*Response to treatment is determined after a 4–6-week trial at the maximal tolerated dose, with a minimum of 80% adherence. In patients who demonstrate partial response, full remission may occur with continuation of treatment for a total of 12 weeks or more.

7

Adequate response per BPRS?

Yes

8

- Continue therapy for 6-12 months, reassessing as needed by unit mental health provider
- After 12-18 months, consider tapering and discontinuing pharmacotherapy

No

9

- If compliance < 80%, counsel on medication compliance
- Re-evaluate diagnosis and need for medication
- Increase dose of current agent to maximal tolerated dose for 4-6 weeks
- If trial at max tolerated dose is partially effective, consider continuing this dose and reassessing response in another 4-6 weeks
- If trial at max tolerated dose is ineffective, switch to another formulary agent (Table 1), or consider pharmacotherapy consult

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.

Medication Selection
Patients should be evaluated for use of formulary agents when possible. Providers should consider history of response, contraindications, co-morbidities, compliance, and potential for adverse effects and drug interactions when making treatment decisions. When medications are changed, patients should be monitored closely for signs of worsening symptoms and adverse effects.

Table 1: Formulary Antidepressants

Drug Class	Generic Name	Brand Name	Initial Daily Dosage (Range)	Therapeutic Range	Monitoring
Selective Serotonin Reuptake Inhibitors (SSRIs)	Citalopram 20mg, 40mg tablet	Celexa®	20 mg (20 – 40 mg)	N/A	• Emergence of suicidal ideation or behavior • Citalopram: EKG at baseline and as clinically indicated if risk factors for QTc prolongation are present[a] • If QTc is > 450 msec for males or > 470 msec for females, do not initiate citalopram. If pt is on citalopram and QTc is > 500 msec, consider alternative treatment. • Fluoxetine has also been associated with QTc prolognation. EKG monitoring is encouraged if risk factors for QTc prolongation are present.[a]
	Fluoxetine 20mg capsule	Prozac®	20 mg (20 – 60 mg)		
	Sertraline 50mg, 100mg tablet	Zoloft®	50 mg (50 – 200 mg)		
Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)[b]	Venlafaxine XR 75, 150 mg capsule	Effexor XR®	75 mg (75-225 mg)	N/A	• Emergence of suicidal ideation or behavior • Dose-related increases in systolic blood pressure and pulse
	Duloxetine 30, 60 mg capsules	Cymbalta®	30-60 mg 60-120 mg		
Other[c]	Trazodone 50mg, 100mg tablet	Desyrel®	100 – 150 mg (300 – 600 mg)	N/A	• Emergence of suicidal ideation or behavior • Priapism

[a] Risk factors for QTc prolongation include age > 65 years old, use of other concomitant QTc prolonging medications, baseline hypokalemia or hypomagnesemia, or pre-existing cardiovascular impairment.
[b] venlafaxine functions as an SNRI at doses ≥ 150 mg/day. At lower doses, venlafaxine functions more like an SSRI.
[c] Generally not recommended as first line or second line therapy for treatment of anxiety or panic disorder

BRIEF PSYCHIATRIC RATING SCALE (BPRS) - Instructions for the Clinician

The Brief Psychiatric Rating Scale (BPRS) is a widely used instrument for assessing psychopathology at baseline and longitudinally when treatment is introduced. The BPRS is a scale measuring positive symptoms, general psychopathology and affective symptoms. It has proven particularly valuable for documenting efficacy of treatment in patients who have moderate to severe psychopathology. The BPRS has been well validated in clinical literature and is reportedly the most studied psychometric instrument currently in use.

The BPRS should be administered by a clinician who is knowledgeable concerning psychiatric disorders and is able to interpret the constructs used in the assessment. The individual's behavior over the previous 2-3 days should also be considered and can be reported by caregivers. It should be utilized at baseline and at each visit as long as the patient is prescribed a psychotropic medication.

The BPRS utilized in the electronic medical record (EMR) consists of 23 symptom constructs covering a broad array of potential psychopathology. The assessment typically takes 10-20 minutes or less for the interview and scoring.

Instructions for Use and Scoring:
Each item is rated on a seven-point scale (1=not present to 7=extremely severe). Zero (0) is entered if the item is not assessed. The scores of the 23 items should be summed and recorded. The total score should be compared from one evaluation to the next to measure response to treatment. In addition, a single subscale (symptom) or cluster of subscales (e.g., grandiosity, elevated mood, excitement, distractibility) can be followed over time.

Brief Psychiatric Rating Scale (BPRS)

Patient Name _____ Patient Number _____ Date_____

Facility _____ Practitioner _____

Enter the score for the term that best describes the patient's condition.

0 = Not assessed, 1 = Not present, 2 = Very mild, 3 = Mild, 4 = Moderate, 5 = Moderately severe, 6 = Severe, 7 = Extremely severe

Score		
____	1.	SOMATIC CONCERN - Preoccupation with physical health, fear of physical illness, hypochondriasis.
____	2.	ANXIETY - Worry, fear, over-concern for present or future, uneasiness
____	3.	EMOTIONAL WITHDRAWAL - Lack of spontaneous interaction, isolation deficiency in relating to others.
____	4.	CONCEPTUAL DISORGANIZATION - Thought processes confused, disconnected, disorganized, disrupted.
____	5.	IMPULSIVENESS
____	6.	MOTOR HYPERACTIVITY - Increase in energy level evidenced in more frequent movement and/or rapid speech. Do not rate if restlessness is due to akathisia.
____	7.	MANNERISMS AND POSTURING - Peculiar, bizarre, unnatural motor behavior (not including tic).
____	8.	GRANDIOSITY - Exaggerated self-opinion, arrogance, conviction of unusual power or abilities.
____	9.	DEPRESSIVE MOOD - Sorrow, sadness, despondency, pessimism.
____	10	HOSTILITY - Animosity, contempt, belligerence, disdain for others.
____	11.	SUSPICIOUSNESS - Mistrust, belief others harbor malicious or discriminatory intent.
____	12.	HALLUCINATORY BEHAVIOR - Perceptions without normal external stimulus correspondence.
____	13.	MOTOR RETARDATION - Slowed, weakened movements or speech, reduced body tone.
____	14.	UNCOOPERATIVENESS - Resistance, guardedness, rejection of authority.
____	15.	UNUSUAL THOUGHT CONTENT - Unusual, odd, strange, bizarre thought content.
____	16.	BLUNTED AFFECT - Reduced emotional tone, reduction in formal intensity of feelings, flatness.
____	17.	EXCITEMENT - Heightened emotional tone, agitation, increased reactivity.
____	18.	DISORIENTATION - Confusion or lack of proper association for person, place or time.
____	19.	ELEVATED MOOD - A pervasive, sustained and exaggerated feeling of well-being, cheerfulness, or euphoria implying a pathological mood. Optimism that is out of proportion to the circumstances.
____	20.	SUICIDALITY - Expressed desire, intent, or actions to harm or kill self.
____	21.	BIZARRE BEHAVIOR - Reports of behaviors which are odd, unusual, or psychotically criminal. Not limited to interview period. Include inappropriate sexual behavior and inappropriate affect.
____	22.	SELF-NEGLECT - Hygiene, appearance, or eating behavior below usual expectations, below socially acceptable standards or life threatening.
____	23.	DISTRACTIBILITY - Degree to which observed sequences of speech and actions are interrupted by stimuli unrelated to the interview. Distractibility is rated when the individual shows a change in the focus of attention as characterized by a pause in speech or a marked shift in gaze. Individual's attention may be drawn to noise in adjoining room, books on a shelf, interviewer's clothing, etc.

Asthma – Acute: Unit Level Management

1

Initial Assessment:

1) Determine degree of symptoms (dyspnea, wheezing, chest tightness, cough), duration of exacerbation, response to self treatment, and medications used for current exacerbation, and estimate of number of previous exacerbations.
2) Examine patient for degree of distress. Listen to chest for breath sounds and note symmetry and depth of respiration. Use of accessory muscles or supra-sternal retractions suggests severe exacerbation.
3) Measure pulse and respiratory rate.
4) Measure peak expiratory flow (PEF) and compare with personal best.
5) Consider potential triggers for symptoms (e.g. acute viral infection, sinusitis, pneumonia, exposure to toxic environment, heart disease).
6) Obtain oxygen (O_2) saturation.

2

FEV_1 or PEF ≥ 50% (Mild-to-Moderate)

- Oxygen to achieve SaO_2 93-95%
- Inhaled SABA by nebulizer or MDI with valve holding chamber, up to 3 doses in first hour
- Prednisone: 40 mg daily x 5 days

3

FEV1 or PEF <50% (Severe)

- May consider transfer to higher level of care.
- Oxygen to achieve SaO_2 *93-95%*
- High-dose inhaled SABA plus ipratropium by nebulizer or MDI with valve holding chamber, every 20 minutes or continuously for 1 hour
- Prednisone: 40 mg daily x 5 days

4

Impending or Actual Respiratory Arrest

- Transfer to higher level of care. Contact Utilization Review or follow unit procedures.
- Oxygen to achieve SaO_2 93-95%
- Nebulized SABA and ipratropium
- Intravenous corticosteroids
- Schedule follow up with unit provider upon return of hospitalization. Refer to Box 11

5

Continue treatment with SABA as needed. **ASSESS RESPONSE AT 1 HOUR** (or earlier if indicated)

6

Good Response

- PEF ≥ 70%
- Response sustained 60 minutes after last treatment
- No distress
- Physical exam: normal

7

Incomplete Response

- PEF 60-70%
- Mild-to-moderate symptoms

8

Poor Response

- PEF <60%
- PCO_2 ≥ 42 mm Hg
- Physical exam: severe symptoms, drowsiness, confusion

9

Discharge

- Continue treatment with inhaled SABA.
- Continue course of oral corticosteroid.
- Consider initiation of an ICS if not currently prescribed.
- Follow up with unit provider within 1 week
- Patient education
  - Review medications, including inhaler technique.
  - Review/initiate action plan
  - Review of environmental triggers
  - Follow up medical appointment

10

Individualize decision for hospitalization based on individual risk factors listed in Table 1, page 2. Refer to Box 11 if patient is discharged.

11

- Transfer to higher level of care. Contact Utilization Review or follow unit procedures.
- Schedule follow up with unit provider upon return of hospitalization. Refer to Box 11.

Exacerbations and poor control should prompt review of treatment plan

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients

SABA=Short-acting beta agonist (e.g., albuterol), MDI=Metered Dose Inhaler, ICS=Inhaled Corticosteroid.

Nurses: DMGs re guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.**

Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee, *Approved January 1999. Reviewed 4/02, 4/03, 3/05, 9/09, 1/11. Revised 10/03, 5/14, 9/19,7/24.*

Table 1. Risk Factors for Death from Asthma*

- A history of near-fatal asthma requiring intubation and mechanical ventilation
- Hospitalization or emergency care visit for asthma in the past year
- Currently using or having recently stopped using oral corticosteroids
- Not currently using inhaled corticosteroids
- Over-use of SABAs, especially use of more than one canister of albuterol monthly
- A history of psychiatric disease or psychosocial problems
- Poor adherence with asthma medications and/ or poor adherence with a written asthma action plan
- Food allergy in a patient with asthma
- Illicit drug use
- Cardiovascular disease
- Other chronic lung disease

*Adapted from National Heart, Lung, and Blood Institute Guidelines for the Diagnosis and Management of Asthma, Expert Panel Report 3 and GINA 2024

Table 2. Dosages of Drugs for Asthma Exacerbations

Medication	Adult Dose	Comments
Albuterol nebulizer Solution (0.083%, 2.5mg/3ml)	2.5-5mg every 20 minutes for 3 doses, then 2.5-10mg every 1-4 hours as needed, or 10-15mg/hour continuously	Use large volume nebulizers for continuous administration. May mix with ipratropium nebulizer solution.
Albuterol MDI (90mcg/puff)	4-8 puffs every 20 minutes up to 4 hours, then every 1-4 hours as needed.	In mild-to-moderate exacerbations, MDI plus valved holding chamber is as effective as nebulized therapy with appropriate administration technique and coaching by trained personnel.
Ipratropium bromide nebulizer solution (0.25mg/ml)	0.5mg every 20 minutes for 3 doses then as needed.	May mix in same nebulizer with albuterol. Should not be used as first-line therapy; should be added to SABA therapy for severe exacerbations.
Ipratropium bromide MDI (18mcg/puff)	8 puffs every 20 minutes as needed up to 3 hours	
Ipratropium with albuterol nebulizer solution (each 3ml vial contains 0.5mg ipratropium bromide and 2.5mg albuterol)	3 ml every 20 minutes for 3 doses, then as needed	May be used for up to 3 hours in the initial management of severe exacerbations.
Prednisone (5mg, 10mg, and 20mg tablets)	40 mg/day in 1 or 2 divided doses until PEF reaches 70% of predicted or personal best	For outpatient "burst," use 40mg in single or 2 divided doses for 5 days

Notes:
•There is no known advantage for higher doses of corticosteroids in severe asthma exacerbations, nor is there any advantage for intravenous administration over oral therapy provided gastrointestinal time or absorption is not impaired.
•The total course of systemic corticosteroids for an asthma exacerbation requiring an emergency department visit or hospitalization may last up to 5 days. For corticosteroid courses of less than 3 weeks, there is generally no need to taper, especially if patients are concurrently taking inhaled corticosteroids (ICS).
•ICSs can be started at any point in the treatment of an asthma exacerbation.

Adapted from National Heart, Lung, and Blood Institute Guidelines for the Diagnosis and Management of Asthma, Expert Panel Report 3

I. Treatment Goals
   A. Correction of significant hypoxemia, in moderate or severe exacerbations, by administering supplemental oxygen.
   B. Rapid reversal of airflow obstruction which is best achieved by repetitive or continuous administration of a short-acting beta-agonist (SABA) (e.g., albuterol) and early in the course of treatment, administration of systemic corticosteroids to patients who have moderate to severe exacerbations or to patients who fail to respond promptly and completely to SABA treatment.
   C. Reduction of the likelihood of relapse of the exacerbation or future recurrence of severe airflow obstruction by intensifying therapy. Often, a short course of systemic corticosteroids is useful.

II. Classifying Asthma Severity (Adapted from National Heart, Lung, and Blood Institute Guidelines for the Diagnosis and Management of Asthma, Expert Panel Report 3)

Table 3. Classifying Asthma Severity

Classification	Dyspnea	Symptoms and Signs	Initial PEF (or FEV_1)	Clinical Course
Mild	Dyspnea only with activity	• Talks in phrases • Not agitated • Increase in respiratory rate • Accessory muscles not used • Pulse Rate: 100-120 bpm • O_2 (on air) 90- 95%	PEF ≥ 70 percent predicted or personal best	• Usually cared for at home • Prompt relief with inhaled SABA • Possible short course of systemic corticosteroids
Moderate	Dyspnea interferes with or limits usual activity		PEF 50-69 percent predicted or personal best	• Usually requires office or ED visit • Relief from frequent inhaled SABA • Oral systemic corticosteroids; some symptoms last 1-2 days after treatment is begun
Severe	Dyspnea at rest; interferes with conversation	• Talks in words • Agitated • Respiratory rate >30/min • Accessory muscles in use • Pulse Rate >120 bpm • O_2 (on air) <90%	PEF < 50 percent predicted or personal best	• Usually requires ED visit and likely hospitalization • Partial relief from frequent inhaled SABA • Oral systemic corticosteroids; some symptoms last for >3 days after treatment is begun
Subset: Life threatening	Too dyspneic to speak; perspiring	Drowsy, confused, or silent chest	PEF < 25 percent predicted or personal best	• Requires ED/hospitalization; possible ICU • Minimal or no relief from frequent inhaled SABA • Intravenous corticosteroids

Key: ED - emergency department; FEV_1 - forced expiratory volume in 1 second; ICU - intensive care unit; PEF - peak expiratory flow; SABA - short-acting $beta_2$ -agonist

III. Monitoring
   A. Serial Measurements of Lung Function - FEV_1 or PEF appear to be more useful in categorizing the severity of the exacerbation, assessing treatment response, and predicting the need for hospitalization. Repeated measurements of PEF or FEV_1 at 1 hour and beyond are useful as isolated assessments in determining who will require hospitalization and who is likely to have sufficient response to allow continued treatment in the emergency room.
   B. Pulse oximetry is indicated for patients in severe distress or have FEV_1 or PEF < 40 percent of predicted, to assess the adequacy of arterial oxygen saturation.
   C. Signs and Symptoms – All patients presenting with a reported asthma exacerbation should be evaluated based on at least vital signs and an overall physical assessment (e.g., ability to breathe well enough to talk). The presence of drowsiness in a patient is a useful predictor of impending respiratory failure and reason to consider transfer to a higher level of care.

IV. Therapy
- A. Oxygen is recommended for most patients. Administer supplemental oxygen (by nasal cannulae or mask, whichever is better tolerated) to maintain an SaO_2 93-95% for adults and 94-98% for children. Monitor SaO_2 until a clear response to bronchodilator therapy has occurred.
- B. Short-acting beta-agonists (e.g, albuterol) are recommended for all patients. The repetitive or continuous administration of SABAs is the most effective treatment for reversing airflow obstruction. Nebulizer therapy may be preferred for patients who are unable to cooperate effectively in using a metered dose inhaler (MDI) because of their age, agitation, or severity of the exacerbation. The onset of action is less than 5 minutes; repetitive administration produces incremental bronchodilation. In about 60-70 percent of patients, response to the initial three doses of therapy will be sufficient to discharge them, and most patients will have a significant response after the first dose. The duration of action of bronchodilation from SABAs in severe asthma exacerbations is not precisely known, but duration can be significantly shorter than that observed in stable asthma.
- C. Ipratropium - Adding multiple high doses of ipratropium bromide (0.5mg nebulizer solution or 8 puffs by MDI in adults) to a selective SABA produces additional bronchodilation, resulting in fewer hospitalizations.
- D. Oral corticosteroids (OCS) are recommended for most patients. Give systemic corticosteroids to patients who have moderate or severe exacerbations and patients who do not respond completely to initial SABA therapy. These medications speed the resolution of airflow obstruction and reduce the relapse rate and may reduce hospitalizations. Patients given systemic corticosteroids should continue oral systemic corticosteroids for 5 days. The need for further corticosteroid therapy should be assessed at a follow up visit. There is generally no need to taper the dose for short courses less than 2~~3~~ weeks.
  - a) OCS can be life saving during severe asthma exacerbation, but there is increasing awareness of risks associated with repeated courses. Therefore, optimizing inhaled treatment, such as ICS-containing therapy, to reduce the risk of future exacerbations requiring OCS is also an important consideration after exacerbation.
- E. Inhaled corticosteroids (ICS) should be considered at discharge in addition to oral corticosteroids. Long-term ICS therapy reduces exacerbations in patients who have persistent asthma. Patients already taking ICS should continue it following discharge.

V. Patient Education
- A. Advise patient to keep follow up appointments
- B. Review medications (e.g., dosing, purpose, side effects) and proper inhaler technique
- C. Advise patient on when to seek medical care if asthma worsens
- D. Review asthma triggers
- E. Review or develop a written plan for managing either relapse of the exacerbation or recurrent symptoms

Asthma (Adults and Children ≥ 12 years)

1

1. Obtain thorough history and perform physical exam.
2. Review history of symptoms witnessed or addressed by healthcare staff.
3. Document peak expiratory flow. Spirometry is suggested when available.
4. Consider transferring the patient to a 24-hour unit if the patient has a history of intubation.
5. Assess the patient's knowledge and skills for self-management.
6. Classify asthma severity to select the most appropriate therapy by assessing impairment and risk.

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

2

Components of Severity		Classification			
		Intermittent	**Persistent Mild**	**Persistent Moderate**	**Persistent Severe**
Impairment Normal FEV_1/FVC: 8-19 yr = 85% 20-39 yr = 80% 40-59 yr = 75% 60-80 yr = 70%	Symptoms	≤ 2 days/week	> 2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤ 2 times/month	3-4 times/month	> 1 time/week but not nightly	Often 7 times/week
	SABA for symptom control (not prevention EIB)	≤ 2 days/week	> 2 days/week but not > 1 time/day	Daily	Several times per day
	Interference with normal activity	None	Minor limitations	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 > 80% predicted • FEV_1/FVC normal	• FEV_1 ≥ 80% predicted • FEV_1/FVC normal	• FEV_1 > 60% but < 80% predicted • FEV_1/FVC reduced 5%	• FEV_1 < 60% predicted • FEV_1/FVC reduced > 5%
Risk	Exacerbations requiring oral systemic corticosteroids	0-1/year	≥ 2/year		
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients			
		Relative annual risk of exacerbations may be related to FEV_1			
Treatment	**Long-Term Control Medication** (see table 4 for alternatives)	**STEP 1** None	**STEP 2** **Low dose ICS** Ciclesonide HFA 80 mcg 1 puff BID	**STEP 3** **Low dose ICS + LABA†** Ciclesonide HFA 80 mcg 1 puff BID **plus** Salmeterol* 1 puff bid	**STEP 4** **Medium dose ICS + LABA** Non-formulary combination inhaler: UTMB Mometasone/formoterol (Dulera®)* 100 mcg / 5 mcg 2 puffs BID Texas Tech Fluticasone/salmeterol (Wixela®)* 250 mcg / 50 mcg 1 puff BID **STEP 5** **Consider:** • Specialty referral
	Quick Relief Medication	**SABA as needed for symptoms for all patients for all steps of therapy** Albuterol HFA 2 puffs QID prn			

SABA=short-acting beta2-agonist, LABA=long-acting beta2-agonist, ICS=inhaled corticosteroid, EIB=exercise-induced bronchospasm. * Non-formulary approval required. The Texas Tech sector may request non-formulary fluticasone/salmeterol (Wixela®) in Step 3.

3

Evaluate response to therapy in 2-6 weeks or as clinically indicated. Go to page 2 box #4

Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee. September 1996. Reviewed 3/05. Revised 4/98, 12/98, 4/02, 4/03, 10/03, 7/09, 1/10, 1/13, 1/15, 9/19, 7/21, 11/24. Revised to include children 11/06.

Exacerbations and poor control should prompt review of treatment plan

4

Assess the patient to determine if asthma is well controlled (based on the most severe symptoms during the previous 2-4 weeks and by spirometry or peak flow measures)

5

Well Controlled

- Symptoms: ≤ 2 days/week
- Nighttime awakenings: ≤ 2 x/month
- Limitations of activities: None
- Need for quick relief inhaler: ≤ 2 days/week
- FEV_1 or Peak Flow: >80% predicted/personal best
- Exacerbations requiring oral corticosteroids: 0-1/year

6

Continue current regimen.

- Follow up with peak flow to assess control.
- Consider step down if well controlled for at least 3 months.
- Once stable, follow up at least every 12 months.
- Obtain peak flow at each visit.
- Review medication technique, adherence, environmental control, comorbid conditions, and assess side effects during each visit.
- Review asthma action plan & revise as needed during each visit.
- Consider spirometry every 1-2 years.

7

Not Well Controlled

- Symptoms: > 2 days/week
- Nighttime awakenings: 1-3 x/week
- Limitations of activities: Some
- Need for quick relief inhaler: > 2 days/week
- FEV_1 or Peak Flow: 60% - 80% predicted/personal best
- Exacerbations requiring oral corticosteroids: ≥ 2/year

8

- Before stepping up therapy, review adherence to medication, inhaler technique, environmental control, comorbid conditions and assess side effects.
- Obtain peak flow.
- Step up 1 step.
- Review asthma action plan & revise as needed.
- Consider Respiratory Care referral.
- Follow up in 2-6 weeks or as clinically indicated.

9

Asthma well controlled?

Yes → 10 Go to box # 6

No → 11

11

- Before stepping up therapy, review adherence to medication, inhaler technique, environmental control, comorbid conditions and assess side effects.
- Obtain peak flow.
- Step up 1 step.
- Review asthma action plan & revise as needed.
- Consider Respiratory Care or Specialty Care referral.
- Follow up in 2-6 weeks or as clinically indicated.

12

Very Poorly Controlled

- Symptoms: Throughout the day
- Nighttime awakenings: ≥ 4 x/week
- Limitations of activities: Extremely limited
- Need for quick relief inhaler: Several times per day
- FEV_1 or Peak Flow: < 60% predicted/personal best
- Exacerbations requiring oral corticosteroids: ≥ 2/year

13

- Before stepping up therapy, review adherence to medication, inhaler technique, environmental control, comorbid conditions and assess side effects.
- Obtain peak flow.
- Step up 1 step.
- Consider short course oral systemic corticosteroids.
- Review asthma action plan & revise as needed.
- Consider Respiratory Care or Specialty Care referral.
- Follow up in 2 weeks or as clinically indicated.

14

Asthma well controlled?

Yes → 10 Go to box # 6

No → 15

15

- Before stepping up therapy, review adherence to medication, inhaler technique, environmental control, comorbid conditions and assess side effects.
- Obtain peak flow.
- Consider short course oral systemic corticosteroids.
- Step up 1-2 steps.
- Review asthma action plan & revise as needed.
- Consider Specialty referral
- Follow up in 2 weeks or as clinically indicated.

Nurses: DMGs are to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.**

I. Definition: Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.

II. Diagnosis is based on the following:

A. History
   1. Family history of asthma, allergy, sinusitis, rhinitis, eczema or nasal polyps
   2. Age of onset and diagnosis
   3. Recurrent symptoms such as wheeze, cough, chest tightness, shortness of breath, or difficulty breathing
   4. Pattern of symptoms
      a. Perennial, seasonal, or both
      b. Continual, episodic, or both
   5. Precipitating factors that cause symptoms to occur or worsen
      a. Exercise
      b. Allergen (e.g., mold, pollen, dust mites, animal fur)
      c. Irritant (e.g., smoke, chemicals)
      d. Viral infection
      e. Changes in weather
      f. Menstrual cycles
      g. Strong emotional expression (e.g., stress, laughing or crying hard)
      h. Drugs (e.g., aspirin, NSAIDs, or beta-blockers)
   6. Symptoms occur or worsen at night and awaken the patient
   7. History of exacerbations
      a. Usual prodromal signs and symptoms
      b. Rapidity of onset, duration & frequency
      c. Severity (e.g., need for hospitalization) and life-threatening exacerbations (e.g., intubation)
      d. Number and severity of exacerbations in last year
      e. Usual management of exacerbations
   8. Comorbid conditions that may aggravate asthma (e.g., rhinitis, GERD, obesity, obstructive sleep apnea)

B. Physical exam focusing on the upper respiratory tract, chest, and skin
   1. Hyper-expansion of the chest
   2. Expiratory wheezing (rhonchi) upon auscultation is the most common abnormality
   3. Increased nasal secretion, mucosal swelling, and/or nasal polyps
   4. Atopic dermatitis, eczema, or any other manifestations of an allergic skin condition
   5. Note: Physical examination in patients with asthma is often normal. Lack of wheezing or normal chest examination does not exclude asthma

C. Airflow obstruction is at least partially reversible
   1. Spirometry is used to demonstrate obstruction and assess reversibility
   2. Considered reversible if either an increase in FEV_1 of ≥12 percent from baseline or by an increase ≥10 percent of predicted FEV_1 after inhalation of a short-acting bronchodilator
   3. Spirometry typically measures the maximal volume of air forcibly exhaled from the point of maximal inhalation (FVC) and the volume of air exhaled during the first second of this maneuver (FEV_1)

D. Exclusion of other diagnoses
   1. Adults – COPD, heart failure, pulmonary embolism, mechanical obstruction such as tumor, vocal cord dysfunction, cough secondary to medications such as ACE inhibitors, or pulmonary infiltration
   2. Children – Vocal cord dysfunction, bronchiectasis, cystic fibrosis, congenital heart disease, alpha1-antitrypsin deficiency, inhaled foreign body, chronic upper airway cough syndrome

III. Classification of severity

A. Classify asthma severity to select the most appropriate therapy by assessing impairment and risk.
   1. Impairment: frequency and intensity of symptoms, and functional limitations
      a. Nighttime awakenings
      b. Need for short-acting beta agonist for quick relief of symptoms
      c. School/workdays missed
      d. Ability to engage in normal daily activities
      e. Lung function measured by spirometry
   2. Risk: likelihood of exacerbation, progressive loss of lung function, and risk of adverse effects from medications
      a. Exacerbations requiring oral corticosteroids
      b. Two or more emergency room visits or hospitalizations for asthma in last year
      c. History of intubation or ICU admission especially in last 5 years
      d. Patients report that they feel in danger or frightened by their asthma
      e. Psychosocial factors (e.g., depression, stress)
      f. Severe airflow obstruction by spirometry
      g. Attitudes and beliefs about taking medications

B. Level of severity is determined by assessment of both impairment and risk. Assess impairment by patient's recall of symptoms in previous 2–4 weeks and spirometry. Assign severity to the most severe category in which any feature occurs (See Page 1, box 2)

C. Respiratory Care may be consulted to assist with asthma classification and patient education.

D. Once asthma is well controlled, classify asthma severity by the lowest level of treatment required to maintain control (See Table 1).

Table 1. Classification of Asthma Severity

	Intermittent	Persistent Mild	Persistent Moderate	Persistent Severe
Lowest level of treatment required to maintain control	Step 1	Step 2	Step 3 – 4	Step 5 - 6

Adapted from Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma

IV. Assessing asthma control

A. Level of control is based on the most severe impairment or risk category (Table 2).
   1. Impairment is assessed based on the patient's recall of events during the previous 2-4 weeks and by spirometry or peak flow measures.
   2. Risk is assessed based on events over the last year.

B. Patients who have asthma that is well controlled at the time of a clinical assessment must be monitored over time and treatment should be adjusted accordingly, since asthma can vary in intensity over time.

C. Depending on level of asthma control, the patients is assigned to one of six treatment steps.

D. Therapy is stepped up or stepped down based on how well asthma is controlled and level of severity assessed for both impairment and risk.

E. Any exacerbation should prompt review of maintenance treatment.

F. Note: For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have not-well-controlled asthma, even in the absence of impairment levels consistent with not-well-controlled asthma.

V. Treatment Principles

A. Gain control of asthma as soon as possible.

B. Evaluate causes of poor control before stepping up therapy and increasing doses or adding long-term control medications.
   1. Poor patient inhaler technique
   2. Poor medication adherence
   3. Adverse effects to medications
   4. Exposure to environmental triggers
   5. Comorbidities that may aggravate asthma (e.g., rhinitis, GERD, obesity, obstructive sleep apnea)

C. Goals of therapy are to achieve asthma control by reducing impairment and risk
   1. Reduce impairment
      a. Prevent symptoms
      b. Require infrequent use of quick relief medications (≤ 2 days per week)
      c. Maintain normal activity level
      d. Maintain normal or near normal lung function
   2. Reduce risk
      a. Prevent exacerbations and minimize need for emergency department visits and hospitalizations
      b. Provide optimal treatment with minimal or no adverse effects
      c. Prevent progressive loss of lung function

VI. Treatment

A. Non-pharmacologic
   1. Avoidance of environmental triggers such as allergens or tobacco smoke.
   2. Physical activity should be encouraged because of its general health benefits. Provide advice about exercise-induced bronchoconstriction (EIB).
   3. Weight reduction if obese.
   4. Possibility of occupational asthma should be considered, and sensitizers should be removed if possible.
   5. Avoidance of medications that may worsen asthma (e.g., aspirin, NSAIDs, or nonselective beta-blockers). However, use of these medications are not absolutely contraindicated unless there is a history of previous reactions to them.

B. Pharmacologic
   1. Annual influenza vaccination for patients with mild persistent to severe persistent asthma (i.e., requires chronic medication) OR patients with a history of hospitalization or emergency treatment for asthma. Refer to Infection Control Immunizations Policy B-14.07 for pneumococcal vaccine recommendations.
   2. Consider treatment of comorbid conditions that aggravate asthma especially if asthma is poorly controlled.
   3. Stepwise approach to therapy
      a. Therapy is determined by asthma severity for initiating therapy and the level of asthma control for adjusting therapy
      b. Six treatment steps stepped up or down based on how well asthma is controlled
         i. Step up
            - Optimize dose of long-term control medication; evaluate causes of poor control first
            - Complete resistance to ICS is rare so consider trial of higher dose
            - Use sustained step up for at least 2-3 months if asthma poorly controlled
            - Use short-term step up for 1-2 weeks (e.g., with viral infection or allergen)
         ii. Step down
            - Consider step down after good control is maintained for at least 3 months
            - Goal is to find the minimum effective dose that controls symptoms & prevents exacerbations
            - Complete cessation of inhaled corticosteroids is <u>not</u> advised in adults
      c. **S**ingle **M**aintenance **A**nd **R**eliever **T**herapy (SMART): if recommended by the specialist, utilization of a single combination ICS/LABA inhaler (e.g., Dulera®) for maintenance and rescue treatment may be considered for patients with persistent moderate-severe asthma. SABA and/or single-entity LABA (e.g., salmeterol) should be discontinued in these patients. Nonformulary approval for Dulera® may be requested; separate EHR orders for maintenance and PRN regimens are required.

Table 2. Assessing Asthma Control and Adjusting Therapy

Components of Severity		Well Controlled	Not Well Controlled	Very Poorly Controlled
Impairment	Symptoms	≤ 2 days/week	> 2 days/week	Throughout the day
	Nighttime awakenings	≤ 2 times/month	1-3 times/week	≥ 4 times/week
	SABA for symptom control (not prevention of EIB)	≤ 2 days/week	> 2 days/week	Several times per day
	Interference with normal activity	None	Some limitations	Extremely limited
	FEV[1] or peak flow	> 80% predicted/personal best	60-80% predicted/ personal best	< 60% predicted/personal best
Risk	Exacerbations	0-1/year	≥ 2/year	
		Consider severity & interval since last exacerbation.		
	Treatment-related adverse effects	Not correlated to level of control but should be considered in assessment of therapy.		
Recommended Action		• Maintain current treatment step • Follow up every 6-12 months as needed • Consider step down if well controlled for at least 3 months	• Step up 1 step. • Reevaluate in 2−6 weeks or as clinically indicated.	• Step up 1-2 steps. • Consider short course of oral systemic corticosteroids • Revaluate in 2 weeks or as clinically indicated

Adapted from Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. SABA=short-acting beta2-agonist, EIB=exercise induced bronchospasm.

4. Quick relief medications (Table 3)
   a. Used to provide prompt relief of symptoms
   b. Will <u>not</u> provide long-term asthma control and is prescribed for as needed use
   c. Short-acting beta$_2$-agonist such as albuterol is preferred
   d. If used > 2 days per week (except for exercise-induced asthma), the patient may need to start or increase long-term control medications

Table 3. Quick Relief Medications

Drug	Type of Medication	Adult Dose	Child ≤ 11 Dose	Adverse Effects
Albuterol (Proventil HFA®) 90 mcg/puff 200 puffs/inhaler	Quick relief Short-acting beta$_2$-agonist	**Quick relief**: 2 puffs qid prn (up to 2 puffs every 4 hrs.) **Exacerbation**: 4-8 puffs every 20 minutes for up to 4 hours then every 1-4 hours prn	**Quick relief**: 2 puffs qid prn (up to 2 puffs every 4 hrs.) **Exacerbation**: 4-8 puffs every 20 minutes for 3 doses then every 1-4 hours prn	Tachycardia, tremor, headache
Prednisone (Deltasone®) 5 mg, 10 mg, 20 mg tablets	Quick relief – used short-term for establishing control when initiating therapy or during moderate to severe exacerbations Oral corticosteroid	40-60 mg/day in 1-2 divided doses x 3-10 days	1-2 mg/kg/day divided in 2 doses (maximum 60 mg/day) x 3-10 days	Hyperglycemia, increased appetite, fluid retention, weight gain, facial flushing, mood alteration, hypertension, ulcer

5. Long-term control medications (Table 4)
    a. Taken daily over a long period of time to maintain control of symptoms
    b. Not effective on an as needed (i.e., PRN) basis
    c. Should <u>not</u> be prescribed without a quick relief medication
    d. Used to reduce inflammation, relax airway muscles, and improve symptoms and lung function
    e. Types
        i. Inhaled corticosteroid (ICS) such as ciclesonide
            - Most potent and effective
            - May cause systemic adverse effects at high dose
        ii. Long-acting beta2-agonist (LABA) such as salmeterol
            - Not used alone and must be used in combination with ICS
            - When long-term control combination therapy is warranted, preferred combination is ICS plus LABA
        iii. Leukotriene receptor antagonist (LTRA) such as montelukast
            - Do NOT use LTRA plus LABA as a substitute for combination therapy with ICS plus LABA
        iv. Oral corticosteroid (OCS) such as prednisone
            - Not recommended as a long-term control medication except at Step 6 of treatment due to potential for systemic side effects
            - Generally reserved as a short course (3-10 days) for moderate to severe exacerbations to gain prompt control
            - Tapering is not generally necessary if OCS is prescribed for less than 2 weeks
            - Factors that may be considered for a gradual discontinuation include patient frailty, comorbid illnesses and severely ill patients. If tapering, consider decreasing by increments of 10-20% every 1-2 weeks.
              Example: Patient is on > 40 mg of prednisone per day, decrease by 5 to 10 mg/day every 10 days.
6. Factors that cause non-adherence
    a. Medication Usage
        i. Difficulties using inhalers
        ii. Complex regimens
        iii. Adverse effects
    b. Non-Medication Factors
        i. Misunderstanding or lack of information
        ii. Poor communication
        iii. Fears about adverse effects
        iv. Inappropriate expectations
        v. Underestimation of severity
        vi. Attitudes about health
        vii. Cultural factors

Table 4. Long-term Control Medications

Drug	Type of Medication	Adult Dose	Child ≤ 11 Dose	Adverse Effects
Beclomethasone (Qvar redihaler®) 40 mcg/actuation 80 puffs/actuation **(non-formulary)** **Recommended for HIV patients prescribed a protease inhibitor*	Long-term control ICS	**Low dose**: 80 -240 mcg • 160 mcg = 1 puff bid **Medium dose**: > 240 -480 mcg • 320 mcg = 2 puffs bid • 480 mcg = 3 puffs bid **High dose**: > 480 mcg • 640 mcg = 4 puffs bid	**Low dose**: 80-160 mcg • 160 mcg = 1 puff bid **Medium dose**: >160-320 mcg • 320 mcg = 2 puffs bid **High dose**: > 320 mcg • 480 mcg = 3 puffs bid	Cough, dysphoria, oral thrush Systemic adverse effects may occur at high doses (see oral corticosteroids below for list)
Ciclesonide HFA (Alvesco®) 80 mcg/puff 160 mcg/puff	Long-term control ICS	**Low dose**: 80 – 160 mcg/day • 160 mcg = 1 puff (80 mcg inhaler) bid **Medium dose**: > 160 – 320 mcg /day • 320 mcg = 1 puff (160 mcg inhaler) bid **High dose**: > 320 mcg/day • 640 mcg = 2 puffs (160 mcg inhaler) bid	**Low dose**:* 80 mcg/day • 80 mcg = 1 puff (80 mcg inhaler) once daily **Medium dose**:* 160 mcg/day • 160 mcg = 1 puff (160mcg inhaler) once daily **High dose**:* N/A *Ciclesonide is not FDA-approved for use in children ≤ 11 years old	Cough, dysphoria, oral thrush Systemic adverse effects may occur at high doses (see oral corticosteroids below for list)
Salmeterol Diskus (Serevent®) 50 mcg/puff powder for inhalation 60 puffs/inhaler (**non-formulary**)	Long-term control LABA	1 puff bid • Must be used in combination with ICS • Do NOT wash mouthpiece	1 puff bid • Must be used in combination with ICS • Do NOT wash mouthpiece • Child ≥ 4 years	Tachycardia, tremor, hypokalemia, QTc prolongation, diminished bronchoprotective effect may occur within 1 week Uncommon, severe, life-threatening or fatal exacerbation
Tiotropium (Spiriva Handihaler®) 18mcg/ actuation (**non-formulary**)	Long-term control LAMA	1 puff daily	**6-11 years:** 1 puff daily	Dry mouth, cough, bitter taste
Fluticasone/salmeterol (Wixela®) 100/50 mcg, 250/50 mcg, 500/50 mcg (**non-formulary)** 60 puffs/inhaler Note: Preferred ICS + LABA for Texas Tech sector	Long-term control combination ICS & LABA	**Low dose:** • 1 puff (100/50 mcg inhaler) bid **Medium dose:** • 1 puff (250/50 mcg inhaler) bid • Maximum 2 inhalations **High dose:** • 1 puff (500/50 mcg inhaler) bid • Maximum 2 inhalations	**4-11 years**: 100/50 mcg 1 puff bid	See adverse effects for ICS and LABA Note: Do NOT use in combination with another LABA such as formoterol.
Mometasone/formoterol (Dulera®) 100/5 mcg, 200/5 mcg **(non-formulary)** 120 puffs/inhaler Note: Preferred ICS + LABA for UTMB sector	Long-term control combination ICS & LABA	**Low dose:** • 2 puffs (50/5 mcg inhaler) bid **Medium dose**: • 2 puffs (100/5 mcg inhaler) bid • Maximum 4 inhalations **High dose**: • 2 puffs (200/5 mcg inhaler) BID • Maximum 4 inhalations	Not approved for use in children ≤ 11 years	See adverse effects for ICS and LABA Note: Do NOT use in combination with another LABA such as salmeterol.
Montelukast (Singulair®) 10 mg tablet, 5 mg chewable tablet (**non-formulary**)	Long-term control LTRA	**≥ 15 years - Adult**: 10mg orally once daily in the evening	**6-14 years**: 5mg chewable one daily in the evening	Headache, cough, upper respiratory infection, pharyngitis, abdominal pain **Black Box Warning:** serious neuropsychiatric events
Prednisone (Deltasone®) 5 mg, 10 mg, 20 mg tablets	Long-term control OCS	5-60 mg daily or every other day Note: • Use lowest effective dose	0.25-2 mg/kg daily or every other day Note: • Use lowest effective dose	Short-term: Hyperglycemia, increased appetite, fluid retention, weight gain, facial flushing, mood alteration, hypertension, ulcer Long-term: adrenal suppression, dermal thinning, hypertension, diabetes, Cushing's syndrome, cataracts, muscle weakness, osteoporosis, immunosuppression

ICS=inhaled corticosteroid, LABA=long-acting beta$_2$-agonist, LTRA=leukotriene receptor antagonist, OCS=oral corticosteroid, LAMA=long-acting muscarinic antagonist

Table 5. Long-term control medication alternative treatment options

Intermittent	Persistent				
STEP 1	**STEP 2**	**STEP 3**	**STEP 4**	**STEP 5**	**STEP 6**
	LTRA*† Montelukast	**Low dose ICS + LTRA*†** Ciclesonide HFA plus Montelukast* Or **Medium dose ICS** Ciclesonide HFA	**Medium dose ICS + LTRA*** Ciclesonide HFA plus Montelukast* Or **Medium dose ICS + LAMA*** Ciclesonide HFA plus tiotropium*	**Refer to specialty**	**Refer to specialty**

* Non-formulary medication, † the FDA issued a black box warning for montelukast in March 2020 for serious neuropsychiatric events
SABA=short-acting beta$_2$ agonist, LABA=long-acting beta$_2$ agonist, ICS=inhaled corticosteroid, OCS=oral corticosteroid, LTRA=leukotriene receptor antagonist, LAMA= long-acting muscarinic antagonist, EIB=exercise induced bronchospasm

Table 6. Stepping Down Treatment

Regimen	Action
Low dose ICS	Reduced dose by 25-50% at 3-month intervals
Medium dose or high dose ICS	Reduced dose by 25-50% at 3-month intervals
ICS + LABA	Reduce dose ICS by 50% and continue LABA *If patient remains controlled, reduce to low dose ICS; may reduce ICS to once daily if controlled on low dose twice daily ICS. Continue LABA.
ICS + LABA + OCS	Continue ICS + LABA and reduce dose of OCS

ICS=inhaled corticosteroid, OCS=oral corticosteroid, LABA=long-acting beta2 agonist

VII. Follow-Up

A. Patients with a diagnosis of asthma should be seen based on acuity and clinical judgment, but duration between visits may not exceed 12 months.

B. Consider the following for frequency of follow-up visits
   1. Follow-up at 2–6-week intervals when initiating therapy or if asthma is not well controlled therapy
   2. Follow-up at 2-week intervals if asthma is very poorly controlled
   3. Follow-up at 3-month intervals when stepping down therapy

C. Assess asthma classification severity (Table 1) and asthma control (Table 2) during each chronic care visit
   1. Daytime and nighttime signs and symptoms of asthma
   2. Inability or difficulty performing normal activities due to asthma symptoms
   3. Pulmonary function
      a. Peak flow reading should be obtained at every chronic care visit. Consider more frequent peak flow monitoring for patients who:
         i. Have moderate persistent and severe persistent asthma
         ii. Have a history of severe exacerbations (e.g., required intubation)
         iii. Poorly perceive airflow obstruction or worsening asthma
         iv. Have poorly controlled asthma
      b. Consider obtaining spirometry every 1-2 years.
   4. Exacerbations since last visit
   5. Frequency of use of quick relief medication - Monitor use of SABA at each chronic care visit as a measure of disease control. Asthma is not adequately controlled if the patient is using more than 2 times per week.

D. Review medication inhaler technique, adherence, and assess side effects during each chronic care visit
E. Reinforce education
    1. Review asthma action plan and revise as needed
    2. Proper inhaler technique
    3. Importance of adherence with long-term control medications

VIII. Referrals

A. Consider respiratory care referral for a patient for the following purposes:
    1. To assist with asthma classification and patient education
    2. If the patient is not well controlled or is very poorly controlled
B. Consider specialty referral for a patient experiencing any of the following conditions:
    1. Requires Step 5 care or higher and is not meeting goals of therapy
    2. Persistent uncontrolled asthma or frequent exacerbations
    3. Risk factors for asthma related death:
        a. Experienced a life-threatening or near-fatal exacerbation (e.g., ICU admission or mechanical ventilation)
        b. Anaphylaxis or confirmed food allergy with asthma
    4. Other conditions that complicate asthma or its diagnosis

IX. Peak Flow Monitoring

A. The patient's personal best peak flow should be used as the reference value
B. Personal best peak flow number is the highest peak flow number achieved over a 2-week period when asthma is well controlled
C. Steps
    1. Move indicator to the bottom of the numbered scale
    2. Patient should be standing
    3. Patient should take a deep breath, filling their lungs completely
    4. Mouthpiece should be placed in mouth and lips should be closed around it. The tongue should not be placed inside the hole.
    5. Patient should exhale as hard and fast as possible in a single breath
D. Interpretation of results
    1. Green Zone – 80% of personal best number signals good control
    2. Yellow Zone – 50% to < 80% of personal best number signals caution
    3. Red Zone – less than 50% of personal best number signals a medical alert

X. Patient Education

A. Teach patients how to manage their asthma.
    1. Basic facts about the disease
        a. What is asthma
        b. Consequences of poor control
        c. What to expect during an asthma exacerbation
    2. Use of medication
        a. Difference between quick relief and long-term control medications and when to use them
        b. Proper inhaler technique (technique varies between inhalers)
        c. Importance of adherence for control
    3. Self-monitoring to assess level of asthma control and recognize signs of worsening asthma based on symptoms.
    4. Use of a written asthma action plan
        a. How to adjust medications in response to worsening asthma
        b. When to seek medical care if symptoms fail to respond to quick relief medication
    5. Avoidance of environmental triggers that worsen asthma

Instructions for MDI Use
Albuterol HFA (Proventil®, Ventolin®), Ciclesonide HFA (Alvesco®), Mometasone/Formoterol (Dulera®)

Below are general instructions for HFA inhaler use. Please refer to the specific inhaler package insert for complete directions as instructions may vary.

Priming HFA inhaler
1. Shake the inhaler well.
2. Prime the inhaler before using for the first time by releasing 4 test sprays into the air away from face.
3. Repeat the above priming procedure before using only if the inhaler has not been used for more than 2 weeks.

Cleaning HFA inhaler:
1. Remove medication canister. Never get the canister wet.
2. Clean the plastic mouthpiece by running warm water through the top to the bottom for 30 seconds at least once a week.
3. Shake to remove excess water, then air dry thoroughly (such as overnight).

Instructions for taking a dose from your HFA inhaler:
1. Take the cap off the mouthpiece of the inhaler (plastic actuator) and **shake the inhaler well** before each spray.
2. Hold the inhaler upright with the mouthpiece down (see Figure 2). Breathe out through your mouth and push as much air from your lungs as you can. Put the mouthpiece in your mouth and close your lips around it.
3. Push the top of the canister all the way down while you breathe in deeply and slowly through your mouth (see Figure 3). Right after the spray comes out, take your finger off the canister. After you have breathed in all the way, take the inhaler out of your mouth and close your mouth.
4. Hold your breath as long as you can, up to 10 seconds, to allow the drug to reach deeply into your lungs. Then breathe normally.
5. If your provider has prescribed more sprays, wait 1 minute between sprays. Shake the inhaler again and repeat steps 2 through 4.
6. Put the cap back on the mouthpiece after every time you use the inhaler, and make sure it snaps firmly into place.

Important points:
1. Do <u>not</u> use the inhaler after the expiration date, which is on the outside packaging.
2. This technique does not work with dry powder capsule inhalers. It is important to close the mouth tightly around the mouthpiece of the inhaler and to inhale rapidly when using a dry powder inhaler.

Figure 1

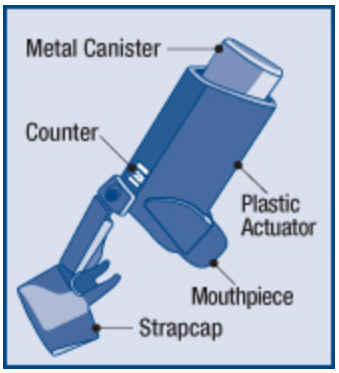


Figure 2

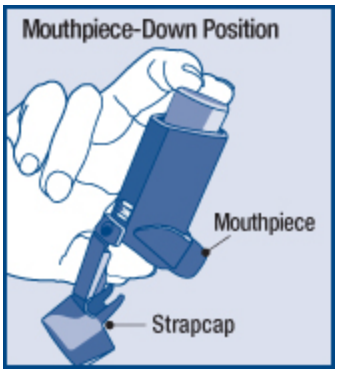
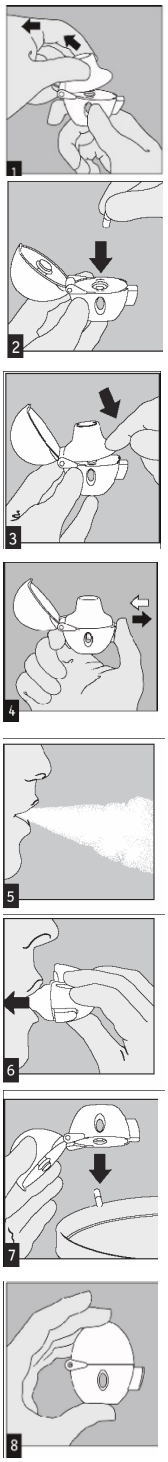


Figure 3

*This is a general diagram depicting an MDI. Counter location and cap mechanism may vary by product.

Tiotropium Handihaler (Spiriva®) Technique:

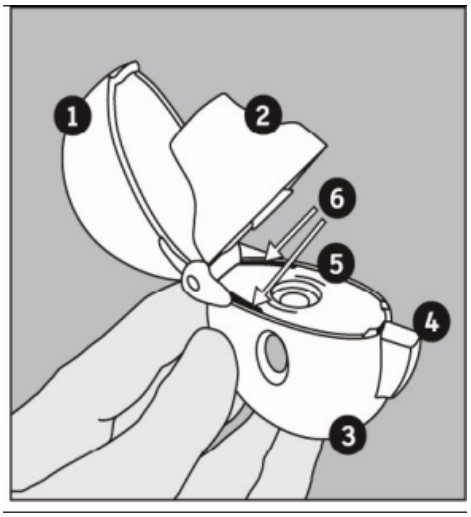
1. Open the inhaler cap by pressing the green piercing button and pulling upwards and then open the mouthpiece.
2. Place 1 capsule in the center chamber.
3. Close the mouthpiece. You will hear a click when it is firmly closed.
4. Hold the inhaler with the mouthpiece upwards and press the piercing button in once. This makes a hole in the capsule and allows the medication inside the capsule to be released.
5. Breathe out completely away from the device.
6. Raise the inhaler to your mouth in a horizontal position and close your lips tightly around the mouthpiece. **Do not** block the air vents. Keep your head in an upright position and breathe in slowly and deeply at a rate sufficient to hear the capsule vibrate. Hold your breath as long as is comfortable.
7. To get your full daily dose, you must again breathe out completely (Picture 5) and for a second time, breathe in (Picture 6) from the same capsule. **Do not** press the green piercing button again.
8. After taking your daily dose, open the mouthpiece and turn the inhaler upside down to discard the capsule without touching it.
9. Close the mouthpiece and inhaler cap for storage.



Notes:

Do not store capsules in the inhaler.

Do not open capsule package until you are ready to use the inhaler.



Inhaler parts:

1. Dust cap
2. Mouthpiece
3. Base
4. Piercing button
5. Center chamber
6. Air intake vents

Salmeterol (Serevent®) Diskus Technique:

1. Open your Diskus: Hold the Diskus in your left hand and place the thumb of your right hand in the thumb grip. Push the thumb grip away from you as far as it will go until the mouthpiece shows and snaps into place (Picture A).
2. Slide the lever until you hear it click. Hold the Diskus in a level, flat position with the mouthpiece towards you. Slide the lever away from the mouthpiece as far as it will go until it clicks. The number on the counter will count down by 1. The Diskus is now ready for use (Picture B).
3. Inhale your medication. Before you breathe in your dose, breathe out as long as you can while you hold the Diskus level and away from your mouth. Do not breathe into the mouthpiece. Put the mouthpiece to your lips. Breathe in quickly and deeply through the Diskus. Do not breathe in through your nose. Remove the Diskus from your mouth and hold your breath for about 10 seconds, or for as long as is comfortable. Breathe out slowly as long as you can (Pictures C and D).
4. Close the Diskus. Place your thumb in the thumb grip and slide it back towards you as far as it will go. Make sure the Diskus clicks shut and you cannot see the mouthpiece. The Diskus is now ready for your next scheduled dose (Picture E).

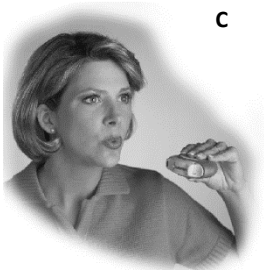
Important notes to avoid accidentally wasting a dose:

- Do not close the Diskus
- Do not tilt the Diskus
- Do not move the lever on the Diskus

A

B

C



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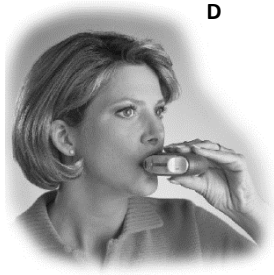
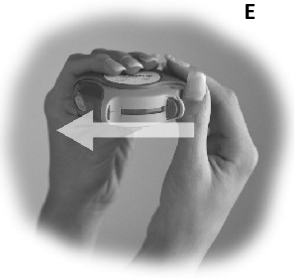


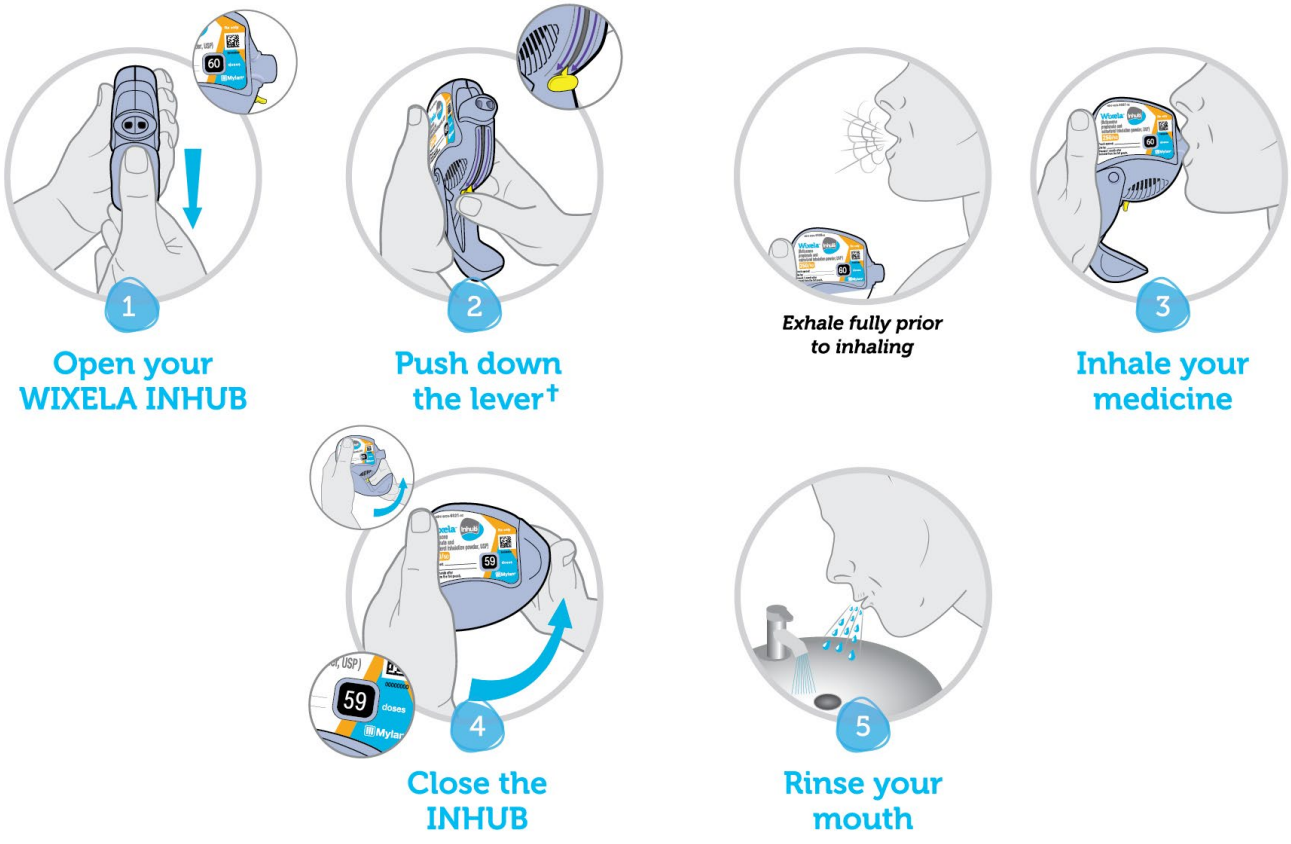
E



Fluticasone / salmeterol (Wixela Inhub®) Technique:

1. Remove the inhaler from the foil pouch. Open the inhaler by lowering the mouthpiece cover (figure 1).
2. Push down the yellow lever following the purple arrows (figure 2).
3. Breathe out completely away from the device. Raise the inhaler to your mouth in a vertical position and close your lips tightly around the mouthpiece. Keep your head in an upright position and breathe in quickly and deeply. Hold your breath for 10 seconds or as long as is comfortable (figure 3).
4. Breathe out slowly for as long as you can.
5. Close the inhaler by pushing the mouthpiece cover up to the closed position (figure 4).
6. Rinse your mouth with water after use. Spit out the water, do not swallow it (figure 5).

Notes:
Store Wixela Inhub® in the unopened foil pouch and only open when ready for use.
Safely throw away Wixela Inhub® in the trash 1 month after you open the foil pouch or when the counter reads **0**, whichever comes first.
Do not wash or rinse the mouthpiece.

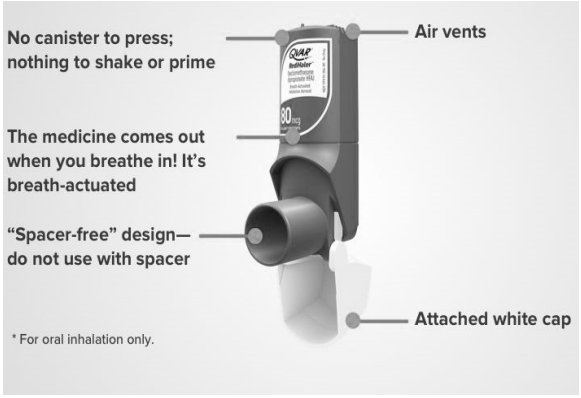


Beclomethasone (QVAR RediHaler®) Technique:

The white cap must be closed to prepare the inhaler before each inhalation or you will not receive your medicine. Do not open the cap until you are ready to take your inhalation.

1. Open the white cap that covers the mouthpiece of the inhaler. Do not open the cap unless you are taking a dose. Breathe out fully.

2. Place the mouthpiece in your mouth and close your lips around it so you form a good seal. To avoid blocking airflow through the device, be sure that your hand doesn't cover the air vent on top of the inhaler. Hold the inhaler and mouthpiece upright as you take your inhalation. Inhale deeply to release the medicine. Remove the inhaler, hold your breath for 5 to 10 seconds, then breathe out slowly, away from the inhaler.



3. Close the white cap after inhaling to prepare your next inhalation.

If your doctor has told you to take more than one inhalation per dose, make sure the white cap is closed and repeat steps 1-3. Do not take extra doses or stop taking QVAR RediHaler® without consulting your medical provider.

After taking your prescribed number of inhalations, rinse your mouth with water without swallowing to help reduce the risk of a fungal infection (thrush) in your mouth.

Be sure to use QVAR RediHaler® 2 times daily, as directed by your medical provider. It may take 3 to 4 weeks after starting QVAR RediHaler® to feel the benefits, although some people may notice a change in asthma symptoms within 24 hours.

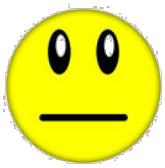
Asthma Action Plan

Completed by: <insert>

Patient Name: <insert>
Patient MRN: <insert>
Date: <insert>

Long-term Control Medicines	How to Take	Other Instructions
1.		
2.		
3.		
4.		
Quick Relief Medicine	**How to Take**	**Other Instructions**
		Take only if needed and in the yellow and red zones or before exercise.

Special instructions when I feel ■ good, ■ not good, and ■ awful.

Green Zone	**I feel good**. • No cough, wheeze, chest tightness, or shortness of breath during the day or night • Can do usual activities.		**PREVENT asthma symptoms everyday**. ❑ Take my long-term control medicines every day. ❑ Before exercise, take ___ puffs of _____ ❑ Avoid known triggers when possible
Yellow Zone	**I do <u>not</u> feel good**. • Cough, wheeze, chest tightness, shortness of breath, or • Waking at night due to asthma symptoms, or • Can do some, but not all, usual activities.		**CAUTION. I should continue taking my long-term control asthma medicines every day AND**: ❑ Take ____ puffs of quick relief medicine. If you still do not feel good within 20-30 minutes, you should take ___ puffs. If you do not feel better within one hour, go to the Red Zone. If you do feel better, ❑ Continue using quick relief medicine every 4 hours as needed for 24 hours. ❑ Increase_____ ❑ Drop a sick call request.
Red Zone	**I feel awful**. • Very short of breath, or • Quick relief medicine has not helped, or • Cannot sleep because of trouble breathing, or • Cannot do usual activities because of trouble breathing		**MEDICAL ALERT! Get help!** ❑ Take quick relief medicine. _____ puffs every ____ minutes ❑ Get help immediately if you are having difficulty walking or talking due to shortness of breath or lips or fingernails are gray or blue. ❑ Increase _____

BENZODIAZEPINE DISCONTINUATION

The pathways do not replace sound clinical judgment, nor are they intended to strictly apply to all patients

1

Intake screening identifies patient on benzodiazepine (BZD). Provider completes assessment of BZD dependence, comorbid conditions, and risk for complicated withdrawal (see Table 1)

2

Risk factors for complicated BZD withdrawal (BZW) present?

No

3

No Risk Factors Present

Discontinue BZD and monitor for signs/symptoms of withdrawal (see Table 2). If signs/symptoms of withdrawal occur, proceed to box #4.

Yes

4

Risk Factors Present

- ≥ 1 risk factors identified from Table 1 requires gradual discontinuation.
- Start equivalent dose of chlordiazepoxide (see Table 3) and administer DOT to avoid BZW symptoms (see Table 2)
- Transfer patient to a 24-hour medical facility.

5

≥ 3 risk factors identified?

No

6

< 3 risk factors identified:

- Begin gradual discontinuation and tapering of chlordiazepoxide. Continue the full dose equivalent for 5 days, then taper the total daily dose by 25% every 5 days until discontinued. The total daily dose should be divided and administered every 12 hours.
- Monitor patient using the BZW Assessment Form every 12 hours.
- Consider collaboration with Mental Health Services for conversion and taper schedule.

Yes

7

≥ 3 risk factors identified:

- Begin gradual discontinuation and tapering of chlordiazepoxide. Continue full dose equivalent for 5 days, then taper the total daily dose by 25% every 5 days until discontinued. The total daily dose should be divided and administered every 8 hours.
- Monitor patient using the BZW Assessment Form every 8 hours
- Consider infirmary admission if more frequent monitoring is indicated.
- Consider collaboration with Mental Health Services for conversion and taper schedule.

8

Signs/symptoms of BZW (Table 2) or sedation?

No

9

Continue taper and monitoring plan.

Yes

10

1. Consider modification of dose to alleviate symptoms.
2. Consider transfer to an inpatient facility.

Nurses: DMGs are to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.**

Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee, Approved January 2000. Reviewed 8/03, 1/10, 5/12, 5/14. Revised 1/07, 5/08, 3/09, 11/09, 9/14, 3/18, 3/23.

Table 1. Risk Factors for Complicated BZW

- Long duration of daily BZD use (≥ 4 weeks)
- Higher dose/frequency (> 1.25x's FDA approved daily maximum)
- Use of BZD with short half-life
- Comorbid medical conditions exacerbated by adrenergic state (i.e., COPD, DM, HTN, CAD, and history of CVA)
- History of seizure disorder
- Comorbid psychiatric illness
- History of complicated BZD or alcohol withdrawal
- Concomitant dependence to barbiturates, opioids, or alcohol

Table 2. Signs and Symptoms of BZW

Anxiety	Nausea
Agitation	Vomiting
Convulsions	Blood Pressure lability
Tremor	Delirium
Tachycardia	Hallucinations
Perspiration	

*The likelihood and severity of withdrawal symptoms is a function of drug, dose, and duration of exposure.

Table 3. BZD Equivalents (Estimates) & Withdrawal Data

Generic Name	Brand Name	Approx. Equivalent Dose (mg)*	FDA Adult Max Daily Dose (mg/day)	Elimination Half-Life (hours)
Alprazolam†	Xanax	0.5	4	12-15
Chlordiazepoxide	Librium	10	100	15-40
Clonazepam	Klonopin	0.25	20	18-50
Clorazepate	Tranxene	7.5	60	50-100
Diazepam	Valium	5	40	20-80
Estazolam†	ProSom	0.5	2	10-24
Flurazepam	Dalmane	15	60	40-100
Lorazepam†	Ativan	1	10	10-20
Oxazepam†	Serax	15	120	10-20
Quazepam	Doral	5	15	30-100
Temazepam†	Restoril	7.5	30	10-40
Triazolam†	Halcion	0.25	0.25	2-3

*Approximate equivalent doses may vary by source. † Short acting agent

Table 4. Example Taper Schedule: Patient arrives on lorazepam 8 mg/day and is switched to chlordiazepoxide 80 mg/day. Total daily dose should be divided and administered every 8 or 12 hours depending on risk stratification. For example, 1 mg lorazepam = 10 mg chlordiazepoxide, therefore 8 mg lorazepam = 80 mg chlordiazepoxide

Approximate Chlordiazepoxide Dose Reductions*	Dose with Formulary Chlordiazepoxide 10 mg Capsules
80 mg/day	Eight 10 mg capsules x 5 days
60 mg/day	Six 10 mg capsules x 5 days
40 mg/day	Four 10 mg capsules x 5 days
30 mg/day	Three 10 mg capsules x 5 days
20 mg/day	Two 10 mg capsules x 5 days
10 mg/day	One 10 mg capsule x 5 days

*Dose reductions are approximate to 25%.

Benzodiazepine Withdrawal (BZW) Assessment Form Page 1

Name:_____

TDCJ #_____

	Date							
	Time							
	Initials of Staff Assessing							
Perspiration	0 no sweating 1 palms moist 2 palms/fore-head moist 3 sweat beads on face 4 drenching sweats							
Tremor	0 none 1 none 2 mild visible tremor 3 moderate-arms out severe- arms 4 at side							
Restlessness/ agitation	0 none 1 uneasy 2 restless 3 excitable-purposeless activity 4 pacing-unable to sit							
Level of Consciousness	0 unimpaired 1 alert-obeys commands 2 confused-responds to speech 3 stuporous-responds to pain 4 semi-comatose 5 comatose							

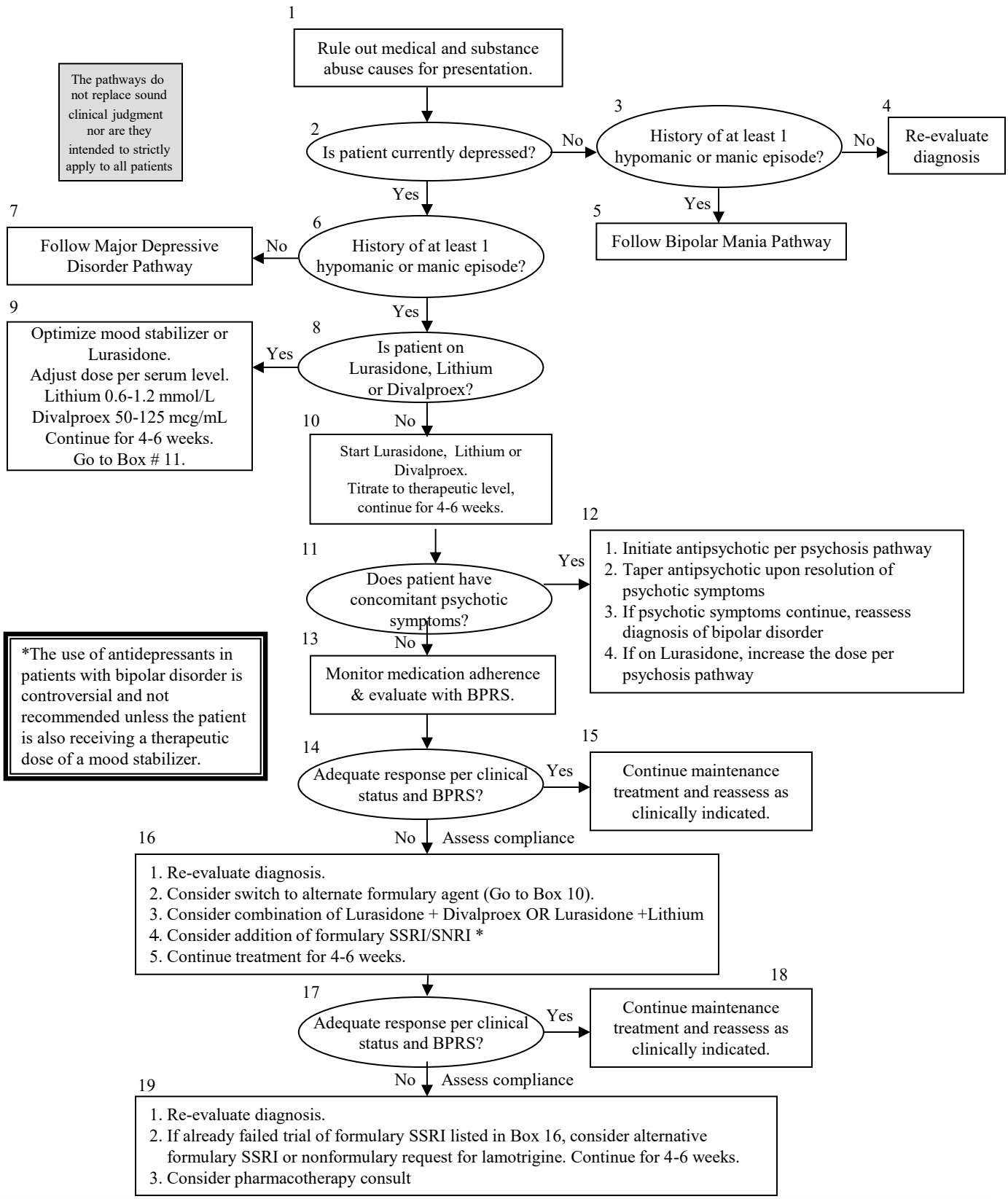
Benzodiazepine Withdrawal (BZW) Name_____
Data Collection Form Page 2 TDCJ #_____

Nausea or Vomiting	0 none 1 mild 2 moderate 3 severe 4 very severe							
Baseline (Admission)								
Blood Pressure								
Pulse								
Temperature								
Respirations								

Pearls:

- Monitor BZW Observation parameters based on setting guidelines
- Baseline (on admission) vital sign observation: those assessed prior to initiating tapering regimen
- Hyperthermia: any temperature exceeding 99.5 degrees F or 37.5 degrees C
- Tachycardia: heart rate > 90 BPM or an increase of $\geq$ 20 BPM from baseline heart rate on admission
- Blood pressure lability: change in systolic or diastolic of 20mm Hg from baseline on admission
- Severe n/v, blood pressure-pulse lability, hyperthermia, restlessness, tremor, perspiration, or agitation will require provider oversight and ***may indicate*** need for dose/titration adjustment.

BIPOLAR DEPRESSION



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Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee. Approved 1/99, revised 5/02, 2/03, 4/03, 9/05, 5/09, 7/09, 5/12, 1/15, 5/20., 11/24, 7/25

BIPOLAR DEPRESSION

Monitoring Parameters

I. **Lithium**
- A. Cardiac – obtain ECG at baseline if patient is > 40 or has pre-existing heart disease
- B. Metabolic
  1. Obtain electrolytes, BUN, SCr, TSH, and T4 at baseline.
  2. Repeat every 6 – 12 months.
- C. Trough Serum Drug Levels
  1. Obtain 5 – 7 days after lithium initiation.
  2. Monitor every 2 – 6 months once patient and levels are stabilized.
  3. Monitor weekly if patient begins to destabilize.
  4. Levels should be drawn 5-7 days (or more often if clinically indicated) after a dosage change, with the addition or deletion of drugs that increase/decrease lithium renal clearance (e.g., ACE inhibitors, calcium-channel blockers, diuretics, NSAIDs, SSRIs, theophylline), or if there is a change in renal function.
  5. Therapeutic Range: 0.6-1.2 mmol/L for maintenance, 0.8 – 1.2 mmol/L for acute stabilization. Determine by serum trough level in the morning, 10 – 12 hours after last dose.

II. **Divalproex**
- A. Hematologic
  1. CBC with differential – obtain at baseline, then monthly for first 2 months, then every 6 months thereafter.
  2. Platelets – obtain at baseline, then every 6 - 12 months thereafter.
- B. Chemistry – obtain LFTs at baseline, then monthly for first 2 months, then yearly thereafter. If LFTs are elevated on repeat testing, consider obtaining ammonia level and monitor for cognitive dysfunction.
- C. Serum Drug Level
  1. Obtain 5-7 days weeks following initiation, change in dose, addition of other CNS agents to the patient's regimen, or observed signs/symptoms of toxicity. Then obtain every 6 – 12 months thereafter.
  2. Therapeutic Range: 50 – 125 mcg/mL, dose not to exceed 60 mg/kg/day.
  3. Standard draw time is 12 hours after the last dose.

III. **Lamotrigine** (Requires Nonformulary Approval for use)
- A. Dosing
  1. Monotherapy (No concurrent enzyme-inducing or enzyme-inhibiting medications)
     a. 25 mg/day for 2 weeks, then 50 mg/day for 2 weeks, then 100 mg/day for 1 week; thereafter, daily dose may be increased to 200 mg/day.
  2. Adjunctive therapy in patient receiving enzyme-inducing medications (eg, carbamazepine, phenytoin, ritonavir, lopinavir/ritonavir)
     a. 50 mg/day for 2 weeks, then 100 mg/day (in divided doses) for 2 weeks, followed by 200 mg/day (in divided doses) for 1 week, followed by 300 mg/day (in divided doses) for 1 week. May increase to 400 mg/day (in divided doses) during week 7 and thereafter.
     b. NOTE: if enzyme-inducing medication is discontinued, the daily dose of lamotrigine will need to be decreased in 100 mg increments at weekly intervals until daily dosage of 200 mg is attained.
  3. Adjunctive therapy in patients receiving enzyme-inhibiting medications (eg, valproate, sertraline)
     a. 25 mg every other day for 2 weeks, followed by 25 mg/day for 2 weeks, followed by 50 mg/day for 1 week, followed by 100 mg/day.
     b. NOTE: if enzyme-inhibiting medication is discontinued, increase daily lamotrigine dose in 50 mg increments at weekly intervals until daily dosage of 200 mg is attained.

III. **Lamotrigine continued** (Requires Nonformulary Approval for use)

B. Physical Findings

1. Rash
   a. Lamotrigine therapy should be discontinued at the first sign of a rash. If the cause of the rash has been clearly identified as not drug-related then lamotrigine does not need to be discontinued.
   b. Dosing schedule should be strictly followed to decrease risk of rash.
   c. Majority of rash cases occur within the first 8 weeks of therapy.
2. Hypersensitivity Reaction
   a. Fever and lymphadenopathy without rash. Hypersensitivity may progress to multiorgan failure/dysfunction.
   b. Lamotrigine should be discontinued if other causes for hypersensitivity are ruled out.

Table 1: Mood Stabilizers

Medication: Daily Dose Range	**Contraindications**	**Toxicity Starting At Trough Serum Levels of:**	**Signs/symptoms of toxicity (dose-related)**	**Signs/symptoms of toxicity (NOT dose-related)**
Lithium: Initially 900 – 1200 mg daily in 1 to 3 divided doses. **Dose to stay between 0.6 mEq/L and 1.2 mEq/L.** **It is advised to not order doses > 1200 mg daily**	• Hypersensitivity to lithium • Severe cardiovascular or renal disease • Severe debilitation • Dehydration • Sodium depletion • Pregnancy Category D	> 1 – 1.2 mmol/L Patients who are sensitive to lithium may manifest toxicity at serum levels < 1 mmol/L. *Note: A rise in white blood cell count is to be expected.*	Lithium toxicity can be FATAL **Acute:** • Apathy • Coarsening hand tremor that spreads to other parts of body while patient sitting still • Confusion / Drowsiness • Dysarthria • Diarrhea, nausea, vomiting • Giddiness **Acute To Severe:** • Blurred vision • Deep tendon reflexes increased • Muscle rigidity / fasciculations • Mild ataxia • Profound lethargy • Tinnitus • Vertical nystagmus • Vomiting **Severe Intoxication:** • Arrythmias • Impaired consciousness • Increased fasciculations and ataxia • CV collapse with oliguria and anuria • Coarse / irregular limb tremors or muscle contractions • Choreoathetoid movements • Cogwheel rigidity • Coma • Generalized tonic-clonic seizures	Not applicable

BIPOLAR DEPRESSION

Table 1 continued: Mood Stabilizers

Medication: Daily Dose Range	Contraindications	Toxicity Starting At Trough Serum Levels of:	Signs/symptoms of toxicity (dose-related)	Signs/symptoms of toxicity (NOT dose-related)
Divalproex: 20mg/kg/day, given in divided doses **Dose to stay between 50 mcg/mL and 125 mcg/mL** **It is not recommended to exceed 60mg/kg/day**	• Hypersensitivity to VPA • Hepatic dysfunction • Urea cycle disorder • Pregnancy Category D	> 100-125 mcg/mL	**Acute** • Somnolence • Heart block • Deep coma • Hyperbilirubinemia • Lethargy • Vomiting • Changes in mental status • Thrombocytopenia • Prolongation of bleeding time • Hepatotoxicity	• Pancreatitis - DO NOT RECHALLENGE • Hyperammonemic encephalopathy • Hepatotoxicity, severe or fatal • Stevens-Johnson Syndrome • Toxic Epidermal Necrolysis • Polycystic ovarian syndrome (PCOS)
Lamotrigine: 25 – 400 mg/day (Dosing depends on concomitant medication due to significant drug interactions)	• Hypersensitivity to Lamotrigine • Pregnancy Category C	Therapeutic plasma concentration has not been established.	• Rash (maculopapular and erythematous) • Tourette's Syndrome in children • Blood dyscrasias	• Fever • Lymphadenopathy • Multiorgan dysfunction • Stevens-Johnson Syndrome • Toxic Epidermal Necrolysis

Table 2: SSRI/SNRI Antidepressants

Formulary Medications	Initial Dose (Dose Range) mg/day	Significant Drug Interactions	Monitoring
Citalopram (Celexa®) 20mg, 40mg tablet	20 (20 – 40) Do not exceed 20mg in patients age >60	• QTc prolonging agents • Serotonergic agents • Agents that may increase citalopram levels: azole antifungals, carbamazepine • Antiplatelet / anticoagulant agents	• Emergence of suicidal ideation or behavior • EKG for citalopram if risk factors for QTc prolongation are pre • If QTc is > 450msec for males or > 470msec for females, do not initiate citalopram. If pt is on citalopram and QTc is > 500msec, consider alternative treatment. • Emergence of hypomania/mania
Fluoxetine (Prozac®) 20mg capsule	20 (20 – 60)	• Serotonergic agents • Agents that may increase fluoxetine levels: haloperidol, propranolol • Thioridazine- levels increased by fluoxetine • Antiplatelet / anticoagulant agents	
Sertraline (Zoloft®) 50mg, 100mg tablet	50 (50 – 200)	• Serotonergic agents • Agents that may increase sertraline levels: haloperidol, propranolol • Antiplatelet / anticoagulant agents	
Duloxetine (Cymbalta®)	30-60 (60-120)	• Serotonergic agents • Haloperidol- increase duloxetine level • Thioridazine- levels increased by duloxetine • Antiplatelet / anticoagulant agents	• Emergence of suicidal ideation or behavior • Dose-related increases in systolic blood pressure and pulse • Emergence of hypomania/mania
Venlafaxine XR (Effexor XR ®)	75 (150-225)	• Serotonergic agents • Antiplatelet / anticoagulant agents	

Table 3: Atypical Antipsychotics/Second Generation Antipsychotics Approved for Bipolar Depression – Dosages and Adverse Effects

Agent	Formulary Status	Potency	Dose Range (mg/day)	Adverse Effects				
				Weight Gain	EPS	Sedation	Anticholinergic	Orthostasis
Second Generation Antipsychotics		**5HT2$_a$/D2**						
Cariprazine (Vraylar®)	NF	++/+++#	1.5-6	++	+/++	++	+	+
Lumateperone (Caplyta®)	NF	++++/+++	42	+	++	++++	+	+
Lurasidone (Latuda®)	NF	++++/+++	40-80	+	+	++	+/0	+/0
Olanzapine* (Zyprexa®)	NF	++++/++	5 – 20	+++	0/+	++	++	+
Quetiapine (Seroquel®)	NF	+/+	300 – 800	++	0/+	++/+++	++	+

partial D2 agonist, *In combination with fluoxetine

Antipsychotic Monitoring Parameters

Table 4: Antipsychotic Monitoring Guidelines[1]

Parameter	Baseline	Follow-Up
Weight, Height, BMI	X	BMI every visit for 6 months and quarterly thereafter
Blood Pressure, Pulse, Temperature	X	As clinically indicated
Fasting Blood Glucose[4]	X	At 4 months after initiating new antipsychotic, then annually
Fasting Lipid Profile[4]	X	At 4 months after initiating new antipsychotic, then annually
Complete Metabolic Panel	X	As clinically indicated
CBC	X	As clinically indicated
TSH	X	As clinically indicated
EKG[2]	As clinically indicated	
Prolactin[3]	As clinically indicated	

Providers should consider obtaining any of the laboratories listed above more frequently if clinically indicated.

1. Additional assessments may be necessary based on patient's history, preexisting conditions and clinical circumstances.
2. Providers should consider obtaining an EKG at baseline and periodically when there is a personal or family history of cardiovascular disease or the patient is > 40 years old. Also, consider obtaining EKG prior to treatment with chlorpromazine, iloperidone, pimozide, thioridazine or ziprasidone or with addition of other medications that can affect QTc interval in patients with cardiac risk factors or elevated QTc intervals.
3. Providers should consider obtaining a prolactin level if the patient is complaining of gynecomastia, galactorrhea, irregular or absent menses, or sexual dysfunction. Consider screening for symptoms at each visit until stable and annually if treated with an antipsychotic known to increase prolactin.
   - Routine prolactin levels are **not** recommended unless symptoms are present
   - The normal range of prolactin is 10-20 mcg/L in males and 10-25 mcg/L in females
   - Symptoms typically do not appear until levels reach 60-100 mcg/L
   - Patients should be referred to medical to rule-out other etiologies of hyperprolactinemia

See next page for additional antipsychotic monitoring parameters

BIPOLAR DEPRESSION

Antipsychotic Monitoring Parameters Continued:

4. Providers should consider determining if metabolic syndrome criteria are met at 4 months after initiating a new antipsychotic and annually thereafter. Metabolic syndrome is defined by the presence of at least 3 of the following risk factors: elevated waist circumference(>40.2 inches for males and >34.6 inches for females), elevated triglycerides (≥150 mg/dL)or drug treatment for elevated triglycerides, reduced HDL (<40 mg/dL in men or <50 mg/dL in women) or treatment of low HDL, elevated BP (≥130/85)or antihypertensive treatment and elevated fasting glucose or drug treatment for high glucose.

Table 5: Antipsychotic Outcome and Adverse Effect Monitoring

Assessment	Baseline	Follow-up
AIMS (Abnormal Involuntary Movement Scale) •Acute EPS – Akathisia, dystonia, parkinsonism •Tardive Dyskinesia	X	Baseline and at least every 6 months

Table 6: Antipsychotic Adverse Effect Management

Side Effect	Recommended Management Strategies

Extrapyramidal Symptoms (EPS) for Second Generation Antipsychotics (SGA)	• Lower the dose of the antipsychotic agent to the lowest effective dose **or**
	• Review table 3 and consider selecting an agent with a lower incidence of EPS **or**
	• Switch to an SGA **or**
	• Treat EPS with one of the following agents
	  • Benztropine 1 – 6 mg/day
	  • Diphenhydramine 25 – 100 mg/day
	  • Amantadine 100 – 300 mg/day
	  • Propranolol 20 – 120 mg/day
	  • Short term use of benzodiazepines may be considered in severe cases in an inpatient setting
	  • Increase dose of agent or switch to alternate anti-EPS agent if ineffective

Akathisia	• Lower the dose of the antipsychotic agent to the lowest effective dose **or** • Switch to an SGA **or** • Treat with propranolol 20 – 120 mg/day. Titrate dose as tolerated and as needed.
Tardive dyskinesia	• Diagnosis supported by AIMS? • Switch to an SGA • Consider pharmacotherapy consult for treatment options
Neuroleptic Malignant Syndrome	• Medical emergency • Evaluate through medical department for possible referral to emergency room • Consider STAT CPK • Discontinue antipsychotic

Appropriate use of Anticholinergic Medications

Benztropine and diphenhydramine are associated with significant side effects and may potentially increase the risk of developing tardive dyskinesia, cognitive impairment, anticholinergic side effects, and delirium. Current treatment guidelines recommend **against** the use of anticholinergics for prevention of EPS unless the patient has a history of severe EPS.

- Anticholinergic medications use should be limited to the treatment of confirmed EPS and scheduled prophylactic use should be minimized.
- Lower starting doses of FGA with reasonable titration rates could potentially reduce the risk of treatment-emergent EPS.
- When treating EPS, use of anticholinergic medications should be evaluated every 3 months for possible discontinuation, as most cases of EPS are self-limiting and do not require long-term treatment.

ABNORMAL INVOLUNTARY MOVEMENT SCALE

Complete examination procedure outlined in the instructions before making rating. Rate highest severity observed. Movements occurring upon activation rate one less than those occurring spontaneously.
0 = None 1 = Minimal 2 = Mild 3 = Moderate 4 = Severe

Date of Evaluation									
1	**Muscles of facial expression** e.g., movements of forehead, eyebrows, preorbital area, cheeks, include frowning, blinding, smiling, grimacing								
2	**Lips and perioral area** e.g., puckering, pouting, smacking								
3	**Jaw** e.g., biting, clenching, chewing, mouth opening, lateral movement								
4	**Tongue** Rate only increase in movement both in and out of mouth, not inability to sustain movement								
5	**Upper (arms, wrists, hands, fingers)** Include chronic movements (i.e., rapid objectively purposeless, irregular, spontaneous); athetoid movements (i.e., slow, irregular, complex, serpentine). DO NOT include tremor (i.e., repetitive, regular, rhythmic).								
6	**Lower (legs, knees, ankles, toes)** e.g., lateral knee movement, foot tapping, heel dropping, foot squirming, inversion, and eversion of foot								
7	**Neck shoulders, hips** e.g., rocking, twisting, squirming, pelvic gyrations								
8	**Severity of abnormal movements**								
9	**Incapacitation due to abnormal movements**								
10	**Patient's awareness of abnormal movements** Rate only patient's report: No awareness=0 Aware, no distress=1 Aware, mild distress=2 Aware, moderate distress=3 Aware, severe distress=4								
11	**Current problems with teeth &/or dentures?** No=0 Yes=1								
12	**Does patient usually wear dentures?** No=0 Yes=1								
13	**COMMENTS:**								

BRIEF PSYCHIATRIC RATING SCALE (BPRS) - Instructions for the Clinician

Background: The Brief Psychiatric Rating Scale (BPRS) is a widely used instrument for assessing psychopathology at baseline and longitudinally as an outcome measurement when treatment is introduced. The BPRS is a scale measuring positive symptoms, general psychopathology and affective symptoms. It has proven particularly valuable for documenting the efficacy of treatment in patients who have moderate to severe psychopathology. The BPRS has been well validated in the clinical literature and is reportedly the most studied psychometric instrument currently in use.

The BPRS should be administered by a clinician who is knowledgeable concerning psychiatric disorders and is able to interpret the constructs used in the assessment. The individual's behavior over the previous 2-3 days should also be considered and can be reported by the patient's caregivers or teachers. It should be utilized at baseline and then at each visit as long as the patient is prescribed an antipsychotic.

The BPRS utilized in the electronic medical record (EMR) consists of a range of 23 symptom constructs covering a broad array of potential psychopathology. The assessment typically takes 10-20 minutes or less for the interview and scoring.

Instructions for Use and Scoring: Each item is rated on a seven-point scale (1=not present to 7=extremely severe). Zero (0) is entered if the item is not assessed. The scores of the 23 items should be summed and recorded. The total score should be compared to the total score from one evaluation to the next as a measure of response to treatment. In addition, a single subscale (symptom) or cluster of subscales (e.g., grandiosity, elevated mood, excitement, distractibility) can be followed over time.

Brief Psychiatric Rating Scale (BPRS)

Patient Name _____ Patient Number _____ Date_____

Facility _____ Practitioner _____

Enter the score for the term that best describes the patient's condition.

0 = Not assessed, 1 = Not present, 2 = Very mild, 3 = Mild, 4 = Moderate, 5 = Moderately severe, 6 = Severe, 7 = Extremely severe

Score		
____	1.	SOMATIC CONCERN - Preoccupation with physical health, fear of physical illness, hypochondriasis.
____	2.	ANXIETY - Worry, fear, over-concern for present or future, uneasiness
____	3.	EMOTIONAL WITHDRAWAL - Lack of spontaneous interaction, isolation deficiency in relating to others.
____	4.	CONCEPTUAL DISORGANIZATION - Thought processes confused, disconnected, disorganized, disrupted.
____	5.	IMPULSIVENESS
____	6.	MOTOR HYPERACTIVITY - Increase in energy level evidenced in more frequent movement and/or rapid speech. Do not rate if restlessness is due to akathisia.
____	7.	MANNERISMS AND POSTURING - Peculiar, bizarre, unnatural motor behavior (not including tic).
____	8.	GRANDIOSITY - Exaggerated self-opinion, arrogance, conviction of unusual power or abilities.
____	9.	DEPRESSIVE MOOD - Sorrow, sadness, despondency, pessimism.
____	10	HOSTILITY - Animosity, contempt, belligerence, disdain for others.
____	11.	SUSPICIOUSNESS - Mistrust, belief others harbor malicious or discriminatory intent.
____	12.	HALLUCINATORY BEHAVIOR - Perceptions without normal external stimulus correspondence.
____	13.	MOTOR RETARDATION - Slowed, weakened movements or speech, reduced body tone.
____	14.	UNCOOPERATIVENESS - Resistance, guardedness, rejection of authority.
____	15.	UNUSUAL THOUGHT CONTENT - Unusual, odd, strange, bizarre thought content.
____	16.	BLUNTED AFFECT - Reduced emotional tone, reduction in formal intensity of feelings, flatness.
____	17.	EXCITEMENT - Heightened emotional tone, agitation, increased reactivity.
____	18.	DISORIENTATION - Confusion or lack of proper association for person, place or time.
____	19.	ELEVATED MOOD - A pervasive, sustained and exaggerated feeling of well-being, cheerfulness, or euphoria implying a pathological mood. Optimism that is out of proportion to the circumstances.
____	20.	SUICIDALITY - Expressed desire, intent, or actions to harm or kill self.
____	21.	BIZARRE BEHAVIOR - Reports of behaviors which are odd, unusual, or psychotically criminal. Not limited to interview period. Include inappropriate sexual behavior and inappropriate affect.
____	22.	SELF-NEGLECT - Hygiene, appearance, or eating behavior below usual expectations, below socially acceptable standards or life threatening.
____	23.	DISTRACTIBILITY - Degree to which observed sequences of speech and actions are interrupted by stimuli unrelated to the interview. Distractibility is rated when the individual shows a change in the focus of attention as characterized by a pause in speech or a marked shift in gaze. Individual's attention may be drawn to noise in adjoining room, books on a shelf, interviewer's clothing, etc.

BIPOLAR DISORDER: MANIA

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

1 Rule out medical and substance causes for presentation.

2 Meets criteria for Manic or Hypomanic Episode as defined in DSM-5?

No → 3 Re-evaluate diagnosis and treat underlying causes.

Yes

4 Is patient currently on an antidepressant?

Yes → 5 Consider antidepressant discontinuation or tapering dose.

No

6 Is patient currently on a mood stabilizer **or** antipsychotic*?

Yes → 7 Optimize mood stabilizer. Adjust dose per serum level. Lithium 0.6 – 1.2 mmol/L, Divalproex 50 – 125 mcg/mL, continue for 4 – 6 weeks.
or
Maximize dose of antipsychotic, continue for 4 – 6 weeks.

No

8 Initiate treatment with mood stabilizer or Aripiprazole, Risperidone or Ziprasidone, titrate to therapeutic level/dose (see box 7). Continue for 4-6 weeks.

9 Adequate response per clinical status and BPRS?

Yes → 10 Continue current therapy.

Partial → 11 Consider combination therapy:
- Lithium plus Divalproex
- Lithium or Divalproex plus Aripiprazole
  or
- Lithium or Divalproex plus Risperidone
  or
- Lithium or Divalproex plus Ziprasidone

No, Assess compliance

12 Discontinue current therapy and switch to the alternative mood stabilizer or antipsychotic for 4 – 6 weeks at therapeutic doses.

13 Adequate response per clinical status and BPRS?

Yes → 14 Continue current therapy.

No, Assess compliance

15
1. Consider combination therapy:
   - Lithium plus Divalproex
     or
   - Lithium or Divalproex plus Aripiprazole or Risperidone or Ziprasidone
2. Consider carbamazepine. Target levels between 4 – 12 mcg/mL for 4 – 6 weeks.

16 Adequate response per clinical status and BPRS?

Yes → 17 Continue current therapy.

No → 18
1. Re-evaluate diagnosis
2. Counsel regarding medication adherence
3. Consider use of combination therapy with lithium, divalproex, carbamazepine, aripiprazole, risperidone or ziprasidone
4. Consider Pharmacotherapy consult

*Antipsychotic agents may be preferred in patients with significant psychotic features.

If psychotic symptoms persist, reassess diagnosis of bipolar disorder.

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.

Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee. Approved 1/99; revised 5/02, 1/10, 3/12, 1/15, 5/20, 9/20;11/24 *reviewed 4/03, 9/05.*

BIPOLAR DISORDER: MANIA

Recommended Laboratory Monitoring

I. **Lithium**
- A. Cardiac – obtain ECG at baseline if patient is > 40 or has pre-existing heart disease
- B. Metabolic
  1. Obtain electrolytes, BUN, SCr, TSH, and T4 at baseline.
  2. Repeat every 6 – 12 months.
- C. Trough Serum Drug Levels
  1. Obtain 5 – 7 days after lithium initiation.
  2. Monitor every 2 – 6 months once patient and levels are stabilized.
  3. Monitor weekly if patient begins to destabilize.
  4. Levels should be drawn *5-7* days (or more often if clinically indicated) after a dosage change, with the addition or deletion of drugs that increase/decrease lithium renal clearance (e.g., ACE inhibitors, calcium-channel blockers, diuretics, NSAIDs, SSRIs, theophylline), or if there is a change in renal function.
  5. Therapeutic Range: 0.6-1.2 mmol/L for maintenance, 0.8 – 1.2 mmol/L for acute stabilization. Determine by serum trough level in the morning, 10 – 12 hours after last dose.

II. **Divalproex**
- A. Hematologic
  1. CBC with differential – obtain at baseline, then monthly for first 2 months, then every 6 months thereafter.
  2. Platelets – obtain at baseline, then every 6 - 12 months thereafter.
- B. Chemistry – obtain LFTs at baseline, then monthly for first 2 months, then yearly thereafter. If LFTs are elevated on repeat testing, consider obtaining ammonia level and monitor for cognitive dysfunction.
- C. Serum Drug Level
  1. Obtain 5-7 days following initiation, change in dose, addition of other CNS agents to the patient's regimen, or observed signs/symptoms of toxicity. Then obtain every 6 – 12 months thereafter.
  2. Therapeutic Range: 50 – 125 mcg/mL, dose not to exceed 60 mg/kg/day.
  3. Standard draw time is 12 hours after the last dose.

III. **Carbamazepine**
- A. Cardiac – obtain ECG at baseline if patient is > 40 or has pre-existing heart disease
- B. Hematologic – CBC with differential and platelets; obtain baseline, then monthly for first 2 months, then every 6 months thereafter and as clinically indicated
- C. Chemistry – emphasis hepatic function, renal function, and electrolytes; obtain at baseline, 3 months, then annually and as clinically indicated
- D. Ophthalmic – perform baseline and periodic eye examinations. Use with caution in patients with increased intraocular pressure.
- E. Serum Drug Level
  1. Obtain a level at 2 weeks, one month, then annually or as clinically indicated.
  2. Therapeutic Range: 4-12 mcg/mL
  3. Onset of auto-induction occurs in about 3 days from first dose, with maximum effect at about 30 days.
  4. Draw serum trough levels just prior to the next dose.
- F. Genetic testing – recommended for people with Asian ancestry
  1. Serious skin reactions (e.g., Stevens Johnson Syndrome) are more common in people with the HLA-B 1502 variant, a mutation found primarily in Asians. Reactions have been fatal.
  2. Carbamazepine should not be prescribed for patients with Asian ancestry unless no other reasonable alternative exists. If so, patients must undergo genetic testing for the mutation before being prescribed carbamazepine. Providers must obtain approval from their Regional Medical Director prior to ordering the test.
  3. The risk versus benefits of carbamazepine therapy should be weighed in patients that test positive, and discussed with the Regional Medical Director prior to initiating therapy.
  4. Carbamazepine therapy may be continued in intake Asian patients or Asian patients already taking the medication for $\geq$ 3 months if they have not experienced adverse effects.

Table 1: Mood Stabilizers

Medication: Daily Dose Range	Contraindications	Toxicity Starting At Trough Serum Levels of:	Signs/symptoms of toxicity (dose-related)	Signs/symptoms of toxicity (NOT dose-related)
Lithium: Initially 900 – 1200 mg daily in 1 to 3 divided doses. **Dose to stay between 0.6 mEq/L and 1.2 mEq/L.** **It is advised to not order doses > 1200 mg daily**	• Hypersensitivity to lithium • Severe cardiovascular or renal disease • Severe debilitation • Dehydration • Sodium depletion • Pregnancy Category D	> 1 – 1.2 mmol/L Patients who are sensitive to lithium may manifest toxicity at serum levels < 1 mmol/L. *Note: A rise in white blood cell count is to be expected.*	Lithium toxicity can be FATAL **Acute:** • Apathy • Coarsening hand tremor that spreads to other parts of body while patient sitting still • Confusion / Drowsiness • Dysarthria • Diarrhea, nausea, vomiting • Giddiness **Acute To Severe:** • Blurred vision • Deep tendon reflexes increased • Muscle rigidity / fasciculations • Mild ataxia • Profound lethargy • Tinnitus • Vertical nystagmus • Vomiting **Severe Intoxication:** • Arrythmias • Impaired consciousness • Increased fasciculations and ataxia • CV collapse with oliguria and anuria • Coarse / irregular limb tremors or muscle contractions • Choreoathetoid movements • Cogwheel rigidity • Coma • Generalized tonic-clonic seizures	Not applicable
Divalproex: 20mg/kg/day, given in divided doses **Dose to stay between 50 mcg/mL and 125 mcg/mL** **It is not recommended to exceed 60 mg/kg/day**	• Hypersensitivity to VPA • Hepatic dysfunction • Urea cycle disorder • Pregnancy Category D	> 100-125 mcg/mL	**Acute** • Somnolence • Heart block • Deep coma • Hyperbilirubinemia • Lethargy • Vomiting • Changes in mental status • Thrombocytopenia • Prolongation of bleeding time • Hepatotoxicity	• Pancreatitis - DO NOT RECHALLENGE • Hyperammonemic encephalopathy • Hepatotoxicity, severe or fatal • Stevens-Johnson Syndrome • Toxic Epidermal Necrolysis • Polycystic ovarian syndrome (PCOS)

Table 1: Mood Stabilizers Continued

Drug: Daily Dose Range	Contraindications	Toxicity Seen Starting At Trough Serum Levels of:	Signs/symptoms of toxicity (dose-related)	Signs/symptoms of toxicity (NOT dose-related)
Carbamazepine: 600 – 1600 mg, given in divided doses **Dose to stay between 4 mcg/mL and 12 mcg/mL**	• Hypersensitivity to carbamazepine or TCAs • Bone marrow depression • In combination with or within 14 days of MAOIs • Pregnancy Category D	> 12 mcg/mL	• Abnormal reflex response • Acetonuria • Agitation / restlessness • Ataxia / dizziness • Blurred vision / diplopia/mydriasis • Cardiac dysrhythmias • Coma • Cyanosis • Disorientation • Extreme lethargy or drowsiness • Flushing • Glycosuria • Involuntary muscle movements • Nausea / vomiting • Nystagmus • Opisthotonos • Tremor • Urinary retention	• Arrhythmias • Blood cell dyscrasias • Chest pain • CHF • Nausea / vomiting • Photosensitivity • SIADH (Syndrome of Inappropriate ADH Secretion) • Stevens-Johnson Syndrome • Toxic epidermal necrolysis

Table 2: Antipsychotics

Drug: Daily Dose Range	Contraindications	Adverse Drug Reactions
Aripiprazole: 10-30 mg, given once daily	• Hypersensitivity to aripiprazole	• Akathisia • Anxiety • Blurred vision • Constipation • Dizziness • Extrapyramidal symptoms • Fatigue • Headache • Insomnia • Nausea • Orthostatic hypotension • Restlessness • Sedation • Tremor • Vomiting • Weight gain

Table 2: Antipsychotics continued.

Risperidone: 1 to 6 mg daily, given once to twice daily	• Hypersensitivity to risperidone or paliperidone	• Anxiety • Blurred vision • Constipation • Diarrhea • Dizziness • Extrapyramidal Symptoms • Fatigue • Hyperprolactinemia • Increased appetite • Nausea • Rash • Respiratory symptoms (cough, nasal congestion) • Sedation • Tremor • Upper abdominal pain • Vomiting • Weight gain • Xerostomia
Ziprasidone: 80 to 160 mg daily, given twice daily	• Hypersensitivity to Ziprasidone • Uncompensated heart failure • Acute or recent myocardial infarction • History of QT prolongation • Concomitant administration with drugs that cause QT prolongation	• Abnormal vision • Anxiety • Asthenia • Constipation • Diarrhea • Dizziness • Extrapyramidal Symptoms • Headache • Indigestion • Nausea • Reduced motor activity • Respiratory tract infection • Somnolence • Tremor • Vomiting • Weight gain

Antipsychotic Monitoring Parameters

Table 3: Metabolic and Endocrine Monitoring Guidelines

Parameter	Baseline	Follow-Up
Weight, Height, BMI	X	BMI every visit for 6 months and quarterly thereafter
Blood Pressure, Pulse, Temperature	X	As clinically indicated
Fasting Blood Glucose[4]	X	At 4 months after initiating new antipsychotic, then annually
Fasting Lipid Profile[4]	X	At 4 months after initiating new antipsychotic, then annually
Complete Metabolic Panel	X	As clinically indicated
CBC	X	As clinically indicated
TSH	X	As clinically indicated
EKG[2]	As clinically indicated	
Prolactin[3]	As clinically indicated	

Providers should consider obtaining any of the laboratories listed above more frequently if clinically indicated.

1. Additional assessments may be necessary based on patient's history, preexisting conditions and clinical circumstances.
2. Providers should consider obtaining an EKG at baseline and periodically when there is a personal or family history of cardiovascular disease or the patient is > 40 years old. Also, consider obtaining EKG prior to treatment with ziprasidone or with addition of other medications that can affect QTc interval in patients with cardiac risk factors or elevated QTc intervals.
3. Providers should consider obtaining a prolactin level if the patient is complaining of gynecomastia, galactorrhea, irregular or absent menses, or sexual dysfunction. Consider screening for symptoms at each visit until stable and annually if treated with an antipsychotic known to increase prolactin.
   - Routine prolactin levels are **not** recommended unless symptoms are present
   - The normal range of prolactin is 10-20 mcg/L in males and 10-25 mcg/L in females
   - Symptoms typically do not appear until levels reach 60-100 mcg/L
   - Patients should be referred to medical to rule-out other etiologies of hyperprolactinemia
4. Providers should consider determining if metabolic syndrome criteria are met at 4 months after initiating a new antipsychotic and annually thereafter. Metabolic syndrome is defined by the presence of at least 3 of the following risk factors: elevated waist circumference(>40.2 inches for males and >34.6 inches for females), elevated triglycerides ($\geq$150 mg/dL)or drug treatment for elevated triglycerides, reduced HDL (<40 mg/dL in men or <50 mg/dL in women) or treatment of low HDL, elevated BP ($\geq$130/85)or antihypertensive treatment and elevated fasting glucose or drug treatment for high glucose.

Additional Monitoring Parameters for Specific Agents

- Ziprasidone (Geodon®) - EKG at baseline then annually or as clinically indicated
- Quetiapine (Seroquel®) - Ophthalmic exam checking for cataracts every 6 months

Table 4: Outcome and Adverse Effect Monitoring

Assessment	**Baseline**	**Follow-up**
AIMS (Abnormal Involuntary Movement Scale) •Acute EPS – Akathisia, dystonia, parkinsonism •Tardive Dyskinesia	X	Baseline and at least every 6 months
Mental Status Exam	X	Baseline and at least every 6 months
BPRS (Brief Psychiatric Rating Scale)	X	• Baseline and at least every 6 months • Medication is started, changed or discontinued

Table 5: Atypical Antipsychotics Approved for Bipolar Mania - Dosages and Adverse Effects

Agent	Formulary Status	Traditional Equivalents (approx.mg)	Dose Range (mg/day)	Adverse Effects				
				Weight Gain	EPS	Sedation	Anticholinergic	Orthostasis
Aripiprazole (Abilify®)	F	7.5	10 – 30	0/+	0/+	+	0/+	0/+
Asenapine (Saphris ®)	NF	?	5-20	++	+	++	+	+
Cariprazine (Vraylar®)	*NF*	*?*	*1.5 - 6*	++	+/++	++	+	+
Olanzapine (Zyprexa®)	NF	5	5 – 20	+++	0/+	++	++	+
Quetiapine (Seroquel®)	NF	125	300 – 800	++	0/+	++/+++	++	+
Risperidone (Risperdal®)	F	2	0.5-6	+	0/+++§	++	+	++
Ziprasidone (Geodon®)	F	60	120 -160	0/+	++	++	+	++

§ dose-dependent

BRIEF PSYCHIATRIC RATING SCALE (BPRS) - Instructions for the Clinician

Background: The Brief Psychiatric Rating Scale (BPRS) is a widely used instrument for assessing psychopathology at baseline and longitudinally as an outcome measurement when treatment is introduced. The BPRS is a scale measuring positive symptoms, general psychopathology and affective symptoms. It has proven particularly valuable for documenting the efficacy of treatment in patients who have moderate to severe psychopathology. The BPRS has been well validated in the clinical literature and is reportedly the most studied psychometric instrument currently in use.

The BPRS should be administered by a clinician who is knowledgeable concerning psychiatric disorders and is able to interpret the constructs used in the assessment. The individual's behavior over the previous 2-3 days should also be considered and can be reported by the patient's caregivers or teachers. It should be utilized at baseline and then at each visit as long as the patient is prescribed an antipsychotic.

The BPRS utilized in the electronic medical record (EMR) consists of a range of 23 symptom constructs covering a broad array of potential psychopathology. The assessment typically takes 10-20 minutes or less for the interview and scoring.

Instructions for Use and Scoring: Each item is rated on a seven-point scale (1=not present to 7=extremely severe). Zero (0) is entered if the item is not assessed. The scores of the 23 items should be summed and recorded. The total score should be compared to the total score from one evaluation to the next as a measure of response to treatment. In addition, a single subscale (symptom) or cluster of subscales (e.g., grandiosity, elevated mood, excitement, distractibility) can be followed over time.

Brief Psychiatric Rating Scale (BPRS)

Patient Name _____ Patient Number _____ Date_____

Facility _____ Practitioner _____

Enter the score for the term that best describes the patient's condition.

0 = Not assessed, 1 = Not present, 2 = Very mild, 3 = Mild, 4 = Moderate, 5 = Moderately severe, 6 = Severe, 7 = Extremely severe

Score		
____	1.	SOMATIC CONCERN - Preoccupation with physical health, fear of physical illness, hypochondriasis.
____	2.	ANXIETY - Worry, fear, over-concern for present or future, uneasiness
____	3.	EMOTIONAL WITHDRAWAL - Lack of spontaneous interaction, isolation deficiency in relating to others.
____	4.	CONCEPTUAL DISORGANIZATION - Thought processes confused, disconnected, disorganized, disrupted.
____	5.	IMPULSIVENESS
____	6.	MOTOR HYPERACTIVITY - Increase in energy level evidenced in more frequent movement and/or rapid speech. Do not rate if restlessness is due to akathisia.
____	7.	MANNERISMS AND POSTURING - Peculiar, bizarre, unnatural motor behavior (not including tic).
____	8.	GRANDIOSITY - Exaggerated self-opinion, arrogance, conviction of unusual power or abilities.
____	9.	DEPRESSIVE MOOD - Sorrow, sadness, despondency, pessimism.
____	10	HOSTILITY - Animosity, contempt, belligerence, disdain for others.
____	11.	SUSPICIOUSNESS - Mistrust, belief others harbor malicious or discriminatory intent.
____	12.	HALLUCINATORY BEHAVIOR - Perceptions without normal external stimulus correspondence.
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____	15.	UNUSUAL THOUGHT CONTENT - Unusual, odd, strange, bizarre thought content.
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____	18.	DISORIENTATION - Confusion or lack of proper association for person, place or time.
____	19.	ELEVATED MOOD - A pervasive, sustained and exaggerated feeling of well-being, cheerfulness, or euphoria implying a pathological mood. Optimism that is out of proportion to the circumstances.
____	20.	SUICIDALITY - Expressed desire, intent, or actions to harm or kill self.
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____	23.	DISTRACTIBILITY - Degree to which observed sequences of speech and actions are interrupted by stimuli unrelated to the interview. Distractibility is rated when the individual shows a change in the focus of attention as characterized by a pause in speech or a marked shift in gaze. Individual's attention may be drawn to noise in adjoining room, books on a shelf, interviewer's clothing, etc.

ABNORMAL INVOLUNTARY MOVEMENT SCALE

Complete examination procedure outlined in the instructions before making rating. Rate highest severity observed. Movements occurring upon activation rate one less than those occurring spontaneously.
0 = None 1 = Minimal 2 = Mild 3 = Moderate 4 = Severe

Date of Evaluation									
1	**Muscles of facial expression** e.g. movements of forehead, eyebrows, preorbital area, cheeks, include frowning, blinding, smiling, grimacing								
2	**Lips and perioral area** e.g. puckering, pouting, smacking								
3	**Jaw** e.g. biting, clenching, chewing, mouth opening, lateral movement								
4	**Tongue** Rate only increase in movement both in and out of mouth, not inability to sustain movement								
5	**Upper (arms, wrists, hands, fingers)** Include chronic movements (i.e. rapid objectively purposeless, irregular, spontaneous); athetoid movements (i.e. slow, irregular, complex, serpentine). DO NOT include tremor (i.e. repetitive, regular, rhythmic).								
6	**Lower (legs, knees, ankles, toes)** e.g. lateral knee movement, foot tapping, heel dropping, foot squirming, inversion, and eversion of foot								
7	**Neck shoulders, hips** e.g., rocking, twisting, squirming, pelvic gyrations								
8	**Severity of abnormal movements**								
9	**Incapacitation due to abnormal movements**								
10	**Patient's awareness of abnormal movements** Rate only patient's report: No awareness=0 Aware, no distress=1 Aware, mild distress=2 Aware, moderate distress=3 Aware, severe distress=4								
11	**Current problems with teeth &/or dentures?** No=0 Yes=1								
12	**Does patient usually wear dentures?** No=0 Yes=1								
13	**COMMENTS:**								

BUPRENORPHINE AND METHADONE DISCONTINUATION FOR MEDICATION ASSISTED TREATMENT

1

- Counsel the patient on signs and symptoms of opioid withdrawal
- Evaluate patient's withdrawal symptoms with the Clinical Opiate Withdrawal Scale (COWS); refer to page 6. The COWS can be found in the EHR under Notebuilder Templates
- Do not discontinue methadone or buprenorphine in a pregnant patient (See Page 2 for management)
- For patients on buprenorphine or methadone, if taper deemed necessary, patients will be transferred to the following designated facilities with request for a medical hold:
  - UTMB: Beto for males, Plane for females
  - Texas Tech: Middleton

2

Does the patient have underlying cardiac disease, i.e., CAD, heart failure, or history of arrhythmias?

Yes

3

- Order baseline EKG and repeat as clinically indicated.
- Go to box #6.

No

4

Does the patient have acute psychiatric issues warranting crisis management or psychiatric admission?

Yes

5

- Transfer patient to an inpatient psychiatric facility.
- Go to box #6.

No

6

Was patient on buprenorphine or methadone for medication assisted treatment (MAT) on intake?

Yes

7

- See page 3 and 4 for taper recommendations regarding buprenorphine and methadone

No

8

See Opioid Discontinuation DMG for more information

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

12

Is patient having moderately severe withdrawal symptoms (score of ≥25 on the COWS)?

Yes

13

- Administer clonidine 0.1 mg TID up to 0.3 mg TID for 7 days; taper over additional 3 days. Maximum total daily dose should not exceed 1 mg/day.
- Monitor vital signs before every administration of clonidine. Clonidine should be held if systolic blood pressure (SBP) < 90mmHg, diastolic blood pressure (DBP) < 60mmHg, or pulse rate (PR) < 50 bpm.
- Provide supportive care for pain, nausea, vomiting, and diarrhea as clinically indicated.
- If patient is experiencing significant withdrawal symptoms, the taper may be paused or slowed as needed.

No

14

- Monitor vital signs as clinically indicated.
- Provide supportive care for pain, nausea, vomiting, and diarrhea as clinically indicated

15

Monitor patient for severe complications, i.e., signs of dehydration and acute mental status changes. If present, transfer to higher level of care.

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.

Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee, July 2025

DISCONTINUATION TAPER

- Buprenorphine and methadone tapers require approval from a Regional Medical Director (RMD).
- Pharmacy Clinical Practice Specialists (PCPS) may approve non-formulary requests short-term pending RMD approval
- **Monitor withdrawal symptoms with COWS prior to every dose reduction**. See page 1, box 12.
- Purpose of tapers is to minimize opioid withdrawal symptoms and signs. Rate of tapering should be individualized based on patient's clinical situation. See Tables 1 and 2 for tapering recommendations and examples.
- Per CDC guidelines, patients who are not taking prescribed opioids (e.g., patients who are diverting all opioids they obtain) do not require tapers.
- Postpartum Taper:
    - Do not discontinue methadone or buprenorphine in a pregnant patient. Therapy should be tapered and discontinued postpartum.
    - Patient may receive postpartum taper at the following units: Young or Plane
    - Patient should be discharged from the hospital on whichever agent they received while pregnant (e.g., methadone or buprenorphine), as part of the postpartum discharge orders.

BUPRENORPHINE TAPER

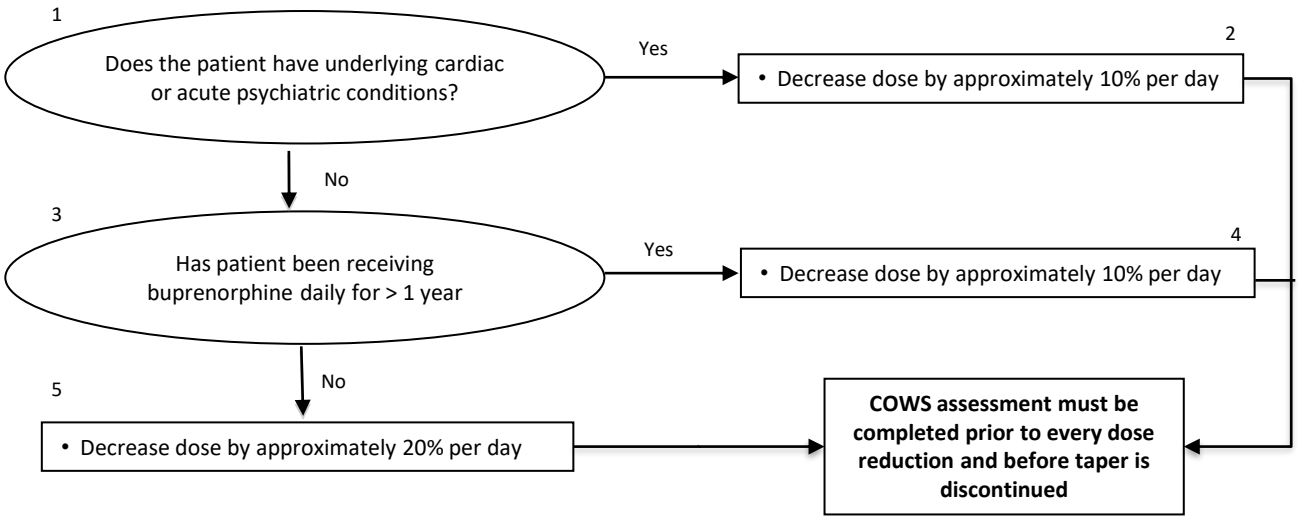

Table 1. Example of Buprenorphine Tapering Schedule

Consider tapering schedule if patient receiving buprenorphine daily for ≤ 1 year and does not have cardiac or acute psychiatric conditions		Consider tapering schedule if patient receiving buprenorphine daily for >1 year **or** has cardiac or acute psychiatric conditions	
• Decrease dose by approximately 20% per day.* • Example 12 mg/day		• Decrease dose by approximately 10% per day.* • Example 12 mg/day	
Day 1	10 mg	Day 1	10 mg
Day 2	8 mg	Day 2	10 mg
Day 3	6 mg	Day 3	8 mg
Day 4	4 mg	Day 4	8 mg
Day 5	4 mg	Day 5	8 mg
Day 6	2 mg	Day 6	6 mg
Day 7	2 mg	Day 7	6 mg
Day 8	Discontinue	Day 8	6 mg
		Day 9	4 mg
		Day 10	4 mg
		Day 11	4 mg
		Day 12	2 mg
		Day 13	2 mg
		Day 14	2 mg
		Day 15	Discontinue

*Round to the most appropriate tablet strength, 2 mg sublingual (SL) tablets available at select units

METHADONE TAPER

- Decrease dose by approximately 20% every 3 days
  - Methadone withdrawal typically begins 36 to 48 hours after the last dose, peaks after about 3 days
- Then once reach 40 mg, reduce dose by 5 mg every 3 days
  - According to Substance Abuse and Mental Health Services Administration (SAMHSA) Treatment Improvement Protocol (TIP) 43, "regardless of the rate of withdrawal from methadone, a point usually is reached at which stead-state occupancy of opiate receptors is no longer complete and discomfort, often with drug hunger and craving, emerges. This point may occur at any dosage but is more common with methadone when the dosage is below 40 mg per day."
- **COWS assessment must be completed prior to every dose reduction, before taper is discontinued, and 72 hours after last dose has been administered**

Table 2. Example of Methadone Tapering Schedule

Example 50 mg/day		Example 100 mg/day		Example 150 mg/day		Example 200 mg/day	
Day 1	40 mg	Day 1	80 mg	Day 1	120 mg	Day 1	160 mg
Day 2	40 mg	Day 2	80 mg	Day 2	120 mg	Day 2	160 mg
Day 3	40 mg	Day 3	80 mg	Day 3	120 mg	Day 3	160 mg
Day 4	35 mg	Day 4	65 mg	Day 4	95 mg	Day 4	130 mg
Day 5	35 mg	Day 5	65 mg	Day 5	95 mg	Day 5	130 mg
Day 6	35 mg	Day 6	65 mg	Day 6	95 mg	Day 6	130 mg
Day 7	30 mg	Day 7	50 mg	Day 7	75 mg	Day 7	100 mg
Day 8	30 mg	Day 8	50 mg	Day 8	75 mg	Day 8	100 mg
Day 9	30 mg	Day 9	50 mg	Day 9	75 mg	Day 9	100 mg
Day 10	25 mg	Day 10	40 mg	Day 10	60 mg	Day 10	80 mg
Day 11	25 mg	Day 11	40 mg	Day 11	60 mg	Day 11	80 mg
Day 12	25 mg	Day 12	40 mg	Day 12	60 mg	Day 12	80 mg
Day 13	20 mg	Day 13	35 mg	Day 13	50 mg	Day 13	65 mg
Day 14	20 mg	Day 14	35 mg	Day 14	50 mg	Day 14	65 mg
Day 15	20 mg	Day 15	35 mg	Day 15	50 mg	Day 15	65 mg
Day 16	15 mg	Day 16	30 mg	Day 16	40 mg	Day 16	50 mg
Day 17	15 mg	Day 17	30 mg	Day 17	40 mg	Day 17	50 mg
Day 18	15 mg	Day 18	30 mg	Day 18	40 mg	Day 18	50 mg
Day 19	10 mg	Day 19	25 mg	Day 19	35 mg	Day 19	40 mg
Day 20	10 mg	Day 20	25 mg	Day 20	35 mg	Day 20	40 mg
Day 21	10 mg	Day 21	25 mg	Day 21	35 mg	Day 21	40 mg
Day 22	5 mg	Day 22	20 mg	Day 22	30 mg	Day 22	35 mg
Day 23	5 mg	Day 23	20 mg	Day 23	30 mg	Day 23	35 mg
Day 24	5 mg	Day 24	20 mg	Day 24	30 mg	Day 24	35 mg
Day 25	Discontinue	Day 25	15 mg	Day 25	25 mg	Day 25	30 mg
		Day 26	15 mg	Day 26	25 mg	Day 26	30 mg
		Day 27	15 mg	Day 27	25 mg	Day 27	30 mg
		Day 28	10 mg	Day 28	20 mg	Day 28	25 mg
		Day 29	10 mg	Day 29	20 mg	Day 29	25 mg
		Day 30	10 mg	Day 30	20 mg	Day 30	25 mg
		Day 31	5 mg	Day 31	15 mg	Day 31	20 mg
		Day 32	5 mg	Day 32	15 mg	Day 32	20 mg
		Day 33	5 mg	Day 33	15 mg	Day 33	20 mg
		Day 34	Discontinue	Day 34	10 mg	Day 34	15 mg
				Day 35	10 mg	Day 35	15 mg
				Day 36	10 mg	Day 36	15 mg
				Day 37	5 mg	Day 37	10 mg
				Day 38	5 mg	Day 38	10 mg
				Day 39	5 mg	Day 39	10 mg
				Day 40	Discontinue	Day 40	5 mg
						Day 41	5 mg
						Day 42	5 mg
						Day 43	Discontinue

*Round to the most appropriate tablet strength, 5 and 10 mg tablets available as floor stock at select units

Withdrawal Symptoms

A. Definition – clinical syndrome produced by discontinuation of an opioid drug from an opioid-dependent patient

B. Onset of symptoms – initial signs and symptoms may occur in a few hours or up to 48 hours after cessation or reduction in dosage of an opioid, depending upon the half-life of the drug concerned. Withdrawal of longer-acting opioids produces a withdrawal syndrome with a more delayed onset, milder severity and prolonged duration. Methadone withdrawal typically begins 36 to 48 hours after the last dose, peaks after about 3 days, and gradually subsides over a period of 3 weeks or longer depending on the dose and duration of use.

C. Symptoms
   1. Usually are self-limiting and generally non-life threatening, unless there is a concurrent serious medical condition
   2. Milder symptoms may include restlessness, mydriasis, lacrimation, rhinorrhea, sneezing, piloerection, yawning, perspiration, restless sleep and aggressive behavior
   3. More severe symptoms may include muscle spasms, back aches, abdominal cramps, hot and cold flashes, insomnia, nausea, vomiting, diarrhea, tachypnea, hypertension, hypotension, tachycardia, bradycardia and cardiac arrhythmias

D. Management
   1. Educate on signs and symptoms of withdrawal
   2. Monitor the following:
      a. Vital signs as clinically indicated
      b. Signs of dehydration, acute mental changes and aggravation of underlying cardiac disease
   3. Provide supportive care if needed
      a. Pain - ibuprofen, acetaminophen
      b. Nausea and vomiting - promethazine
      c. Diarrhea - loperamide
      d. Clonidine may be used to alleviate severe symptoms
         i. Usual Dose - 0.1 mg PO TID up to 0.3 mg PO TID (0.006 mg/kg/day in divided doses, maximum 1 mg/day). Severity of withdrawal symptoms and baseline blood pressure should be considered when initiating clonidine
         ii. Continue effective dose for 7 days, then taper and discontinue over the next 3 days
         iii. Vital signs should be checked before every administration of clonidine
            - Clonidine should be held if SBP <90mmHg, DBP <60mmHg, or PR< 50 bpm

Clinical Opiate Withdrawal Scale

The Clinical Opiate Withdrawal Scale (COWS) is an 11-item scale. This tool can be used in both inpatient and outpatient settings to rate common signs and symptoms of opiate withdrawal. The summed score for the complete scale can be used to help determine the stage or severity of opiate withdrawal and assess the level of physical dependence on opioids.

For each item, write in the number that best describes the patient's signs or symptoms.

Score:
- Mild = 5-12
- Moderate = 13-24
- Moderately severe = 25-36
- Severe ≥ 37

Patient Name: _____ Patient MRN #: _____
Current Vitals (BP, RR, HR):_____ Date:_____ Time:_____
Observer: _____

Signs & Symptoms	Score
Resting Pulse Rate: (record beats per minute) *Measured after patient is sitting or lying down for one minute* 0 = pulse rate 80 or below 1 = pulse rate 81–100 2 = pulse rate 101–120 4 = pulse rate greater than 120	
Sweating: over past ½ hour not accounted for by room temperature or patient activity 0 = no report of chills or flushing 1 = subjective report of chills or flushing 2 = flushed or observable moistness on face 3 = beads of sweat on brow or face 4 = sweat streaming off face	
Restlessness: observation during assessment 0 = able to sit still 1 = reports difficulty sitting still, but is able to do so 3 = frequent shifting or extraneous movement of legs/arms 5 = unable to sit still for more than a few seconds	
Pupil size 0 = pupils pinned or normal size for room light 1 = pupils possibly larger than normal for room light 2 = pupils moderately dilated 5 = pupils so dilated that only the rim of the iris is visible	
Bone or joint aches: if patient was having pain previously, only the additional component attributed to opiate withdrawal is scored 0 not present 1 mild/diffuse discomfort 2 patient reports severe diffuse aching of joints/muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	
Cont. next page	

COWS cont.

Signs & Symptoms	Score
Runny nose or tearing: not accounted for by cold symptoms or allergy 0 = none present 1 = nasal stuffiness or unusually moist eyes 2 = nose running or tearing 4 = nose constantly running or tears streaming down cheeks	
GI upset: over last ½ hour 0 = no GI symptoms 1 = stomach cramps 2 = nausea or loose stool 3 = vomiting or diarrhea 5 = multiple episodes of diarrhea or vomiting	
Tremor: observation of outstretched hands 0 = no tremor 1 = tremor can be felt, but not observed 2 = slight tremor observable 4 = gross tremor or muscle twitching	
Yawning: observation during assessment 0 = no yawning 1 = yawning once or twice during assessment 2 = yawning three or more times during assessment 4 = yawning several times/minute	
Anxiety or irritability 0 = none 1 = patient reports increasing irritability or anxiousness 2 = patient obviously irritable or anxious 4 = patient so irritable or anxious that participation in the assessment is difficult	
Gooseflesh skin 0 = skin is smooth 3 = piloerrection of skin can be felt or hairs standing up on arms 5 = prominent piloerrection	
Total Score	

*COWS adapted from National Institute on Drug Abuse. http://www.drugabuse.gov/nidamed-medical-health-professionals

CATHETER RESTORATION FOR HEMODIALYSIS PATIENTS

This protocol pertains to registered nurses who have received training and been validated in the procedure

The protocol does not replace sound clinical judgement nor is it intended to strictly apply to all patients.

1 Assessment of occlusion:
1. Rule out mechanical obstruction
2. Attempt to aspirate blood
3. Attempt to flush the catheter with 5-10 mL of normal saline (0.9% Sodium Chloride)

2 Is catheter occluded?

No → 3 Continue catheter use

Yes → 4 Notify provider and obtain order for Cathflo®.

Nurses: DMGs are guidelines to assist providers in ~~m~~ making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.

5 Explain procedure to patient.

6

PREPARATION OF CATHFLO® (ALTEPLASE, TPA) SOLUTION	
ACTION	NOTES
1. Wash hands thoroughly. Put on PPE.	Hand washing protects the patient and health care staff from cross contamination. PPE is worn for health care staff protection.
2. Aseptically withdraw 2.2 mL of Sterile Water for injection, USP.	Do **not** use Bacteriostatic Water for injection.
3. Inject the 2.2 mL of Sterile Water for injection into the Cathflo® vial. The diluent stream should be directed into the powder.	Slight foaming may occur.
4. Let the vial stand undisturbed until foaming dissipates.	Allows large bubbles to dissipate prior to administration.
5. Mix by gently swirling the vial until the contents are completely dissolved. Complete dissolution should occur within 3 minutes. **DO NOT SHAKE**.	The reconstituted solution is colorless to pale yellow transparent solution. The final concentration is 1mg/1mL. pH is approximately 7.3.
6. Inspect the reconstituted solution prior to administration for foreign matter or discoloration. If any seen, discard the vial. **DO NOT USE**.	Should be reconstituted immediately prior to use or used within 8 hours after being reconstituted and stored at 2-30 °C or 36-86 °F.
7. No other medications should be added to the solution containing Cathflo®	

7 Go to Page 2

Prepared by the Correctional Managed Care Pharmacy and Therapeutics Committee. January 2005. Reviewed 1/08, 01/11, 9/14, 1/19, 9/23.

8

INSTILLATION OF CATHFLO® (ALTEPLASE, TPA) SOLUTION		
ACTION		NOTES
1.	Inspect the reconstituted solution prior to administration for foreign matter or discoloration.	If any seen, discard the vial. **DO NOT USE**.
2.	Aseptically withdraw the reconstituted solution from the vial.	Dose to be determined by the provider. The usual dose is 2mg (2mL) for patients ≥ 30 kg.
3.	Wash hands thoroughly. Put on PPE.	Hand washing protects the patient and health care staff from cross contamination. PPE is worn for health care staff protection.
4.	Slowly instill the appropriate dose of Cathflo into the occluded catheter.	Excessive pressure should be avoided when instilled into the catheter, because excessive force could cause rupture of the catheter or expulsion of the clot into circulation.
5.	Assess catheter function by attempting to aspirate blood after 60 minutes of catheter dwell time. *If the catheter is functional, go to step 8 *If the catheter is <u>not</u> functional, go to step 6	Vigorous suction should not be applied during attempts to assess catheter function, because of the risk of damage or collapse.
6.	Wait an additional 60 minutes for a total of 120 minutes dwell time. Assess catheter function by attempting to aspirate blood. *If the catheter is functional, go to step 8 *If the catheter is <u>not</u> functional, go to step 7	
7.	A second dose of Cathflo® may be given upon the receipt of a provider order for a second dose if catheter function is not restored. Repeat the procedure beginning with Step 1 under PREPARATION OF CATHFLO® (ALTEPLASE, TPA) SOLUTION in box 6 on page 1.	An order <u>must</u> be obtained from the provider to administer a second dose.
8.	If successful, remove 4 to 5 mL of blood with a syringe to remove Cathflo® and residual clot. Then gently flush the catheter with 10 to 12 mL of normal saline (0.9% Sodium Chloride).	
9.	Discard any unused Cathflo® solution.	
10.	Document administration in the patient medial record.	Documentation should include drug, dose, route, time administered, patient response, & signature and title of person administering the drug.

9

Catheter function restored?

Yes → Resume catheter use

10

No → Provider should be notified and a decision made regarding catheter viability. Referral of patient to a higher level of care should be considered.

11

Health Care Personnel Education

A. Types of catheter occlusions
   1. Intraluminal occlusion – Occlusion occurs within the catheter lumen
   2. Fibrin sheath occlusion – Occlusion occurs as a layer around the outside of the catheter
   3. Fibrin tail occlusion – Occlusion occurs over the tip of the catheter
   4. Mural occlusion – Occlusion occurs as an extension from the wall of the blood vessel to the catheter

B. Contributing factors – The changes listed below lead to vasoconstriction, platelet aggregation, and activation of the clotting cascade resulting in thrombus formation.
   1. Changes in blood flow – venous stasis
   2. Changes in coagulability
   3. Changes in vessel wall – trauma to the vessel

C. Signs & symptoms of thrombotic occlusion
   1. May develop without symptoms
   2. Sluggish flow may be seen as thrombus develops
   3. Pump alarms may sound frequently as thrombus progresses
   4. It may be possible to infuse fluid in some instances, but fluid withdrawal is impaired

D. Rationale for fibrinolytic therapy - Low dose fibrinolysis with alteplase can lyse clot and re-establish flow in occluded catheter resulting in catheter salvage. Catheter salvage is preferred over replacement for the following reasons:
   1. Limit interruption of hemodialysis
   2. Reduce risk of trauma and complication to patient
   3. Preserve site for future access
   4. Reduce cost (e.g., avoid transportation cost & hospitalization)

E. Treatment Goals
   1. Re-establish flow in catheter
   2. Resume hemodialysis
   3. Avoid catheter replacement

F. Treatment – Cathflo® (Alteplase, TPA)
   1. Availability – 2mg single dose vial
   2. Storage - Refrigerate vial (2-8 °C, 36-46 ° F) and protect from light
   3. Stability of reconstituted solution – Reconstituted solution must be used within 8 hours if stored at 2-30 °C or 36-86 °F. Any unused solution should be discarded.
   4. Usual Dose is 2mg (2mL) for patients ≥ 30 kg. A second dose may be given after 120 minutes if catheter function is not restored.
   5. Adverse Effects
      a. Infection (e.g., sepsis)
      b. Bleeding (e.g., from site, gastrointestinal)
      c. Venous thrombosis
      d. Allergic reactions have not been reported. If occurs, notify provider and manage appropriately.

CHEST PAIN, ACUTE

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients

1

Patient Presents to Medical Department with Chest Pain

2

Clinical Assessment

A focused cardiovascular examination including characteristics and duration of symptoms as well as cardiovascular risk factors should be performed initially to aid in the diagnosis of acute coronary syndrome (ACS) or other potentially serious causes of chest pain (e.g., aortic dissection, aneurysm, pericarditis, pneumonia, pneumothorax, or pulmonary embolism)

- Clinical characteristics with a higher likelihood for suspicion of ACS include:
  - 2 or more cardiac risk factors*
  - Chest pain that is substernal, radiates, squeezes, poorly localized or described as uncomfortable pressure
  - Nausea, shortness of breath, diaphoresis, dizziness, syncope, or palpitations
  - If patient has diabetes mellitus, is elderly, or female, observe for nausea or mid-epigastric discomfort, as chest pain may be masked or sharp/stabbing in nature

3

- Obtain an EKG
- NTG SL up to 3 doses as tolerated by blood pressure if necessary
- Chew aspirin 325 mg
- Administer oxygen if O_2 sat < 92%
- Obtain initial troponin level
- Consider serial EKGs (q 15-30 minutes for 1 hour) if high suspicion of ACS.

***Cardiac Risk Factors:**

- Prior coronary intervention (i.e., PCI, stent, CABG, etc.)
- Family history premature of CHD (first degree male relative < 55 or female relative < 65)
- Age ≥ 45 males, 55 females
- HTN ≥ 140/90 mmHg or on antihypertensive medication
- Smoker within the last 2 years
- Hyperlipidemia or on statin medication
- History of diabetes
- BMI > 30

4

EKG abnormal?

Yes

No

5

STEMI

- New ST elevation or left bundle branch block

UA / NSTEMI

- New ST depression, QT changes, significant Q-waves, inverted T-wave, or changes from previous EKGs

or

- NTG SL x 3 ineffective

or

- Positive Troponin

6

Low-/Intermediate-risk ACS

If patient has CHD OR ≥ 2 cardiac risk factors*

- Repeat EKG in 2 hours
- Maintain in observation for at least 6 hours
- Repeat troponin level in 3 hours & in 6-12 hours if EKG changes or presentation confers ACS suspicion.

If < 2 cardiac risk factors & atypical presentation of chest pain that is not suspected to be cardiac in origin, ascertain & treat etiology

8

Changes in cardiac parameters?

Yes

No

7

Transfer to nearest Emergency Room

- Call 911 and follow unit protocol. *For UTMB, if ambulance is not immediately available call 911.*
- Start normal saline IV infusion
- Consider morphine sulfate IV if pain is not relieved after 3 doses of NTG SL.

9

Discharge from Medical Department. Follow up next morning with provider with instructions to return as needed for chest pain.

ACS: Acute Coronary Syndrome; PCI: Percutaneous Coronary Intervention; CABG: Coronary Artery Bypass Graft; CHD: Coronary Heart Disease; HTN: Hypertension; EKG: Electrocardiogram; NTG: Nitroglycerin; SL: Sublingual; STEMI: ST-Elevation Myocardial Infarction; NSTEMI: Non-ST-Elevation Myocardial Infarction; UA: Unstable Angina

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider**.

Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee. Approved February 2001; Reviewed 11/02, 1/07, 1/15; Revised 4/03, 3/08, 5/11, 7/11, 1/19, 1/24.

CHECKLIST FOR SECONDARY PREVENTION OF CHRONIC CORONARY DISEASE

Chronic Coronary Disease (CCD) definition includes the following patients below in an outpatient setting:

- Discharged after admission for an acute coronary syndrome (ACS)* or coronary revascularization procedure and after stabilization of all acute cardiovascular issues
- Left ventricular systolic dysfunction and known or suspected coronary artery disease (CAD)** or those with established cardiomyopathy
- Stable angina symptoms medically managed
    - If patient's CCD risk is solely stable angina, please refer to Chronic Stable Angina disease management guideline (DMG)
- Patients with angina symptoms and evidence of coronary vasospasm or microvascular angina
- Diagnosed with CCD based on results of screening study (stress test, coronary computed tomography angiography [CTA]) and treating clinician concludes patient has coronary disease

The treatment of a patient whose only manifestation of cardiovascular risk is diabetes (DM) is not covered by this guideline. Please refer to the DM DMG.

*ACS is defined an event where blood supplied to the heart muscle is suddenly blocked, such as a heart attack/myocardial infarction (MI), non-ST segment elevation myocardial infarction (NSTEMI), ST segment elevation myocardial infarction (STEMI), or unstable angina

**CAD is defined as the narrowing of the coronary arteries, due to plaque buildup, limiting blood flow to the heart

LIFESTYLE MODIFICATIONS	
ACHIEVED?	GOAL
☐ Yes ☐ No	Smoking cessation achieved?
☐ Yes ☐ No	Weight management achieved? • Body mass index (BMI): 18.5 to 24.9 kg/m2 • Waist circumference: < 40 inches in men < 35 inches in women
☐ Yes ☐ No	Physical activity achieved? • Minimum 150 minutes per week of moderate intensity exercise or 75 minutes per week of high intensity exercise
☐ Yes ☐ No	Diet for health initiated (or other diet as clinically indicated)? • Limit consumption of carbohydrates, salt, and fat • Emphasize vegetables, fruits, legumes, nuts, whole grains • Avoid baked goods and fried foods
☐ Yes ☐ No	Dental evaluation annually?
☐ Yes ☐ No	Nutrition supplements reviewed? • The following nutrition supplements are NOT beneficial in reducing risk of acute events: nonprescription or dietary supplements such as omega-3 fatty acid, vitamin C, D, E, beta-carotene, and calcium, is not beneficial to reduce risk of acute events

The protocol does not replace sound clinical judgment nor is it intended to strictly apply to all patients.

Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee, Approved May 2008.
Revised 9/09, 05/12, 05/16, 1/19, 7/24

CHECKLIST FOR SECONDARY PREVENTION OF CHRONIC CORONARY DISEASE

PATIENTS WITH HISTORY OF PCI or ACS EVENT

ACHIEVED?	GOAL

☐ Yes ☐ No	Antiplatelet therapy initiated?
	• No percutaneous coronary intervention (PCI) or > 12 months from ACS:
	  • Utilize monotherapy with low-dose aspirin (ASA) long term. May utilize clopidogrel if ASA is contraindicated.
	• Recent ACS event with or without PCI:
	  • Utilize dual antiplatelet therapy (DAPT) consisting of ASA AND clopidogrel for at least 12 months
	  • In consultation with Cardiology and as clinically appropriate, for long term treatment de-escalate to single antiplatelet therapy (SAPT) of either ASA OR clopidogrel
	• Recent elective PCI without ACS:
	  • Determination of bleeding and ischemic risk should be done in consultation with Cardiology.
	  • Low-moderate risk bleeding or ischemic risk with a drug eluting stent (DES): utilize DAPT (ASA AND clopidogrel) for 6 months, then de-escalate to SAPT (ASA OR clopidogrel) for long term
	  • High risk bleeding with a DES: utilize DAPT for 1-3 months, then de-escalate to clopidogrel monotherapy for 9 months, then de-escalate to SAPT (ASA OR clopidogrel) for long term
	• Continuation of DAPT longer than the recommended duration should be done in consultation with Cardiology

☐ Yes ☐ No	Oral Anticoagulation (OAC) medication reviewed?
	• Ensure patient has an appropriate indication for oral anticoagulant (e.g., atrial fibrillation and/or venous thromboembolism [VTE])
	• Recent PCI and on a direct-acting oral anticoagulant (DOAC):
	  • Utilize triple therapy which includes DOAC, ASA, and clopidogrel for ≤ 1 month after PCI
	  • In consultation with Cardiology and as clinically appropriate, then de-escalate to DOAC and clopidogrel for up to 6 months. Then, de-escalate to DOAC monotherapy long term
	  • Continuation or adjustment of clopidogrel or ASA therapy from the recommended duration should done in consultation with Cardiology
	• No PCI and on a DOAC: utilize DOAC monotherapy long term
	• If patient is concurrently on warfarin and DAPT, please consult Cardiology for duration
	Note: Formulary DOAC = rivaroxaban

<u>Note the contraindications below if other P2Y12 inhibitors other than clopidogrel are prescribed:</u>

- Prasugrel should not be used if CCD patient had previous stroke, transient ischemic attack (TIA), or intracerebral hemorrhage (ICH) due to significant or fatal bleeding.
- Ticagrelor should not be used if CCD patient has increased risk for bradycardic events. Concurrent aspirin maintenance dose should not exceed 100 mg/day.

CHECKLIST FOR SECONDARY PREVENTION OF CHRONIC CORONARY DISEASE

OTHER DISEASE STATE AND MEDICATION MANAGEMENT

ACHIEVED?	GOAL

☐ Yes ☐ No	Blood pressure (BP) goal achieved?
	• < 130/80 mm Hg
	• Refer to hypertension (HTN) disease management guideline (DMG) for therapy recommendations to control BP
	• Betablockers (BB), specifically metoprolol SUCCINATE or carvedilol is recommended long term for those with CCD and left ventricular ejection fraction (LVEF) < 50% .
	  • If initiated on beta blocker therapy for previous MI without a history of current LVEF ≤50%, angina, arrhythmias, uncontrolled HTN, or other primary indication, it may be reasonable to reassess the indication for long-term (>1 year) use of beta-blocker therapy for reducing major adverse cardiovascular events (MACE).
	  • Without previous MI or LVEF ≤50%, the use of beta-blocker therapy is not beneficial in reducing MACE, in the absence of another primary indication.
	• Angiotensin-converting enzyme inhibitor (ACEI) long term is recommended for CCD patients who also have HTN, DM, LVEF ≤ 40%, or chronic kidney disease (CKD)
	  • For ACEI allergy, consider submitting a non-formulary (NF) request for angiotensin receptor blocker (ARB)
	  • Without HTN, DM, or CKD and LVEF >40%, the use of ACEI or ARBs may be considered to reduce cardiovascular (CV) events

☐ Yes ☐ No	Lipid goal achieved? • Refer to the hyperlipidemia (HLD) DMG for therapy recommendations • LDL ≥ 50% reduction to reduce MACE • There is no benefit in reducing cardiovascular risk when adding fenofibrate, dietary supplement such as omega-3 fatty acids, or niacin for CCD patients
☐ Yes ☐ No	Diabetes (DM) goal achieved? • Refer to the DM DMG for therapy recommendations to control diabetes • A1C < 7%, consider a less stringent goal < 8% based on patient specific factors • Initiate sodium-glucose transport protein inhibitor (SGLT2 inhibitor) to reduce risk of MACE
☐ Yes ☐ No	Exhibiting heart failure symptoms or is diagnosed with heart failure (HF)? • Please refer to the HF DMG for therapy recommendations to control symptoms • Initiate SGLT2 inhibitor to reduce risk of CV death and HF hospitalization.
☐ Yes ☐ No	Nonsteroidal anti-inflammatory drug (NSAID) use reviewed? • NSAIDs should not be used due to increased cardiovascular and bleeding complications
☐ Yes ☐ No	Vaccines reviewed? • Encourage influenza vaccine annually (unless contraindicated) • Encourage COVID-19 vaccine per Infection Control Policy B-14.52 (unless contraindicated) • Encourage pneumococcal vaccine per Infection Control Policy B-14.07 (unless contraindicated)

Chronic Stable Angina

1

Meets criteria for Chronic Stable Angina?
[Angina that is not unstable and that has a new onset of >2 months ago, does not occur at rest, and has not distinctly changed in frequency, duration, or threshold within the last 2 months.]
Consider cardiology referral if not previously evaluated by cardiology.

No → 2 See Chest Pain, Acute Pathway

Yes ↓

3 Sublingual NTG effective?

No → 4 See Chest Pain, Acute Pathway

Yes ↓

5 Serious contraindication to Beta-Blocker?

No → 6 Start a Beta Blocker (BB) (e.g., metoprolol succinate, atenolol, propranolol, or carvedilol) and ASA EC 81-325 mg daily. Titrate BB to maximum tolerated dose. If patient remains symptomatic go to box 9.

Yes ↓

7 History of Vasospastic Angina?

Yes → 8 Start Calcium Channel Blocker (CCB) - preferably a non-dihydropyridine (DHP) CCB (e.g., diltiazem, verapamil), if no contraindications present, & ASA EC 81-325 mg daily. Titrate Non-DHP CCB to maximum tolerated dose. If patient continues to be symptomatic, add Long-Acting Nitrate therapy. Go to box 10.

No ↓

9 Allergy to Calcium Channel Blocker?

No → 11 Start Dihydropyridine Calcium Channel Blocker (CCB) – (e.g., amlodipine) and ASA 81-325mg daily. Titrate CCB to maximum tolerated dose.

Yes ↓

10 Start Isosorbide Mononitrate ER 30-60 mg daily and ASA 81-325 mg daily. Titrate per symptoms up to maximum 240mg/day.

11 ↓

12 Still experiencing intermittent chest pain relieved with SL NTG?

Yes → 10

No → 13 Refer to Checklist for Secondary Prevention of Coronary Artery Disease DMG to ensure risk reduction measures are being followed. Aggressively treat the underlying disease.

13 ↓

14 Patient remains symptomatic?

Yes → 16 Refer to Checklist for Secondary Prevention of Coronary Artery Disease DMG to ensure risk reduction measures are being followed. Aggressively treat the underlying disease.

16 → 17 Continue therapy. Initial follow up in 30 days, then 90 days if chest pain is stable. Follow-up at least semi-annually thereafter.

No ↓

15 Consider Cardiology Consult

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

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Prepared by the Correctional Managed Care Pharmacy and Therapeutics Committee. Approved February 2001; Reviewed 11/02, 1/08 Revised 4/03, 9/09, 7/11, 1/15, 1/19, 1/24.

Healthcare Provider Education

Definition of chronic stable angina

A clinical syndrome characterized by discomfort in the chest, jaw, shoulder, back, or arms, typically aggravated by exertion or emotional stress and relieved by rest or nitroglycerin.

Goals of Treatment:

- Relief of symptoms
- Prevention or slowing of disease progression
- Prevention of future cardiac events, i.e., myocardial infarction, unstable angina, need for revascularization
- Improvement in survival

Mainstay of therapy in symptomatic treatment:

- Short acting nitroglycerin – 1st line therapy
- Beta Blockers– 2nd line therapy
    - Cardioselective:
        - Atenolol initiated at 50 mg/day; increase dose as tolerated to desired effect; usual dosage range: 50 to 100 mg/daily
        - Metoprolol succinate initiated at 50 mg/day; increase dose as tolerated to desired effect; usual dosage range: 100 to 200 mg/day
    - Non-Cardioselective:
        - Carvedilol initiated at 6.25 mg BID; increase dose as tolerated to desired effect; usual dosage range: 25 to 50 mg twice daily
        - Propranolol initiated at 80 mg/day in 1 to 4 divided doses; increase dose as tolerated to desired effect; usual dosage range : 80 to 320 mg/day in 1 to 4 divided doses
- Calcium Channel Blockers (CCB) – 3rd line if BBs are not tolerated, contraindicated, or if symptoms are not alleviated with BBs alone.
  Verapamil and diltiazem should not be used in combination with beta-blockers (see drug interaction alert).
    -Diltiazem XR 180-360 mg/day (Non-dihydropyridine CCB)
    -Verapamil 240-480 mg/day in 3-4 divided doses (Non-dihydropyridine CCB)
    -Amlodipine 5-10 mg/day (Dihydropyridine CCB)
- Long-acting nitroglycerin – 4th line agent if BB's and/or CCB's are not tolerated, contraindicated, or if symptoms are not alleviated with BB's and/or CCB's.
    - Isosorbide Mononitrate ER 30-240 mg/day
- Ranolazine – 4th line agent for patients with stable ischemic heart disease; should be used in combination with other established anti-anginal medications titrated up to appropriate doses such as amlodipine, beta-blockers or nitrates; preferably, should only be recommended by a cardiologist (see other educational information below).

Note: Three anti-anginal drugs (excluding short acting NTG) may ~~actually~~ provide less symptomatic protection than two drugs. Thus, the dose of one drug should be optimized before adding another one, and it is advisable to switch drug combinations before attempting a three-drug regimen.

Drug interaction alert:
Concomitant use of non-dihydropyridine calcium channel blockers with beta-blockers can possibly potentiate hypotension, bradycardia, heart failure, and conduction abnormalities. These effects are most prevalent in patients with impaired left ventricular function, cardiac arrhythmias, or aortic stenosis.

Contraindications:

•Beta-blockers
- Sinus bradycardia (HR < 50 bpm)
- Second- or third-degree heart block
- Overt cardiac failure
- Hypersensitivity to BB's

- Calcium Channel Blockers
    - Sick sinus syndrome (Non-dihydropyridine)
    - Second- or third-degree heart block (Non-dihydropyridine)
    - Hypotension (systolic <90mmHg)
    - Hypersensitivity to CCB's
    - ❖ Diltiazem: acute MI or pulmonary congestion
    - ❖ Verapamil: severe left ventricular dysfunction, cardiogenic shock, atrial flutter or fibrillation
    - ❖ Amlodipine: caution in aortic stenosis, hypertrophic cardiomyopathy
- Aspirin
    - Hypersensitivity to NSAIDs
    - Syndrome of asthma, rhinitis, and nasal polyps
    - Inherited or acquired bleeding disorders

Counseling on the use of nitrates:

- Patients should be counseled to come to medical if chest pain or discomfort is unimproved or worsening five minutes after one nitroglycerin dose has been taken.
- If the sublingual nitroglycerin (NTG) is potent, a slight tingling sensation should be felt under the tongue. Tablets that crumble easily should not be used. The sublingual mucosa should be moist for adequate dissolution and absorption of the tablet. A drink of water in patients with dry sublingual mucosa prior to ingestion of the tablet may be necessary.
- NTG tablets are both heat and light sensitive. They should therefore be stored in a tightly capped dark bottle. The prescription should be renewed every three to six months.
- Warn patients about the potential of hypotension when first taking the nitrate and the potential for headaches and flushing.
- NTG can be used for prophylaxis of predictable episodes of angina in response to exertion.
- Isosorbide mononitrate ER should be dosed once a day in the morning, which will allow for a nitrate withdrawal period and prevent tolerance from occurring. Extended-release tablets should not be crushed or chewed.

Mainstay of therapy to improve prognosis in patients with stable angina (please refer to the Checklist for Secondary Prevention of Coronary Artery Disease Management Guideline):

- Aspirin 81-325mg for all patients
- Beta-blockers or Calcium Channel Blocker
- Statins for all patients to achieve target LDL <100 mg/dl, <70 mg/dl for high-risk patients
- Angiotensin Converting Enzyme (ACEI) Inhibitor (see below)

Role of ACEI per 2023 Chronic Coronary Disease ACC/AHA guidelines:

- *ACE inhibitors are recommended for patients with chronic stable angina and a history of myocardial infarction, left ventricular ejection fraction (LVEF) ≤ 40%, hypertension, diabetes, or chronic kidney disease.

*May consider use of non-formulary preferred angiotensin II receptor blocker losartan for those intolerant to formulary lisinopril.

Role of SGLT2 inhibitors per 2023 Chronic Coronary Disease* ACC/AHA guidelines:

- In patients with CCD and type 2 diabetes, use of a SGLT2 inhibitor is recommended to reduce the risk of major adverse cardiovascular events.
- In patients with CCD and heart failure with LVEF ≤40%, use of an SGLT2 inhibitor is recommended to reduce the risk of cardiovascular death and heart failure hospitalization and to improve quality of life, irrespective of diabetes status.

*Definition Chronic Coronary Disease (CCD): CCD encompasses patients with or without angina, a history of coronary revascularization, and previous acute coronary syndrome.

Ranolazine Healthcare Provider Education

- Ranolazine is an anti-angina medication that was recently included in the current stable ischemic heart disease guideline.
- The proposed ranolazine mechanism of action is the inhibition of pathologic increases in late Na^+ current induced during myocardial ischemia. Because of Na^+/Ca^{2+} coupling, this would be expected to reduce ischemia-induced calcium overload, resulting in more normal diastolic relaxation and decreased wall tension. Improved diastolic function decreases oxygen demand and increases coronary blood supply.
- Ranolazine is approved for treatment of patients with chronic angina who have not achieved an adequate response with other antianginal drugs.
- Dosing is 500 mg PO BID initially; may increase to 1,000 mg PO BID, if needed.
- Place in therapy: 4^{th} line agent for patients with stable ischemic heart disease; should be used in combination with other established anti-anginal medications such as amlodipine, beta-blockers or nitrates.
- Due to the risk of QTc prolongation, it should not be used with medications that have high QTc prolongation risk. Preferably, ranolazine should only be recommended by a cardiologist.

CHECKLIST FOR NON-DIALYSIS DEPENDENT CHRONIC KIDNEY DISEASE*

The protocol does not replace sound clinical judgment nor is it intended to strictly apply to all patients.

DISEASE STATE MANAGEMENT	
ACHIEVED?	GOAL
☐ Yes ☐ No	Blood pressure at goal? • < 130/80 mmHg • Consider a systolic blood pressure (SBP) target of < 120 mmHG if tolerable, in CKD stage 1-3 patients who are non-diabetic, aged 50-90 years, and have proteinuria (< 1 g/day) • In CKD stages 4-5, loop diuretics are preferred over thiazide diuretics • Avoid other medications that can cause hyperkalemia if possible (NSAIDs, potassium supplements, potassium-sparing diuretics) • Consider Nephrology Referral if BP is uncontrolled on 3 medications including a diuretic, serum creatinine is abnormal, or potassium is < 3 mEq/L If not, refer to Hypertension algorithm
☐ Yes ☐ No	Lipids already evaluated with the Hyperlipidemia algorithm? • Consider moderate to high intensity statin • Determine which statin to use based on patient's 10-year ASCVD risk If not, refer to Hyperlipidemia algorithm
☐ Yes ☐ No	Diabetes goal achieved? • HgbA1c ~7.0% • Recommend not treating to an HgbA1c target of < 7.0% in patients at risk of hypoglycemia • Insulin and medication clearance is decreased in CKD. Closely monitor blood glucose levels and for symptoms of hypoglycemia • Use caution and/or discontinue metformin in CKD stages 3 - 5 If not, refer to Diabetes algorithm
SECONDARY COMPLICATIONS	
PRESENT?	
☐ Yes ☐ No	Proteinuria • Albumin/creatinine ratio ≥ 3,000 mcg/mmol or 30 mg/g • Spot urine protein/spot urine creatinine < 0.5, repeat in 4-6 weeks. > 0.5 check for HIV, HCV, ANA, C3 and C4 levels, and renal ultrasound. • Consider Nephrology Referral if proteinuria is persistent after 4-6 weeks (≥ 2 positive quantitative tests temporally spaced by 1-2 weeks). Expedite referral if associated with significant hematuria or increased serum creatinine. If present, initiate lisinopril
☐ Yes ☐ No	Metabolic acidosis • Defined as CO_2 levels below 22 mmol/L. Goal CO_2 range is 23-29 mmol/L If present, treat with oral bicarbonate solution
☐ Yes ☐ No	Hyperphosphatemia • Defined as phosphate levels > 4.5 mg/dL. Goal phosphate range is 2.5-4.5 mg/dL • Base therapeutic decisions on trends rather than single values If present, counsel on dietary modifications

Nurses: DMGs re guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.**

Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee, Approved November 2021.

SECONDARY COMPLICATIONS continued	
PRESENT?	
☐ Yes ☐ No	Hypocalcemia • Calcium < 8.4 mg/dL If present, treat with calcium supplementation
☐ Yes ☐ No	Hyperkalemia • Potassium 5.2 - 6.0 mEq/L • Discontinue any medications that may be contributing to the increased potassium after assessing risk vs benefit If present, initiate Nephrology Referral • Administer kayexalate 30 gm with lactulose 15 mL and recheck potassium level next day • Potassium > 6.0 mEq/L: call UR for direct admit
☐ Yes ☐ No	Hypokalemia • Potassium < 3.0 mEq/L despite replacement If present, initiate Nephrology Referral
☐ Yes ☐ No	Hyperparathyroidism • Patients with levels of intact PTH above the upper normal limit of the assay (>100) should be evaluated for hyperphosphatemia and hypocalcemia If present, consider calcium supplementation and calcitriol
☐ Yes ☐ No	Anemia • Hemoglobin (Hgb) < 10.0 g/dL with anemia-related symptoms If present, refer to Anemia in non-dialysis CKD algorithm
☐ Yes ☐ No	GFR decline • Rate of decline should be estimated by comparing past GFR levels with current GFR level and ascertaining risk factors If present, consider lisinopril 2.5-40mg/day • **Consider referral to nephrology for the following:** abrupt sustained fall in GFR (> 30% from baseline within 4 weeks), GFR < 25 mL/min/1.73m^2, significant findings of albuminuria and hematuria despite optimum risk stratification, progression of CKD (drop in GFR category and/or a 25% or greater drop from baseline in one year), CKD and HTN refractory to treatment with 3 or more antihypertensive agents, and persistently abnormal serum potassium
☐ Yes ☐ No	Acute increase in serum creatinine • Increase of ≥ 30% from baseline If present, expedite Nephrology Referral • Discontinue new or nephrotoxic medications after assessing risk vs benefits. Recheck in 1-2 days.

*Patients covered by this guideline include those with established non-dialysis dependent chronic kidney disease.

I. Definition of chronic kidney disease (CKD)

A. Abnormalities of kidney structure or function, present for > 3 months, with implications for health.
   1. Classified based on cause, glomerular filtration rate (GFR) category, and albuminuria category

Table 1. GFR Categories in CKD

GFR Category	GFR (ml/min/1.73m^2)	Terms
G1	> 90	Normal or high
G2	60 – 89	Mildly decreased
G3a	45 – 59	Mildly to moderately decreased
G3b	30 – 44	Moderately to severely decreased
G4	15 – 29	Severely decreased
G5	< 15	Kidney failure

Note: In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

Table 2. Albuminuria Categories in CKD

Category	AER (mg/24 hours)	ACR (mg/mmol)	Terms
A1	< 30	< 3	Normal to mildly increased
A2	30 – 100	3 – 30	Moderately increased
A3	> 300	> 30	Severely increased*

AER = albumin excretion rate; ACR = albumin-to-creatinine ratio
*Including nephrotic syndrome (albumin excretion usually > 220 mg/24 hours)

   2. Criteria for CKD is met when either of the following are present for > 3 months
      a. Decreased GFR: GFR < 60 mL/min/1.73m^2
      b. Markers of kidney damage (one or more):
         i. Albuminuria (AER $\geq$ 30 mg/24 hours, ACR $\geq$ 3 mg/mmol)
         ii. Urine sediment abnormalities
         iii. Electrolyte and other abnormalities due to tubular disorders
         iv. Abnormalities detected by histology
         v. Structural abnormalities detected by imaging
         vi. History of kidney transplantation

II. Risk factors for CKD

A. Diabetes
B. Hypertension
C. Autoimmune diseases
D. Systemic infections
E. Urinary stones
F. Lower urinary tract obstruction
G. Neoplasia
H. Family history of CKD
I. Recovery from acute kidney failure
J. Reduction in kidney mass
K. Exposure to certain drugs
L. Low birth weight
M. Older age
N. US ethnic minorities: African American, American Indian, Hispanic, Asian, or Pacific Islander
O. Exposure to certain chemical and environmental conditions

III. Secondary complications

A. Metabolic acidosis
1. Commonly occurs when GFR declines to less than 40-50 mL/min
2. Chronic metabolic acidosis is also associated with increase protein catabolism, uremic bone disease, muscle wasting, chronic inflammation, impaired glucose homeostasis, and impaired cardiac function
3. Goal: CO_2 23 – 29 mmol/L
4. Recommended drug treatment options:
   a. Bicitra® oral solution 15 mL up to TID (nonformulary)
   b. Sodium bicarbonate 650 mg tablets up to TID (nonformulary)
5. Recommend close monitoring of $C0_2$ levels while receiving treatment for evaluation of treatment continuation.

B. Hyperphosphatemia
1. Base therapeutic decisions on trends rather than one single value
2. Patients with GFR < 60 mL/min/1.73 m^2 should be evaluated for bone disease and calcium and phosphorous metabolism disorders
3. Evaluate individual values of serum calcium and phosphorus together rather than using the calcium-phosphorus product equation.
4. Counsel the patient on limiting dietary phosphate consumption. Sources of phosphorus in the diet include meats, dairy products, dark sodas (Coke, Dr. Pepper), and common snacks such as power bars, and some trail mixes (see "Renal Diet" handout on Clinical Education Department homepage)
5. Recommended drug treatment options:
   a. Calcium carbonate 500 mg TID with meals
   b. Alternative: Calcium carbonate/ vitamin D 600 mg/400 IU BID with meals
6. In patients with persistent hypercalcemia (> 10.2 mg/dL), consider reducing and/or discontinuing calcium and/or calcitriol or switching patients to a non-calcium-based binder such as sevelamer (Renvela®)
   a. Sevelamer 800 – 1600 mg TID 10 – 15 minutes prior to meals (nonformulary)

C. Hypocalcemia
1. Patients with GFR < 60 mL/min/1.73 m^2 should be evaluated for bone disease and calcium and phosphorous metabolism disorders
2. For patients with calcium (Ca) below < 8.4 mg/dL, calcium supplementation is warranted and should be treated to bring levels into range
3. Recommended drug treatment options:
   a. Calcium carbonate 500 mg TID with meals
   b. Calcitriol 0.25 mcg daily

D. Hyperparathyroidism
1. Patients with GFR < 60 mL/min/1.73 m^2 should be evaluated for bone disease and calcium and phosphorous metabolism disorders
2. Patients with levels of intact PTH above the upper normal limit of the assay (>100) should be evaluated for hyperphosphatemia and hypocalcemia
3. Patient should be counseled on dietary phosphate reduction (see "Renal Diet" handout on Clinical Education Department homepage)
4. Calcium supplements may be used to correct underlying hyperphosphatemia or hypocalcemia
5. Dose adjustments should be made when iPTH falls below target range, serum levels of corrected total Ca > 9.5, or serum PO4 > 4.6
6. Calcitriol and calcium supplements may be used as combination therapy. Monitor for hypercalcemia.
7. Check Vitamin D levels in patients with elevated PTH and normal Phosphorus and Calcium levels. Refer the patient to Nephrology if patient has low Vitamin D levels.

E. Anemia
1. Patients with GFR < 60 mL/min/1.73 m^2 should be evaluated for anemia
2. Diagnose anemia in adults with CKD when the Hgb concentration is < 13.0 g/dL (< 130 g/L) in males and < 12.0 g/dL (< 120 g/L) in females. Treatment should be considered when Hgb < 10 g/dL and anemia-related symptoms are present.
3. For CKD patients without anemia, measure Hgb concentration when clinically indicated and at least annually in patients with CKD Stage 3 and at least twice per year in patients with CKD stages 4 - 5 and not receiving dialysis
4. For CKD patients with anemia not being treated with an ESA, measure Hgb concentration when clinically indicated and at least every 3 months in patients with CKD stages 3 - 5 and not receiving dialysis.
5. In patients with CKD and anemia (regardless of age and CKD stage), include the following tests in initial evaluation of the anemia:
   a. Complete blood count (CBC), which should include Hgb concentration, red cell indices, white blood cell count and differential, and platelet count
   b. Serum ferritin level
   c. Serum transferrin saturation (TSAT)
   d. Serum vitamin B12 and folate levels
6. Recommended drug treatment options:
   a. Ferrous sulfate 325mg PO TID x 3 months
   b. Epoetin alfa 5,000 – 10,000 units SUBQ weekly (nonformulary)
   c. R**efer to the "Anemia in Non-Dialysis Dependent Chronic Kidney Disease" algorithm for specifics**.

F. GFR decline
1. The rate of GFR decline should be estimated by comparing past and current GFR levels and ascertaining risk factors for faster vs. slower decline including type of kidney disease and non-modifiable and modifiable risk factors
2. Measurements of serum creatinine for estimation of GFR should be obtained at least quarterly in patients with chronic kidney disease
3. Causes of acute decline include the following:
   a. Volume depletion
   b. Intravenous radiographic contrast
   c. Selected antimicrobial agents (e.g., aminoglycosides and amphotericin B)
   d. NSAIDs including cyclo-oxygenase type 2 inhibitors (e.g., ibuprofen, naproxen, celecoxib)
   e. ACE inhibitors or ARBs (e.g., lisinopril, losartan)
   f. Cyclosporine and tacrolimus
   g. Obstruction of the urinary tract
4. Factors that have been shown to slow decline include:
   a. Strict blood glucose control in diabetes
   b. Strict blood pressure control
   c. ACE inhibitors or ARBs
5. Recommended drug treatment: lisinopril 2.5 – 40 mg/day in divided doses
6. **Consider referral to nephrology in the following circumstances:**
   a. Abrupt sustained fall in GFR (>30% from baseline within 4 Weeks)
   b. GFR < 25 mL/min/1.73m^2
   c. Significant findings of albuminuria and hematuria despite optimum risk stratification
   d. Progression of CKD (drop in GFR category and/or a 25% or greater drop from baseline in one year)
   e. CKD and HTN refractory to treatment with 3 or more antihypertensive agents
   f. Persistent abnormalities of serum potassium

ACUTE COPD EXACERBATION

A.

Signs and symptoms of acute exacerbation:
- Increased breathlessness
- Increased cough
- Increased sputum production
- Change of sputum color and/or tenacity
- Tachypnea
- Wheezing
- Chest tightness

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients

1 Patient presents with signs & symptoms of acute COPD exacerbation (Box A)

2 Stabilize the patient
- Assess severity of signs & symptoms
- Obtain oxygen saturation
- Administer oxygen therapy

3 Does patient have characteristics of a severe exacerbation? (Table 1, pg 4)
- Yes → 4 Consider transfer to a higher level of care.
- No ↓

5 Does patient have characteristics of a moderate exacerbation? (Table 1, pg 4)
- No → 6 Treat as mild exacerbation:
  - Albuterol +/- ipratropium by nebulizer or MDI* with valve holding chamber PRN. May repeat every 20 minutes x 2.
  - Discharge patient when clinically stable with nebulized albuterol +/- ipratropium PRN up to 3 days or restart regular treatment with MDI* as tolerated.
  - Go to Box # 15
- Yes ↓

7 Treat as moderate exacerbation:
- Albuterol +/- ipratropium by nebulizer or MDI* with valve holding chamber as needed (PRN). May repeat every 20 minutes x 2.

8 Is the patient responding?
- No → 9 Transfer to a higher level of care if the patient has severe dyspnea and did not respond adequately to initial therapy.
- Yes ↓

***MDI = Metered Dose Inhaler**

10 Signs of bacterial infection?
(increased sputum purulence, PLUS either increased dyspnea or increased sputum volume)
- No → 12 Continue treatment and monitor patient closely
  - Discharge patient when clinically stable
  - Albuterol +/- ipratropium by nebulizer or MDI* with valve holding chamber as needed up to 3 days or restart regular treatment with MDI* as tolerated
  - Prednisone 40 mg daily x 5 days
  - Prior authorization Tiotropium 1 capsule inhaled daily
  - Follow up with unit provider in 3 days or sooner if clinically indicated
  - Go to Box # 15
- Yes ↓

11 Does the patient have risk factors for more severe infection?
(≥2 exacerbations in the last year, antibiotic within the last 3 months, or severe COPD)
- Yes → 13 Continue treatment and monitor the patient closely
  - Discharge patient when clinically stable
  - Albuterol +/- ipratropium by nebulizer or MDI* with valve holding chamber as needed up to 3 days or restart regular treatment with MDI* as tolerated
  - Prednisone 40 mg daily x 5 days
  - Prior authorization Tiotropium 1 capsule inhaled daily
  - Consider obtaining sputum culture and non-formulary approval for antibiotic: Augmentin 875 mg bid x 5 days OR Levofloxacin 500 mg daily x 5 days
  - Follow up with unit provider in 3 days or sooner if clinically indicated
  - Go to Box #15
- No → 14 Continue treatment and monitor patient closely
  - Discharge patient when clinically stable
  - Albuterol +/- ipratropium by nebulizer or MDI* with valve holding chamber as needed up to 3 days or restart regular treatment with MDI* as tolerated
  - Prednisone 40 mg daily x 5 days
  - Prior authorization Tiotropium 1 capsule inhaled daily
  - Antibiotic: Amoxicillin 1000 mg bid x 5 days OR Minocycline 100 mg bid x 5 days
  - Follow up with unit provider in 3 days or sooner if clinically indicated
  - Go to Box #16

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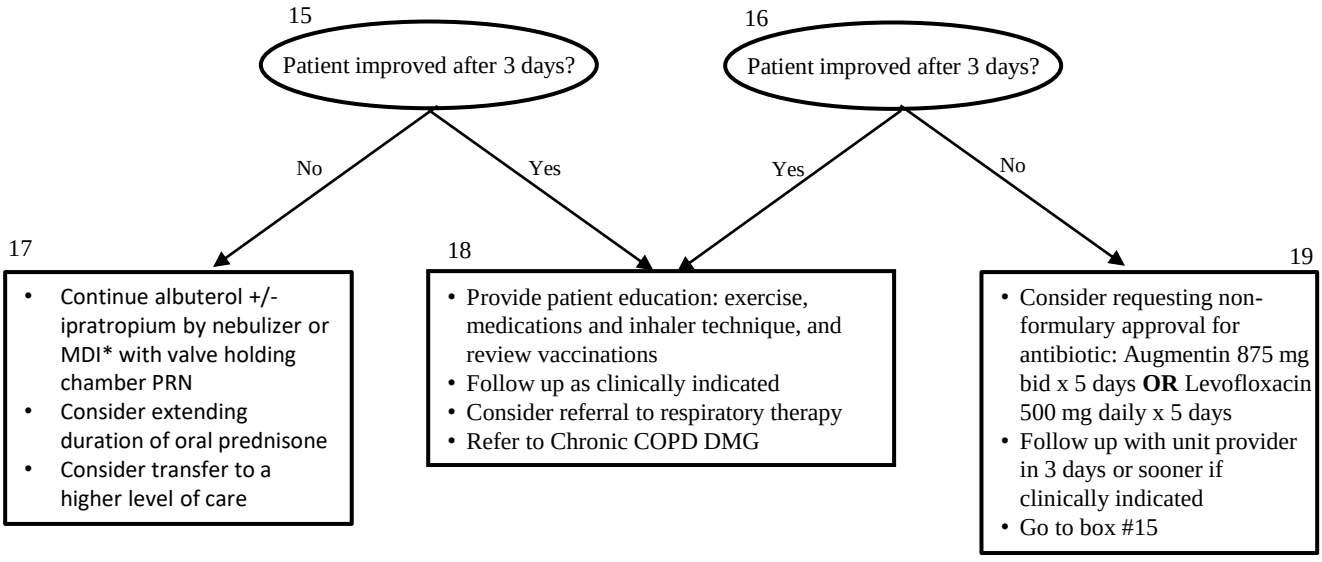
Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee, January 2007, reviewed 1/09, revised 9/12, 11/15, 3/19, 5/23.

ACUTE COPD EXACERBATION continued



I. Definition

A. COPD exacerbation: an event characterized by dyspnea and/or cough and sputum that worsen over <14 days. Exacerbations of COPD are often associated with increased local and systemic inflammation caused by airway infection, pollution, or other insults to the lungs. The goals for treatment of COPD exacerbations are to minimize the negative impact of the current exacerbation and to prevent subsequent events.

1. COPD exacerbations are important events because of the following:
    a. Negatively impact quality of life
    b. Increase rates of hospitalization and readmission
    c. Accelerate rate of lung function decline and disease progression
    d. Associated with significant mortality, particularly if results in hospitalization

II. Risk factors for COPD exacerbation

A. Bacterial and viral infections
B. Environmental conditions: pollution, ambient temperature
C. Lack of compliance with long-term oxygen therapy
D. Risk factors for relapse:
    1. Low pre-treatment FEV_1 (severe baseline COPD: FEV1/FVC <0.7, FEV1 <50)
    2. Need to increase bronchodilator or corticosteroid
    3. History of exacerbations (≥2 in the prior year)
    4. Prior antibiotic treatment
    5. Presence of comorbid conditions (heart failure, coronary artery disease, chronic renal or liver failure)

III. Diagnosis

A. Medical History
    1. Severity of COPD based on degree of airflow limitation
    2. Duration of worsening or new symptoms
    3. Number of previous episodes (total hospitalizations)
    4. Comorbidities
    5. Present treatment regimen
    6. Previous use of mechanical ventilation
B. Physical Exam:
    1. Symptoms:
        a. Cardiac: chest tightness, tachycardia
        b. Musculoskeletal: decreased exercise tolerance
        c. Psychiatric: confusion, depression, insomnia or sleepiness
        d. Pulmonary: change in volume, color, or tenacity of sputum, cough, dyspnea, tachypnea, wheezing
        e. Systemic: fatigue, fever, malaise
    2. Signs of severity include use of accessory respiratory muscles, paradoxical chest wall movements, worsening or new onset central cyanosis, development of peripheral edema, hemodynamic instability, deteriorated mental status
C. Diagnostic Procedures
    1. Pulse oximetry to track and/or adjust supplemental oxygen therapy
    2. Chest x-ray to exclude alternative diagnosis (e.g., pneumonia, PE, or fluid overload from HF)
    3. ECG to aid in detecting coexisting cardiac condition
    4. Blood tests – CBC (may identify polycythemia, anemia, or leukocytosis), serum electrolytes, renal and liver function
    5. Sputum culture – consider if patient has severe underlying COPD, frequent exacerbations or had recent antibiotic use (within past 3 months) or patient does not respond to initial antibiotic therapy

IV. Classification of exacerbation severity: determined by the following variables

A. Dyspnea
B. Respiration rate (RR)
C. Heart rate (HR)
D. Resting SaO_2
E. C-reactive protein (CRP) – if obtained

Table 1. Classification of Severity

Class	Description	Treatment
Mild (default)	• Dyspnea VAS < 5 • RR < 24 breaths/min • HR < 95 bpm • Resting $SaO_2 \geq$ 92% breathing ambient air AND change < 3% (when known)	Short-acting bronchodilators only
Moderate (meets at least 3 of 5)	• Dyspnea VAS $\geq$ 5 • RR $\geq$ 24 breaths/min • HR $\geq$ 95 bpm • Resting $SaO_2 \leq$ 92% breathing ambient air AND change $\geq$ 3% (when known) • CRP $\geq$ 10 mg/L (if obtained)	Short-acting bronchodilators + antibiotics and/or oral steroids
Severe (only assessable in hospitalized patients)	• Dyspnea, RR, HR, SaO_2 and CRP same as moderate • ABG show hypercapnia and acidosis ($PaCO_2$ > 45 mmHg and pH < 7.35)	Hospitalization or emergency room visit required

VAS: visual analog dyspnea scale, with 0 = no shortness of breath at all to 10 = worst shortness of breath every experienced; RR: respiratory rate; HR: heart rate; CRP: C-reactive protein; ABG: arterial blood gases; SaO2: saturated oxygen; PaO2: partial pressure of oxygen; PaCO2: partial pressure of carbon dioxide

V. Risk factors for more severe infections with P. aeruginosa, K. pneumonia, beta-lactamase producing bacteria that require broader-spectrum antibiotics:

A. Older age (>65 years old)
B. Comorbid cardiac diseases
C. Severe underlying COPD (FEV1 <50% predicted, FEV1/FVC<0.7)
D. Frequent exacerbations (2 or more per year)
E. Antimicrobial therapy in the past 3 months
F. Chronic use of oral steroids (doses above 10 mg daily and used for longer than 3 weeks)

VI. Treatment: more than 80% of exacerbations can be managed on an outpatient basis with pharmacologic therapy including bronchodilators, corticosteroids and antibiotics.

A. Supplemental oxygen should be titrated to improve hypoxemia with a target saturation of 88-92%.

B. Nebulizer treatment may be more convenient for sicker patients but produces no significant differences in FEV1 compared to metered dose inhalers.

C. Albuterol, with or without ipratropium, are recommended as the initial bronchodilators to treat an acute exacerbation. Once patient is stable, maintenance therapy with tiotropium should be initiated.

D. Oral prednisone can improve lung function, oxygenation, and shorten recovery time and hospitalization duration. The recommended duration of therapy is 5 days.

E. Antibiotic treatment for 5 days should be given to patients that meet the below criteria:

1. **Three** symptoms - increase in dyspnea, sputum volume, and sputum purulence
   Or
2. **Two** symptoms if increased sputum purulence is one of the two symptoms
   Or
3. Require mechanical ventilation

F. Non-invasive mechanical ventilation should be the first mode of ventilation utilized in COPD patients with acute respiratory failure exhibiting no contraindications

G. Adjunct therapies, including an appropriate fluid balance, use of diuretics when clinically indicated, anticoagulants, treatment of comorbidities, and nutritional aspects, should be considered depending on the clinical condition of the patient

Table 2: Pharmacologic treatment

Treatment	Dose	Therapy side effects
Bronchodilators	Nebulized albuterol 2.5 mg every 1-4 hours or albuterol MDI with valve holding chamber one to two puffs every 2 hours With or without Nebulized ipratropium 500 mcg every 4 hours	Headache, nausea, palpitation, tremor, vomiting Dry mouth, tremor, urinary retention
Systemic corticosteroid	Prednisone 40 mg by mouth daily x 5 days	GI bleed, GERD, hyperglycemia, infections, mood swings, myopathy
Narrow spectrum antibiotics (targeting H. influenza, M. catarrhalis, S. pneumonia)	Amoxicillin 1000 mg by mouth BID x 5 days **OR** Minocycline 100 mg by mouth BID x 5 days	Rash, diarrhea, yeast vaginitis, increased risk of antibiotic resistance Minocycline: tooth discoloration
Broad spectrum antibiotics for resistant pathogens	Non-formulary: Augmentin 875 mg by mouth BID x 5 days **OR** Levofloxacin 500 mg by mouth daily x 5 days	

VII. Follow-up after initial treatment

A. Response to initial treatment:
   1. Restart bronchodilator MDI PRN if tolerated
   2. Restart maintenance therapy with long-acting bronchodilator tiotropium if patient had moderate or severe exacerbation
   3. Complete oral steroid and antibiotic courses if applicable
   4. Follow-up in 3 days or sooner if clinically indicated, then as needed

B. Failure to respond to initial treatment:
   1. Continue bronchodilators by nebulizer or MDI with valve holding chamber
   2. Transfer to a higher level of care

C. Continued symptoms at follow-up visit (3 days later or sooner if clinically indicated)
   1. Continue bronchodilators by nebulizer or MDI with valve holding chamber
   2. Consider switching to broad spectrum antibiotic if currently on narrow spectrum antibiotic
   3. Consider extending duration of oral prednisone
   4. Follow-up in 3 more days or sooner if clinically indicated, or transfer to a higher level of care if necessary

D. Post-hospital discharge
   1. Follow-up on the next clinical day or sooner if clinically indicated

VIII. Prognosis

A. The long-term prognosis following hospitalization for a COPD exacerbation is poor with a five-year mortality rate of ~50%.

B. Factors independently associated with poor outcome include:
   1. Older age
   2. Lower body mass index
   3. Comorbidities (e.g., cardiovascular disease or lung cancer)
   4. Previous hospitalizations for COPD exacerbation
   5. Clinical severity of index exacerbation and need for long-term oxygen therapy at discharge
   6. Higher prevalence and severity of respiratory symptoms
   7. Poorer quality of life
   8. Worsening lung function
   9. Lower exercise capacity
   10. Lower lung density and thickened bronchial walls

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients

CHRONIC COPD

Box A.

COPD risk factors*:
- Tobacco smoke
- Alpha-1 anti-trypsin deficiency
- Exposure to Occupational dusts and chemicals

1

Assess symptoms. Consider COPD in any patient over 40 years old who has dyspnea, recurrent lower respiratory tract infections, chronic cough or sputum production, and a history of exposure to risk factors for the disease (See Box A). For acute respiratory symptoms beyond normal day-to-day variation, see acute COPD DMG.

2

Assess airflow limitation to confirm diagnosis.
- Spirometry should be obtained to diagnose airflow obstruction with respiratory symptoms.
- A post-bronchodilator FEV1/FVC < 70% confirms the presence of persistent airflow limitation.
- See Table 1 on page 4 for Gold classification of airflow limitation severity.

3

Assess symptoms/risk of exacerbation.
- Complete the COPD Assessment Test (CAT) in Appendix A.
- Use the patient's CAT score and number of moderate to severe exacerbations, including hospitalizations in the last year to determine ABE classification (Table 2 on page 4).
- Use classification to determine treatment.
- All patients should receive education on proper inhaler technique and risk factor avoidance.

4

Group A: Mild
(SABA + LAMA)
- Initiate albuterol HFA 2 puffs PRN up to QID
and
- Tudorza® Pressair (aclidinium) 1 puff BID
- Follow-up within 90 days

5

Group B: Moderate
(SABA + LAMA + LABA)
- Initiate albuterol HFA 2 puffs PRN up to QID
and
- UTMB: Tudorza® Pressair (aclidinium) 1 puff BID
and
- Request nonformulary Serevent® (salmeterol) 50 mcg 1 inhalation BID KOP
- Texas Tech: Request nonformulary Stiolto Respimat® (tiotropium 2.5 and olodaterol 2.5 mcg) 2 inhalations daily NONKOP
- Follow-up within 90 days

6

Group E: Severe
(SABA + LAMA + LABA)
- Initiate albuterol HFA 2 puffs PRN up to QID
and
- UTMB: Tudorza® Pressair (aclidinium) 1 puff BID
and
- Request nonformulary Serevent® (salmeterol) 50 mcg 1 inhalation BID KOP
- Texas Tech: Request nonformulary Stiolto Respimat® (tiotropium 2.5 and olodaterol 2.5 mcg) 2 inhalations daily NONKOP
- Follow-up within 30 days

7 Symptoms controlled?

No → 10 Escalate therapy: see pg 2, box 15.

Yes → 11
- Continue regimen
- Reinforce patient education
- Follow up at least every 12 months
- Consider Respiratory Therapy (RT) referral for spirometry based on symptoms or at least every 2 years.

8 Symptoms controlled?

Yes → 11 (same as above)

No → 12 Escalate therapy: see pg 2, box 16.

9 Symptoms controlled?

Yes → 13
- Continue regimen
- Reinforce patient education
- Follow up at least every 3 months
- Consider RT referral for spirometry based on symptoms or at least annually.

No → 14 Escalate therapy: see pg 2, box 17.

Prepared By The Correctional Managed Care Pharmacy & Therapeutic Committee, September 1996, Revised 8/98, 12/98,4/02, 4/03, 10/03, 11/06, 3/10, 7/12, 11/15, 5/19, 5/23 7/24. Reviewed 3/05, 1/09.

CHRONIC COPD continued

Group A: Mild cont. from box 10, page 1 (SABA + LAMA)

15

- Reinforce patient education.
- Reassess CAT score
- Escalate maintenance therapy – Request nonformulary Serevent® (salmeterol) 50 mcg 1 inhalation BID KOP
- Texas Tech: Request nonformulary Stiolto Respimat® (tiotropium 2.5 and olodaterol 2.5 mcg) 2 inhalations daily NONKOP
- Consider RT referral for spirometry based on symptoms and exacerbations or at least every 2 years

Group B: Moderate cont. from box 12 page 1 (SABA + LAMA + LABA)

16

- Reinforce patient education.
- Reassess CAT score
- If dyspnea is the primary complaint, consider switching to non-formulary LAMA + LABA Anoro Ellipta® (umeclidinium/ vilanterol) 62.5/5 mcg - 1 inhalation daily KOP for maintenance therapy.
- If exacerbation is the primary complaint, refer to pulmonary specialist.
- Follow-up within 90 days
- Consider RT referral for spirometry based on symptoms and exacerbations or at least every 2 years

*Texas Tech sector ONLY: may request

- non-formulary Stiolto Respimat® 2.5mcg-2.5mcg 2 inhalations daily in place of salmeterol/tiotropium
- non-formulary Wixela Inhub® 250mcg-50mcg 1 inhalation BID in place of Dulera®

Group E: Severe cont. from box 14, page 1 (SABA + LAMA + LABA)

17

- Consider referral to specialist
- Reinforce patient education.
- Reassess CAT score
- Consider LAMA + LABA + ICS in patients with a history of asthma or blood eosinophil count ≥300 cells/mcL:
  - ❑ UTMB: aclidinium AND nonformulary Dulera® (mometasone/formoterol)
  - ❑ TT: aclidinium AND nonformulary Wixela Inhub® (fluticasone/ salmeterol)
- If dyspnea is the primary complaint, consider switching from aclidinium/salmeterol to non-formulary Anoro Ellipta® (umeclidinium/vilanterol) 62.5/5 mcg - 1 inhalation daily KOP for maintenance therapy.
- If exacerbation is the primary complaint, refer to pulmonary specialist.
- Follow up within 30 days
- Consider RT referral for spirometry based on symptoms and exacerbations or at least annually

Preferred Regimens

Category	UTMB	TT	FS
SABA	Albuterol [Ventolin®/Proventil® HFA] 90 mcg/actuation (200 actuations) - 2 puffs PRN up to QID		F
LABA	Salmeterol [Serevent® Diskus] 50 mcg/actuation (60 actuations) - 1 puff BID	N/A	NF
LAMA	Aclidinium [Tudorza® Pressair] 400 mcg/actuation (60 actuations) 1 puff BID		F
LAMA + LABA	Umeclidium/Vilanterol [Anoro Ellipta®] 62.5mcg-25 mcg/actuation (30 actuations)	Tiotropium/Olodaterol [Stiolto Respimat®] 2.5mcg-2.5mcg/actuation (60 actuations) – 2 inhalations daily	NF
ICS + LABA	Mometasone/Fomoterol [Dulera®] 100mcg-5 mcg/actuation (120 actuations) - 2 puffs BID	Fluticasone/Salmeterol [Wixela Inhub®] 250 mcg-50 mcg/actuation (60 actuations) - 1 inhalation BID	NF

SAMA – Short Acting Muscarinic Antagonist
SABA – Short Acting Beta-2 Agonist
LAMA – Long-Acting Muscarinic Antagonist
LABA – Long-Acting Beta-2 Agonist
ICS – Inhaled Corticosteroid

FS – Formulary Status
NF – Non-formulary
PA – Prior Authorization
F - Formulary

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.**

I. **Definitions (adapted from the 2023 GOLD guidelines)**

- Chronic Obstructive Pulmonary Disease (COPD): a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production, exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction.
- COPD exacerbations: an event characterized by increased dyspnea and/or cough and sputum that worsens in < 14 days which may be accompanied by tachypnea and/or tachycardia and is often associated with increased local and systemic inflammation caused by infection, pollution, or other insult in the airways.

II. **Patient Evaluation**

A. Diagnosis:

1. Consider a diagnosis if patient has symptoms consistent with COPD and/or risk factors associated with the disease. If any of the indicators listed below are present in an individual over the age of **40**, consider COPD and perform spirometry. These indicators are not diagnostic themselves, but the presence of multiple key indicators increases the probability of the presence of COPD.
    a. Dyspnea that is progressive over time and is persistent and worsens with exercise
    b. Recurrent wheeze
    c. Recurrent lower respiratory tract infections
    d. Chronic cough: may be intermittent and may be unproductive, as well as recurrent wheezing
    e. History of risk factors
        i. Host factors: genetic factors, congenital/developmental abnormalities
        ii. Tobacco smoke
        iii. Smoke from home cooking and heating fuels
        iv. Occupational dust, vapors, fumes, gases, and other chemicals
2. Diagnosis is confirmed by spirometry: post bronchodilator FEV1/FVC < 70%
3. Peak flow is not recommended for the diagnosis of COPD
4. Chest X-ray is not considered diagnostic, but may be used to exclude other diagnoses
5. Chest CT imaging should be considered for patients with persistent exacerbations, symptoms out of proportion to disease severity on lung function testing, FEV1 < 45% predicted with significant hyperinflation or for those who meet criteria for lung cancer screening.
6. Alpha-1 antitrypsin deficiency screening may be considered in a patient that develops COPD at a young age (< 45 years) or has a family history.

B. Assessment:

1. Detailed history and physical examination
2. Measurement of post-bronchodilator spirometry
3. Assessment of exercise capacity
4. Measurement of health status (CAT score)
5. Assessment of inspiratory and expiratory muscle strength and lower limb strength in patients who suffer from muscle wasting
6. Discussion about individual patient goals and expectations
    a. Once COPD has been diagnosed, effective management should be based on an individualized assessment to reduce both current symptoms and future risk of exacerbations.

C. Goals of COPD assessment:

1. Determine severity of airflow obstruction
2. Improve the patient's overall health and produce healthy outcomes
3. Decrease the risk of future events (such as exacerbations, hospital admissions, or death)
4. Guide therapy

D. Spirometry: the most reproducible and objective measure of airflow limitation
   1. The GOLD guidelines recommend performing spirometry in patients with symptoms and/or risk factors, but not as the only diagnostic test.
      a. In asymptomatic individuals without any significant exposures to tobacco or other noxious stimuli, screening spirometry is probably not indicated.
      b. In symptomatic individuals or those with significant risk factors (e.g., >20 pack-years of smoking or recurrent chest infections), spirometry should be considered.
   2. Spirometry may also be used to assess airflow limitation (FEV1 predicted).
   3. The classification of airflow limitation severity in COPD (Table 1) uses specific spirometric cutoffs.
   4. To minimize variability, spirometry should be performed after the administration of an adequate dose of at least one short-acting inhaled bronchodilator.

Table 1. Classification of Airflow Limitation Severity (in patients with FEV1/FVC < 70)

Gold Stages		FEV1 % Predicted
Gold 1	Mild	>80%
Gold 2	Moderate	50-79%
Gold 3	Severe	30-49%
Gold 4	Very severe	<30%

E. Combined COPD assessment scheme:
   1. Confirm diagnosis spirometrically (post-bronchodilator FEV1/FVC < 0.7)
   2. Assess airflow limitation severity (Table 1)
   3. Assess symptoms/risk of exacerbation using the COPD Assessment Test (CAT) (Appendix A)
   4. Record history of moderate and severe exacerbations (including hospitalizations) (Table 2)

The number (Gold stage 1-4) provides information regarding severity of airflow limitation, while the letter (groups A, B, E) provides information regarding symptom burden and risk of exacerbation, which can be used to guide therapy.

Table 2. ABE Patient Assessment

A	0 or 1 moderate exacerbation not leading to hospital admission	<10
B	0 or 1 moderate exacerbation not leading to hospital admission	>10
E	≥2 moderate exacerbations or ≥1 leading to hospitalization	

III. **Treatment**
   A. Goals of therapy
      1. Prevent disease progression
      2. Relieve symptoms
      3. Improve exercise tolerance
      4. Improve health status
      5. Prevent and treat exacerbations
      6. Reduce mortality

B. Non-pharmacologic treatment
   1. Risk factor avoidance (e.g., smoking cessation)
   2. Pulmonary rehabilitation: Encourage exercise at least twice a week
   3. Education and self-management: Smoking cessation, correct use of inhaler devices, early recognition of exacerbation, decision-making and taking action, and when to seek medical attention
   4. Oxygen therapy: long-term administration of oxygen (> 15 hours/day) to patients with chronic respiratory failure has been shown to increase survival in patients with severe resting hypoxemia
      a. In patients with stable COPD and moderate resting or exercise-induced desaturation, long-term oxygen does not lengthen time to death or first hospitalization or provide sustained benefit in health status and lung function
      b. Supplemental oxygen should be considered and titrated to keep SaO2 ≥ 90% in patients with:
         - PaO_2 < 55mmHg (8kPa) or SaO_2 < 88% **OR**
         - PaO_2 > 55 but < 60mmHg (>7.3 kPa but < 8kPa) with right heart failure or erythrocytosis

C. Pharmacologic treatment: reduces symptoms and the risk and severity of exacerbations, improves health status, and increases exercise tolerance
   1. Rescue short-acting bronchodilators (e.g., albuterol) should be prescribed to all patients for immediate symptom relief
   2. Long-acting bronchodilators: the mainstay of therapy for COPD
      a. Long-acting beta agonists (LABAs) (e.g., salmeterol) and long-acting muscarinic antagonist (LAMAs) (e.g., aclidinium) are preferred over short-acting agents except for patients with only occasional dyspnea, and for immediate relief of symptoms in patients already on long-acting bronchodilators for maintenance therapy.
      b. The combination of a LAMA and a LABA is preferred for Group B and E patients.
      c. Theophylline is not recommended unless other long-term treatment bronchodilators are unavailable.
   3. Inhaled corticosteroids (ICS): not recommended in COPD except in patients with a history of asthma or blood eosinophil ≥ 300 cells/mcL. If there is an indication for ICS use, then the combination LAMA+LABA+ICS is recommended.
   4. It is essential to provide instruction and to demonstrate proper inhalation technique when prescribing a device, to ensure that inhaler technique is adequate, and to re-check at each visit. Inhaler technique and adherence to therapy should be assessed before concluding that current therapy requires modification.
   5. Vaccinations
      a. Influenza and pneumococcal vaccinations can reduce serious illnesses, such as lower respiratory infections requiring hospitalization and death in COPD patients (Infection Control Policy B-14.07).
      b. COVID-19 vaccination is recommended to reduce the risk of SARS-CoV-2 infection requiring hospitalization, ICU admission, or an emergency department or urgent care clinic visit.
      c. Tdap vaccination should be considered in COPD patients who were not vaccinated in adolescence.

D. Follow-up:
   1. Inquire about changes in symptoms at each visit including cough and sputum, breathlessness, fatigue, activity limitation, and sleep disturbances
   2. Review current treatment including medication dosages, adherence, inhaler technique, effectiveness of the current regimen at controlling symptoms, and adverse effects
   3. Evaluate the frequency, severity, and likely causes of exacerbations
   4. Monitor comorbidities which can potentially complicate management of COPD

Table 3. Pharmacologic Recommendations

Group A	**LAMA** Aclidinium (Turdorza®) 400 mcg 1 inhalation BID KOP	**LAMA + LABA** Aclidinium (Turdorza®) 400 mcg 1 inhalation BID KOP AND Non-formulary salmeterol (Serevent®) 50 mcg - 1 inhalation BID KOP Texas Tech ONLY: nonformulary LAMA/LABA combo inhaler: Stiolto Respimat® (tiotropium/olodaterol) 2.5-2.5 mcg – 2 inhalations daily may be used in place of tiotropium/salmeterol		**+ SABA** Albuterol (Ventolin®, Proventil®) 2 puffs QID as needed as a rescue inhaler
Group B	**LAMA + LABA** Aclidinium (Turdorza®) 400 mcg 1 inhalation BID KOP AND Non-formulary salmeterol (Serevent®) 50 mcg - 1 inhalation BID KOP Texas Tech ONLY: nonformulary LAMA/LABA combo inhaler: Stiolto Respimat® (tiotropium/olodaterol) 2.5-2.5 mcg – 2 inhalations daily may be used in place of tiotropium/salmeterol	**LAMA + LABA** If dyspnea is the primary complaint, consider switching from aclidinium/salmeterol to non-formulary Anoro Ellipta® (umeclidinium/vilanterol) 62.5/5 mcg – 1 inhalation daily KOP for maintenance therapy Or If exacerbation is the primary complaint, refer to specialist		
Group E	**LAMA + LABA** Aclidinium (Turdorza®) 400 mcg 1 inhalation BID KOP AND Non-formulary salmeterol (Serevent®) 50 mcg – 1 inhalation BID KOP Texas Tech ONLY: nonformulary LAMA/LABA combo inhaler: Stiolto Respimat® (tiotropium/olodaterol) 2.5-2.5 mcg – 2 inhalations daily may be used in place of tiotropium/salmeterol	**LAMA + LABA** If dyspnea is the primary complaint, consider switching from aclidinium/salmeterol to non-formulary Anoro Ellipta® (umeclidinium/vilanterol) 62.5/5 mcg – 1 inhalation daily KOP for maintenance therapy Or If exacerbation is the primary complaint, refer to specialist	**LAMA + LABA + ICS** Consider in patients with a history of asthma or blood eosinophil count ≥300 cells/mcL: UTMB: aclidinium (Tudorza®) AND non-formulary Dulera® (mometasone/formoterol) Texas Tech: aclidinium (Tudorza®) AND non-formulary Wixela Inhub® (fluticasone/salmeterol)	

Instructions for MDI Inhaler Use
(Albuterol® HFA, Ventolin ® HFA, Dulera®)

Below are general instructions for HFA inhaler use. Please refer to the specific inhaler package insert for complete directions as instructions may vary.

Priming HFA inhaler:
1. Shake the inhaler well.
2. Prime the inhaler before using for the first time by releasing 4 test sprays into the air away from face.
3. Repeat the above priming procedure before using only if the inhaler has not been used for more than 2 weeks.

Cleaning HFA inhaler:
1. Remove medication canister. Never get the canister wet.
2. Clean the plastic mouthpiece by running warm water through the top to the bottom for 30 seconds at least once a week.
3. Shake to remove excess water, then air dry thoroughly (such as overnight).

Instructions for taking a dose from your HFA inhaler:
1. Take the cap off the mouthpiece of the inhaler (plastic actuator) and **shake the inhaler well** before each spray.
2. Hold the inhaler upright with the mouthpiece down (see Figure 2). Breathe out through your mouth and push as much air from your lungs as you can. Put the mouthpiece in your mouth and close your lips around it.
3. Push the top of the canister all the way down while you breathe in deeply and slowly through your mouth (see Figure 3). Right after the spray comes out, take your finger off the canister. After you have breathed in all the way, take the inhaler out of your mouth and close your mouth.
4. Hold your breath as long as you can, up to 10 seconds, to allow the drug to reach deeply into your lungs. Then breathe normally.
5. If additional sprays have been prescribed, wait 1 minute between sprays. Shake the inhaler again and repeat steps 2 through 4.
6. Put the cap back on the mouthpiece after every time you use the inhaler, and make sure it snaps firmly into place.

Important points:
1. Do <u>not</u> use the inhaler after the expiration date, which is on the outside packaging.
2. This technique does not work with dry powder capsule inhalers. It is important to close the mouth tightly around the mouthpiece of the inhaler and to inhale rapidly when using a dry powder inhaler.

Figure 1

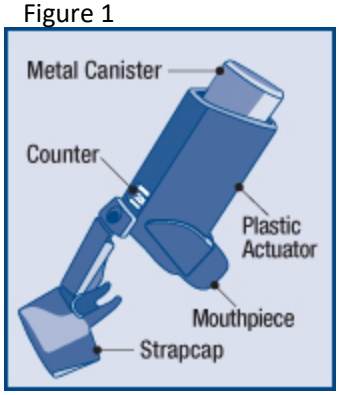


Figure 2

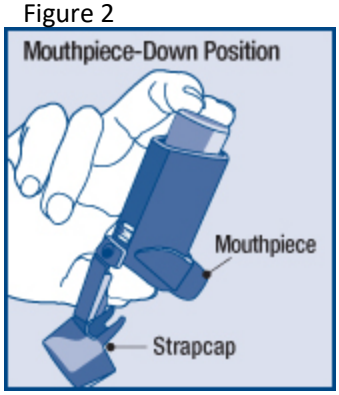


Figure 3

Tudorza® Pressair (aclidinium) Inhaler Technique

READY BEFORE INHALATION

- Remove cap and hold upright.
- **PRESS** and **RELEASE** the green button.
- Check the color-controlled window. **GREEN** means the medicine is **READY** for inhalation.
- Before you put the inhaler in your mouth, breathe out completely. Do not breathe out into the inhaler. Then place your lips tightly around the mouthpiece.

DURING INHALATION

- **TAKE A STRONG, DEEP BREATH IN.**
- A **"CLICK"** will sound during inhalation when the inhaler is used correctly.
- Keep breathing in as long as possible after you hear the **"CLICK."***

CONFIRM AFTER INHALATION

- Remove the inhaler from your mouth and hold your breath for as long as possible, and then slowly breathe out, away from the inhaler.
- **CONFIRM** the color-controlled window has turned from green to **RED** to ensure the full dose has been inhaled correctly.

Salmeterol Diskus Technique:

1. Open your Diskus: Hold the Diskus in your left hand and place the thumb of your right hand in the thumb grip. Push the thumb grip away from you as far as it will go until the mouthpiece shows and snaps into place (Picture A).
2. Slide the lever until you hear it click. Hold the Diskus in a level, flat position with the mouthpiece towards you. Slide the lever away from the mouthpiece as far as it will go until it clicks. The number on the counter will count down by 1. The Diskus is now ready for use (Picture B).
3. Inhale your medication. Before you breathe in your dose, breathe out as long as you can while you hold the Diskus level and away from your mouth. Do not breathe into the mouthpiece. Put the mouthpiece to your lips. Breathe in quickly and deeply through the Diskus. Do not breathe in through your nose. Remove the Diskus from your mouth and hold your breath for about 10 seconds, or for as long as is comfortable. Breathe out slowly as long as you can (Pictures C and D).
4. Close the Diskus. Place your thumb in the thumb grip and slide it back towards you as far as it will go. Make sure the Diskus clicks shut and you cannot see the mouthpiece. The Diskus is now ready for your next scheduled dose (Picture E).

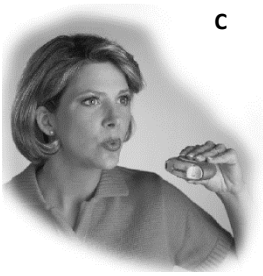
Important notes to avoid accidentally wasting a dose:

- Do not close the Diskus
- Do not tilt the Diskus
- Do not move the lever on the Diskus

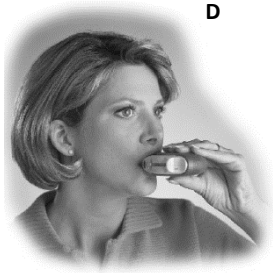
A

B

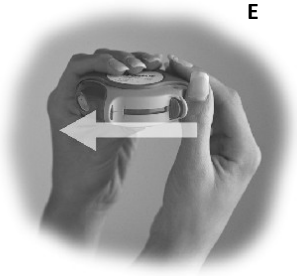
C



D



E

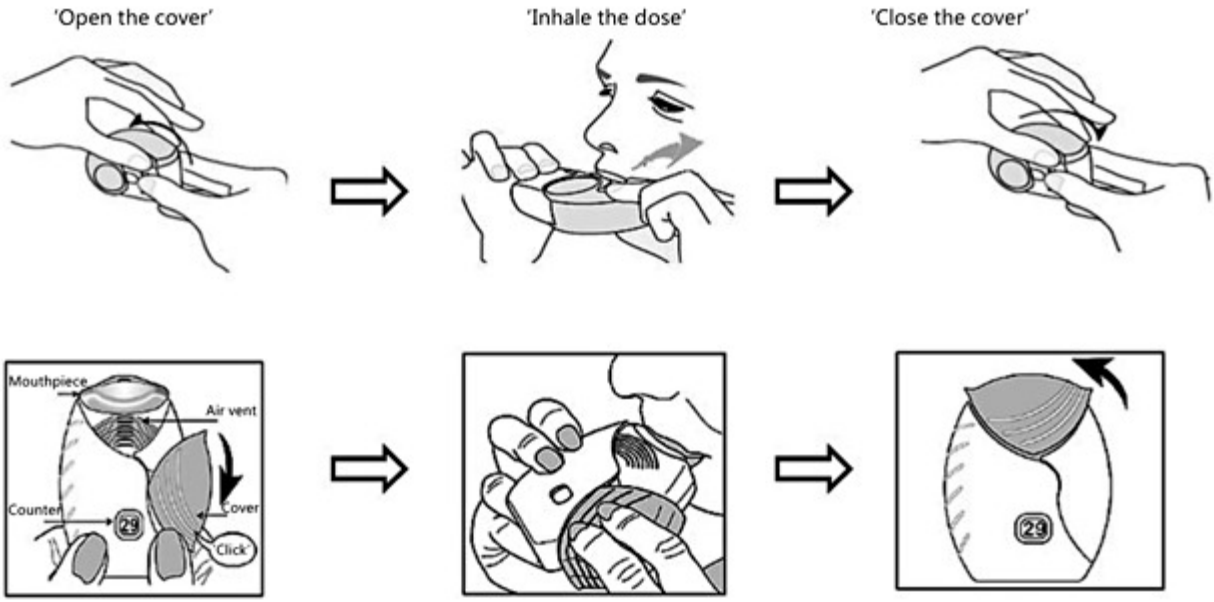


Anoro Ellipta® Technique:

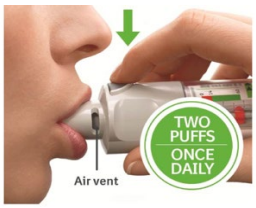
1. Activate the inhaler by sliding the cover down until you hear a "click" to prepare a dose.
2. The dose counter will now count down by one number.
3. While holding the inhaler away from your mouth, exhale a complete breath (i.e., breathe out as far as is comfortable. Do not breathe out into the inhaler.
4. Put the mouthpiece between your lips and close lips firmly around it. Do not block the air vent with your fingers.
5. Take one long, steady, deep breath in. Hold this breath for as long as possible (minimum 3-4 seconds).
6. Remove the inhaler from your mouth. Exhale slowly and gently. Continue to breathe normally.
7. You can clean the mouthpiece of the inhaler with a clean, dry tissue after use.
8. Close the inhaler by sliding the cover upwards as far as it will go over the mouthpiece.

Notes:

1. Keep the cover closed until you are ready to inhale a dose.
2. Do not shake the Ellipta inhaler at any point during use.

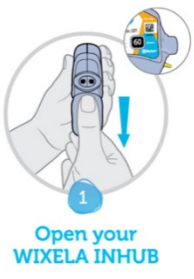


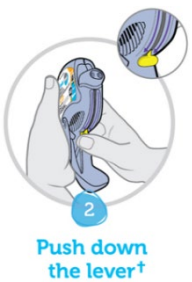
Stiolto® Respimat

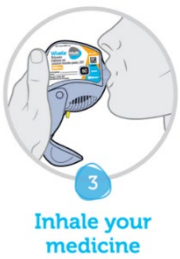


1. Hold the inhaler upright with the orange cap closed. Turn the clear base in the direction of the white arrows until it clicks.
2. Flip the orange cap until it fully snaps open.
3. **Turn your head away from the inhaler and breathe out fully.**
4. **Seal your lips** around the mouthpiece without covering the holes on the side of the mouthpiece **Breathe in slowly and deeply while pressing the dark gray dose-release button**, then hold your breath for about **10 seconds**. Then breathe out. Wait 30 seconds and **repeat this step** for the 2nd dose.
5. Place the cap back on the inhaler.

Wixela® Inhub







1. Hold your Wixela Inhub in one hand, and put the thumb of your other hand on the thumb grip. Slide the thumb grip down until the mouthpiece appears.
2. **Slide the yellow lever down to the end of the purple arrows.** You will hear a click. The medicine is now ready for you to take.
3. **Turn your head away from the inhaler and breathe out fully.** Do not breathe into the Inhub device. **Seal your lips** around the mouthpiece. **Breathe in quickly and deeply**, then hold your breath for about **10 seconds**. Then breathe out.
4. Slide the cover back to the closed position.
5. **Rinse your mouth and throat** with water to prevent a fungal infection (thrush).

Appendix A.

Your name:

Today's date:

CAT
COPD Assessment Test

How is your COPD? Take the COPD AssessmentTest™ (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers, and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

Example: I am very happy	0 X 2 3 4 5	I am very sad	
			SCORE
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	
			TOTAL SCORE

Last Updated: February 24, 2012

Appendix A. continued

CAT Score Interpretation

CAT Score	Impact Level	Broad clinical picture of the impact of COPD by CAT score	Management Considerations
>20	High-Very High	• COPD may inhibit the patient performing ADLs or it may take them a long time to do these activities (e.g., taking showers) • Patients are breathless walking, performing ADLs, as well as talking • Cough makes them tired and chest symptoms disturb their sleep on most nights • "Everything they do seems too much effort"	• Referral to specialist care • Additional pharmacological treatment • Consider referral for pulmonary rehabilitation • Ensure best approaches to minimizing and managing exacerbations
10-20	Medium	• Cough up sputum most days • 1-2 exacerbations a year • Breathless > 3 days /week • Usually wake up with chest tightness or wheezing • Breathless on bending over and can only walk up a flight of stairs slowly • Patients require elongated breaks (rest time) while performing daily activities	• Review maintenance therapy-is it optimal? • Consider referral for pulmonary rehabilitation • Review COPD risk factors • Ensure best approaches to minimizing and managing exacerbations
<10	Low	• Breathless < 3 days/week • Cough several days a week • Breathless when exercising or doing physical activities • Patients have to slow down or rest when walking up hills • Patients get exhausted very easily	• Annual influenza vaccination • Reduce exposure to exacerbation risk factors • Therapy as warranted by further clinical assessment
5		• Upper limit of normal in healthy non-smokers	

DENTAL STREPTOCOCCAL INFECTIVE ENDOCARDITIS PREVENTION

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

1

Does the patient have any of the following underlying conditions?

1. Prosthetic cardiac valve or valve repair with prosthetic valve material
   - Prosthetic of cardiac prosthetic valve
   - Transcatheter implantation of prosthetic valves
   - Cardiac valve repair with prosthetic material (including annuloplasty rings or clips)
   - Left ventricular assist devices or implantable heart
2. Previous, relapsed, or recurrent infective endocarditis.
3. Certain types of congenital heart disease including:
   - Unrepaired cyanotic congenital heart disease, including patients with palliative shunts and conduits
   - Completely repaired congenital heart defect with prosthetic material or device (eg, septal closure device), during the first six months after surgical or transcatheter placement
   - Repaired congenital heart disease with residual defect at the site or adjacent to the site of a prosthetic patch or prosthetic device
   - Surgical or transcatheter pulmonary artery valve or conduit placement (e.g. Melody valve and Contegra conduit)
4. Cardiac transplant recipients who develop cardiac valvulopathy

Yes

No

2

Is the patient undergoing a dental procedure that involves the manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa?

No

3

No antibiotic prophylaxis is suggested.

Yes

4

Refer to Table 1 on page 2 for antibiotic prophylaxis regimens.

Nurses: DMGs are to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.**

DENTAL STREPTOCOCCAL INFECTIVE ENDOCARDITIS PREVENTION

Table 1. Antibiotic Regimens for a Dental Procedure
(Single dose 30 to 60 minutes before the procedure):

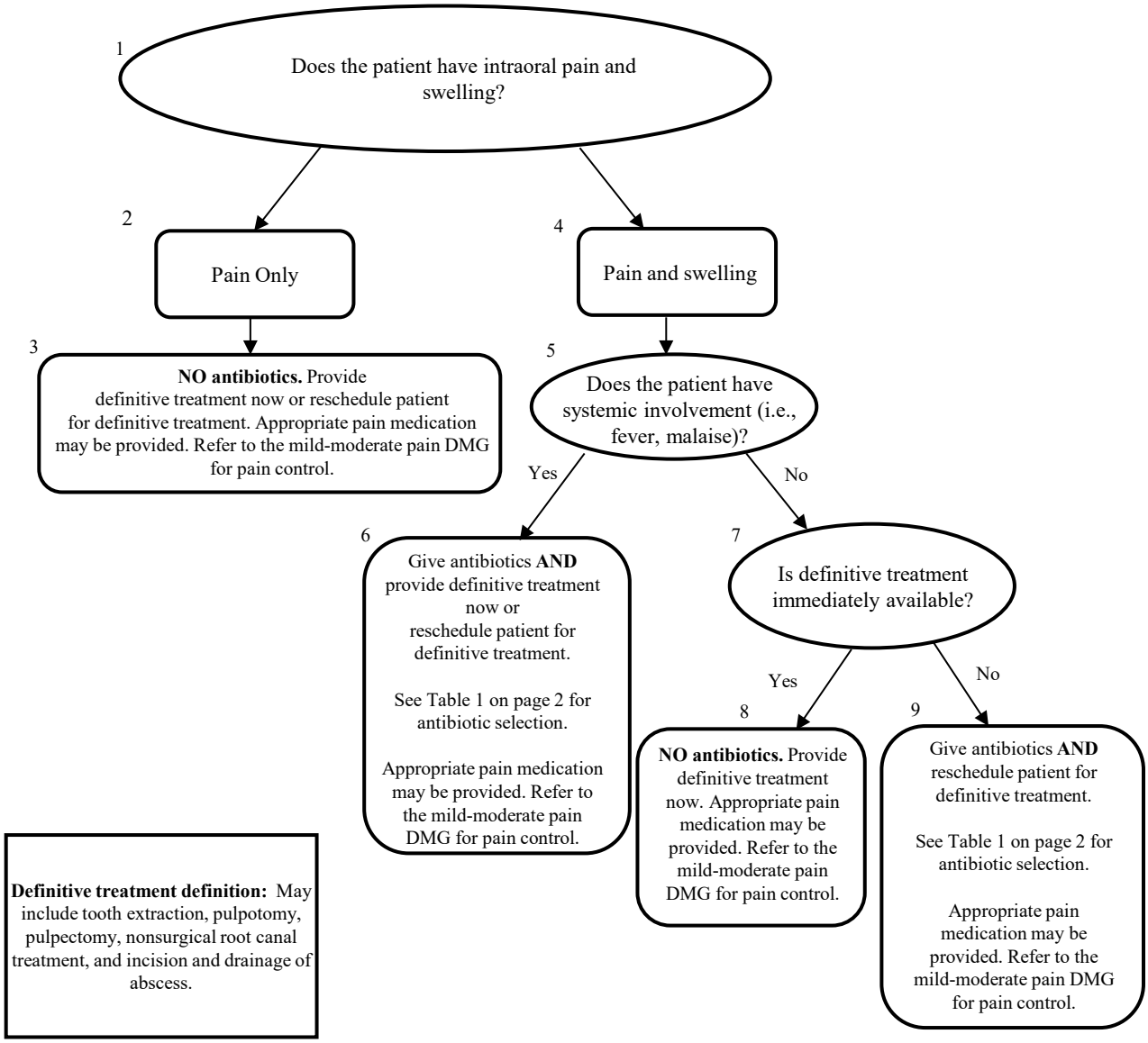
ROUTE:	FORMULARY STATUS:	MEDICATION:	ADULT DOSING:
Preferred Oral	Formulary	Amoxicillin 500mg	2 Grams
Oral and Penicillin Allergic	Formulary	Cephalexin 500mg	2 Grams
	Formulary	Minocyline 100mg	100 mg
	Nonformulary	Azithromycin 500mg	500 mg
Preferred IV (for patients unable to take oral medication)	Formulary	Ampicillin 500mg vial	2 Grams IM or IV
	Formulary	Cefazolin 1gm or Ceftriaxone 1gm vials†*	1 Gram IM or IV
IV and Penicillin Allergic (for patients unable to take oral medication)	Formulary	Cefazolin 1gm or Ceftriaxone 1gm vials†*	1 Gram IM or IV

Antibiotic prophylaxis regimens target prevention of viridans group streptococcal infective endocarditis.
Clindamycin is no longer recommended in antibiotic prophylaxis before a dental procedure.
IM indicates intramuscular; IV indicates intravenous.
†Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema, or urticarial with penicillin or ampicillin.
*Ceftriaxone is restricted to infirmary units and regional medical facilities.

Healthcare Provider Education

- If antibiotic prophylaxis is inadvertently not administered before a dental procedure, then it may be administered up to 2 hours after the procedure.
- Antibiotic prophylaxis is not suggested when providing anesthetic injections through noninfected tissue, taking dental radiographs, placing removable prosthodontic or orthodontic appliances, adjusting orthodontic appliances, placing orthodontic brackets, shedding of primary teeth, or when bleeding from trauma to the lips or oral mucosa.
- When at-risk patients require repeated dental procedures likely to result in bacteremia, either an alternative antibiotic regimen should be used each time, or there should be intervals of at least 4 weeks between treatment sessions.
- In patients who are receiving a short course (7–10 days) of oral antibiotic therapy before a dental procedure, it is preferable to select a different class of antibiotic for prophylaxis.
- If possible, it is preferable to delay an elective dental procedure for at least 10 days after completion of a short course of antibiotic therapy.
- In patients undergoing multiple sequential dental appointments, if possible, it is preferable to delay the next procedure for 10 days after the last dose of antibiotic therapy.
- In patients who are receiving parenteral antimicrobial therapy for infective endocarditis or other infections and require a dental procedure, the same parenteral antibiotic may be continued through the dental procedure.

URGENT MANAGEMENT OF DENTAL PAIN AND INTRAORAL SWELLING



Definitive treatment definition: May include tooth extraction, pulpotomy, pulpectomy, nonsurgical root canal treatment, and incision and drainage of abscess.

The suggested guidelines are for immunocompetent adult patients. These pathways do not replace sound clinical judgement nor are they intended to strictly apply to all patients.

URGENT MANAGEMENT OF DENTAL PAIN AND INTRAORAL SWELLING

Table 1. Antibiotic Regimens

ROUTE:	FORMULARY STATUS:	MEDICATION:	ADULT DOSING:
Oral (1st Line Therapy)	Formulary	Amoxicillin	500 mg 3 times per day
	Formulary	Penicillin VK	500 mg 4 times per day
Oral and Penicillin Allergic	Formulary	Cephalexin†	500 mg 4 times per day
	Formulary	Clindamycin	300 mg 4 times per day
	Non-Formulary	Azithromycin	Loading dose of 500 mg on day 1, followed by 250 mg for an additional 4 days
Oral (2nd Line Add-On Therapy)*	Formulary	Metronidazole	500 mg 3 times per day
Oral (2nd Line Therapy)*	Non-Formulary	Amoxicillin/Clavulanate	500/125 mg 3 times per day
Usual duration of antibiotic therapy is three to seven days.			

† **DO NOT** use in patients who have a history of anaphylaxis, angioedema, or hives with penicillin, ampicillin, or amoxicillin.

*If patient shows no improvement in symptoms or the condition progresses to a more severe state, consider complementing first-line treatment with oral metronidazole to broaden antibiotic therapy **OR** discontinuing first-line treatment and prescribe oral amoxicillin and clavulanate to enhance the efficacy against gram-negative anaerobic organisms.

Healthcare Provider Education

- Examples of definitive treatment include pulpotomy, pulpectomy, nonsurgical root canal treatment, incision and drainage of abscess and tooth extractions*.
- Evidence suggests that nonsteroidal anti-inflammatory drugs (specifically, 400-600 mg ibuprofen plus 1,000 mg acetaminophen) could be effective and less harmful than any opioid-containing medication or medication combination for the temporary relief of dental pain.
- Patients with systemic signs of infection: Providers should reevaluate or follow up with their patient after 3 days to assess if there is resolution of systemic signs and symptoms. The patient should still be referred for definitive therapy despite resolution in symptoms.

**Although the 2019 Journal of the American Dental Association Antibiotics for Dental Pain and Swelling Guideline does not include tooth extractions in definitive treatment, extractions are considered definitive within the scope of care provided.*

1

TYPE 1 DIABETES MELLITUS

- Institute lifestyle modification and provide individual education with specific patient goals: Weight loss (if >10% above ideal body weight (IBW), exercise plan (150 minutes/week), diet for health (DFH)
- Order Complete Metabolic Panel (CMP), urinary albumin-to-creatinine ratio (ACR), thyroid function, lipid panel, and A1C.
- Consider ordering serum C-peptide levels (*with concurrent glucose level; see page 5)* to verify insulin depletion if diagnosis is uncertain or ambiguous (see page 5 for more information).
- Initiate aspirin and statin if indicated and if there are no contraindications to therapy (Table 2, page 12)
- If blood pressure is >140/90 consider starting ACE-Inhibitor or ARB (see Table 2, page 12 and HTN DMG). A lower target of <130/80 mmHg is recommended for those at higher cardiovascular disease risk or with evidence of microvascular complications, particularly renal disease.
- Evaluate for target organ damage and co-morbidities – conduct baseline foot and eye exam
- Refer to Dental for a comprehensive oral/periodontal disease evaluation within 30 days from the initial chronic care visit

2

- Begin **Intensive Insulin Regimen**. Initiate insulin based on 0.5 units/kg/day for Total Daily Dose (TDD).
- Basal regimen: 50% of TDD (*starting recommendation, ratios may change*)
  - Preferred: Insulin glargine (Lantus), administer once or twice daily for basal requirement (see Table 2, page 10)
  - Alternative regimen: If selecting NPH for basal insulin requirement, administer 2/3 of NPH dose in AM and 1/3 in PM.
- Bolus (prandial) regimen: 50% of TDD
  - If on insulin glargine (Lantus), the remainder 50% of TDD is administered as Regular insulin divided equally before breakfast, lunch, and supper (*Lantus and Novolin R cannot be mixed, Lantus regimen may consist of up to 5 injections per day)*
  - If on NPH, the remainder 50% of TDD is administered as Regular insulin divided equally before breakfast and supper
- Order finger sticks (FSBS) two to three times a day, depending on insulin regimen.
- Follow up in 2 weeks

The pathways do not replace sound clinical judgement nor are they intended to strictly apply to all patients

3 Are FBG and PPG at goal (Table A)?

No → 4 Monitor for hypoglycemia. Is patient experiencing hypoglycemia ≥ twice a week? (FSBS <70 mg/dL)?

Yes → 5

1. Determine cause of hypoglycemia. Consider 10-20% dose reduction if appropriate. (see Table 2, page 10 to identify which insulin may need to be adjusted). May also refer to Hypoglycemia DMG for more information. Follow up in 2-4 weeks. Go to circle 3.
2. Consider evaluation of long-acting basal insulin (ex. insulin glargine) if patient continues to experience hypoglycemia, specifically nocturnal (see Table 2, page 10 for dosing). If converting from NPH twice daily to once daily insulin glargine regimen, reduce basal TDD by 20%. Follow up in 2-4 weeks. Go to circle 3.
3. Consider referral to specialist or may consult clinical pharmacist for recommendations if patient continues to be symptomatic of hypoglycemia on long-acting basal insulin.

No → 6

- Reevaluate compliance with medications, exercise and diet.
- Adjust AM and PM NPH/long-acting basal insulin (ex. insulin glargine) or Regular insulin by 10% of total daily dose (TDD) or 2 units every 3-7 days until FBG and PPG FSBS are at goal.
- Follow up every 2 to 4 weeks as needed.
- Consider referral to specialist or may consult clinical pharmacist for recommendations if FBG and PPG are not at goal.
- Go to circle 3.

Yes → 7

- Return to clinic every month until stable, then follow up in Chronic Care Clinic.
- Obtain A1c* every 3 months. Once A1c is at goal for 6 months (two consecutive lab draws) and FBG/PPG are stable, check A1c every 6 months.
- Obtain CMP, lipid panel, and ACR annually
- Conduct foot & eye exam annually

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider

Table A.

Glycemic Control Index			
	Ideal	Goal	Consider action
Fasting Blood Glucose (FBG)	80-120 mg/dL	90-130 mg/dL	<80 mg/dL or >140 mg/dL
Postprandial Blood Glucose (PPG)	100-140 mg/dL	<180 mg/dL	<100 mg/dL or >180 mg/dL
A1C*	<7%	<7%	>7%

***A1c goal needs to be individualized by the provider:**

- **A reasonable A1c goal for many adults is <7%.**
- **Consider a less stringent A1C goal (<8%) in patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions or long-standing diabetes.**
- **Consider a more stringent A1c goal in patients with a short duration of diabetes mellitus, long life expectancy or no significant cardiovascular disease.**

Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee, March 1997, Revised 9/97,6/01, 4/03, 3/04, 9/06, 9/07, 7/08, 3/10, 11/14, 7/16, 11/20, 3/22, 7/25. Reviewed 3/13.

The pathways do not replace sound clinical judgement nor are they intended to strictly apply to all patients

TYPE 2 DIABETES MELLITUS

1

Random plasma glucose ≥200 mg/dL plus classic symptoms of hyperglycemia OR
Based on two abnormal results from different tests (may be obtained at the same time or same test on separate occasions):
Fasting plasma glucose (FPG) ≥126 mg/dL OR
2-hour plasma glucose (2-h PG) ≥200 mg/dL during an oral glucose tolerance test (OGTT) OR
A1c ≥6.5%?

No → 2 Go to Prediabetes DMG

Yes ↓

3

- Institute Lifestyle Modification & Provide Individual Education with Specific Patient Goals: Weight loss (≥ 7% body weight), exercise plan (150 minutes/week), diet for health (DFH)
- Order Complete Metabolic Panel (CMP), urinary albumin-to-creatinine ratio (ACR), thyroid function, lipid panel and A1c.
- **Initiate metformin 500mg qAM to BID up to 1000mg BID, if there are no contraindication to therapy (Table 2, page 8)**.
- Initiate aspirin and statin if indicated and if there are no contraindications to therapy (Table 2, page 12)
- If BP is >140/90, consider starting ACE-Inhibitor or ARB (see Table 2, page 12 and HTN DMG). A lower target of <130/80 mmHg is recommended for those at higher cardiovascular disease risk or with evidence of microvascular complications, particularly renal disease.
- Evaluate for metabolic-dysfunction-associated steatohepatitis liver disease (MASLD)
- Evaluate for target organ damage and co-morbidities – conduct baseline foot and eye exam
- Refer to Dental for a comprehensive oral/periodontal disease evaluation within 30 days from the initial chronic care visit

4 What is the A1c?

5 A1c <7.5%? Yes → 6 Continue monotherapy with metformin. Go to box 14.

7 A1c ≥9% with symptoms of hyperglycemia (FPG >250mg/dL, weight loss or ketonuria)? See Insulin Initiation on page 4.

8 A1c 7.5 to 9%?

9 A1c ≥9% with no symptoms of hyperglycemia?

10 Does the patient have established ASCVD, heart failure (HFrEF or HFpEF) or CKD*?

Yes → 12 **Initiate Dual Therapy with Metformin and Empagliflozin (nonformulary – Table 2, page 7)**
- Follow up in 2-4 weeks to monitor for signs and symptoms of hypoglycemia and ADRs.

No → 11 **Initiate Dual Therapy with Metformin and Glipizide**.
- Follow up in 2-4 weeks to monitor for signs and symptoms of hypoglycemia and ADRs.

13 Recheck A1c in 3 months. Is A1c at goal of <7% (Table A, page 1)?

Yes → 14
- Continue current therapy.
- Obtain A1c every 3 months. Once A1c is at goal for 6 months (two consecutive lab draws) and FBG are stable, check A1c every 6 months. Follow up in CCC every 6 months.
- Obtain CMP, ACR, and lipid panel annually. Conduct foot and eye exam annually.

No → 15
- Reevaluate compliance with medications, diet and exercise plan.

Initiate Triple Therapy
- If patient is on metformin and glipizide, initiate basal insulin (see Insulin Initiation, box 3 on page 4).
- If patient is on metformin and empagliflozin, consider glipizide or basal insulin (see box 3 on page 4).

16 Recheck A1c in 3 months. Is A1c at goal of <7% (Table A, page 1)?

Yes → 17 Go to box 14

No → 18
- Reevaluate compliance with medications, diet and exercise plan.
- **Initiate Insulin**. See Insulin Initiation pathway on page 4.

*ASCVD = Atherosclerotic Cardiovascular Disease
HFrEF = Heart Failure reduced Ejection Fraction
HFpEF = Heart Failure preserved Ejection Fraction
CKD = Chronic Kidney Disease with Diabetes

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Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee, 3/97, Revised 9/97, 6/01, 4/03, 3/04, 9/06, 9/07, 7/08, 3/10 , 3/13, 11/14, 7/16, 11/20, 3/22, 7/25.

PREDIABETES

The pathways do not replace sound clinical judgement nor are they intended to strictly apply to all patients

1

Prediabetes if one of the following:
FPG 100 to 125 mg/dL OR
A1C 5.7 to 6.4% OR
2-h PG following OGTT 140 to 199 mg/dL

Yes

No

2

If all test normal, rescreen in 3 years (see page 5)

3

Is the patient 25-59 years with BMI ≥ 35 kg/m^2, higher FBG ≥ 110 mg/dL, and higher A1c ≥6.0%, or has history of prior gestational diabetes?

Yes

No

4

- Initiate metformin 500mg qAM to BID up to 1000mg BID, if there are no contraindications to therapy (see Table 2, page 8)
- Follow up in 2-4 weeks to monitor for signs and symptoms of hypoglycemia and ADRs.
- Institute Lifestyle Modification & Provide Individual Education with Specific Patient Goals: Weight loss (≥ 7% body weight), exercise plan (150 minutes/week), diet for health (DFH)
- Refer to Hypertension and Hyperlipidemia DMG, if appropriate
- Rescreen A1c, FBG, OGTT at least annually to assess if patient has progressed to T2DM

5

- Institute Lifestyle Modification & Provide Individual Education with Specific Patient Goals: Weight loss (≥ 7% body weight), exercise plan (150 minutes/week), diet for health (DFH)
- Refer to Hypertension and Hyperlipidemia DMG, if appropriate
- Rescreen A1c, FBG, or OGTT annually

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider

INSULIN INITIATION

1

A1c ≥9% plus symptoms of severe hyperglycemia (FPG >250mg/dL, weight loss or ketonuria) present?

No

Yes

2

Has patient been diabetic ≥ 10 years?

Yes

No

3

Initiate Basal Insulin (insulin glargine or evening NPH) in addition to oral agents

- Do not discontinue metformin. Consider conservative insulin doses if patient is on glipizide and/or empagliflozin.
- Initiation: Start 10 units or 0.1-0.2 units/kg per day
- Titration: increase basal insulin dose by 10% or 2 units every 3 to 7 days until FPG is at goal. For hypoglycemia, reduce dose by 10-20%.

4

Recheck A1c in 3 months. Is A1c at goal of <7% (Table A, page 1)?

Yes

5 Go to box 11

No

6

Assess adequacy of basal insulin dose

- Reevaluate compliance with medications, diet and exercise plan.
- For patients on NPH regimen, consider converting evening NPH regimen to a twice daily regimen: divide TDD and administer 2/3 AM dose and 1/3 PM dose
- Titration: Continue adjusting dose by 10% or 2 units every 3 to 7 days until FBG is at goal.
- Monitor for signs and symptoms of hypoglycemia – if symptomatic, decrease glipizide dose, consider switching to insulin glargine regimen, or reduce dose by 10-20% .
- Consider assessing for overbasalization (see page 10)
- Follow up in 2-4 weeks to assess FSBS.

7

Recheck A1c in 3 months. Is A1c at goal of <7% (Table A, page 1)?

Yes

8 Go to box 11

No

9

Add Prandial Insulin (Regular Insulin)

- Reevaluate compliance with medications, diet and exercise plan.
- Initiation: Add Regular insulin 4 units per day or 10% basal insulin dose (one dose with the largest meal or meal with greatest PPG excursion; prandial insulin can be mixed with NPH regimen but not with Lantus) to cover prandial glucose.
- Titration: Adjust dose by 10% or 2 units every 3 to 7 days until FBG and PPG are at goal.
- Discontinue glipizide. Regular insulin and glipizide are not synergistic.
- Monitor for signs and symptoms of hypoglycemia.
- Follow up in 2-4 weeks to assess FSBS.

10

Recheck A1c in 3 months. Is A1c at goal of <7% (Table A, page 1)?

Yes

11

- Continue current therapy.
- Obtain A1c every 3 months. Once A1c is at goal for 6 months (two consecutive lab draws) and FSBS are stable, check A1c every 6 months. Follow up in chronic care clinic every 6 months.
- Obtain CMP, ACR, and lipid panel annually. Conduct foot and eye exam annually.

No

12

- Reevaluate compliance with medications, diet and exercise plan.
- Adjust basal insulin and/or Regular insulin AM or PM by 10% of TDD or 2 units every 3 to 7 days
- In a stepwise fashion, add Regular insulin at other meal-times (ex. breakfast, dinner and/or lunch). *If on insulin glargine (Lantus), patient will likely need TID pre-prandial Regular insulin. Patients on NPH as basal regimen, may achieve blood glucose goals on BID Regular insulin dosing.*
- Initiation: Regular insulin 4 units or 10% basal insulin dose.
- Titration: Adjust dose by 10% or 2 units every 3 to 7 days until FBG and PPG are at goal.
- **If TDD >200 units/day, consider referral to specialist or consult clinical pharmacist for recommendations.**

13

Initiate Dual Therapy with Metformin and Intensive Insulin Regimen

- Discontinue glipizide if patient is on it. Glipizide and Regular insulin should not be used concomitantly. If patient is on empagliflozin, use conservative insulin doses.
- Initiation: Start insulin based on 0.5 units/kg a day for Total Daily Dose (TDD).
- Allocate 50-66% of TDD to basal insulin (*starting recommendation, ratios may change;* see page 10).
  - Consider 66% TDD with NPH. Administer 2/3 of NPH in the AM and 1/3 of NPH dose in the PM.
  - Consider 50% TDD with insulin glargine (Lantus). If on insulin glargine, a dose may be given once or twice daily. (see Table C, page 10).
- The remaining prandial dose (33-50%) of the TDD is allocated to Regular insulin. (*starting recommendation, ratios may change;* see page 10)
  - If on NPH, divide pre-prandial dose equally before breakfast and supper. Consider 33% of TDD for prandial insulin with NPH regimen.
  - If on insulin glargine (Lantus), divide pre-prandial dose equally before breakfast, lunch, and dinner (*if eating all 3 meals*). Consider 50% of TDD for prandial insulin with insulin glargine regimen.
- Titration: Adjust basal insulin regimen or prandial insulin by 10% or 2 units every 3 to 7 days until FBG and PPG are at goal (not all mealtime regular insulin doses may need to be adjusted).
- Monitor for signs and symptoms of hypoglycemia.
- Follow up in 2-4 weeks to assess.
- If patient is not on empagliflozin and has established ASCVD, heart failure (HFrEF or HFpEF), or CKD, initiate empagliflozin (nonformulary, Table 2, page 9, in addition to intensive insulin regimen and metformin.

14

Recheck A1c in 3 months. Is A1c at goal of <7% (Table A, page 1)?

No

15 Go to box 12

Yes

16

If patient is a recently diagnosed diabetic, glucose toxicity, endogenous insulin secretion and insulin sensitivity may improve with the **Intensive Insulin regimen**. It may be possible to reduce and discontinue insulin and manage patient on oral therapy alone in the following order.

1. Decrease and discontinue scheduled regular insulin.
2. Start glipizide 5 mg daily to BID. Titrate slowly up to 20 mg bid over 2-4 weeks as tolerated.
3. Decrease and discontinue AM NPH dose or insulin glargine (Lantus).
4. Decrease and discontinue PM NPH dose or insulin glargine (Lantus).
5. Maintain patient on metformin and glipizide (+/- empagliflozin).
6. Monitor for hypoglycemia and assess blood glucose to ensure they are at goal.
7. Follow up every 2-4 weeks during this transition.

DIABETES DISEASE MANAGEMENT GUIDELINES

I. Assessment

A. Screening

1. Prediabetes: *Screening and early intervention for patients with prediabetes may improve long-term outcomes*
   a) Asymptomatic patients who are overweight or obese (BMI ≥ 25 kg/m² or BMI ≥ 23kg/m² in Asian Americans) and who have one or more additional risk factors:
      i. Physical inactivity
      ii. First-degree relative with diabetes
      iii. Member of high-risk ethnic population (e.g., African-American, Latino, Native American, Asian American, Pacific Islander) Hypertension (≥ 140/90) or on therapy for hypertension
      iv. HDL Cholesterol level ≤ 35 mg/dl and/or a triglyceride level > 250 mg/dl
      v. History of cardiovascular disease
      vi. Other clinical conditions associated with insulin resistance (e.g., polycystic ovary syndrome (PCOS) or acanthosis nigricans)
      i. Medications to consider glucocorticoids, some HIV medications (ex. protease inhibitors), and atypical antipsychotics are known to increase the risk of diabetes (see Table B below)
   b) If do not meet criteria above, testing should begin at age 35 years.
   c) If results indicate prediabetes (A1c 5.7-6.4%, oral glucose tolerance test (OGTT) 140-199 mg/dL, or fasting plasma glucose (FPG) 100-125 mg/dL), repeat screening annually. If tests are normal, repeat every 3 years.

2. Type 1 Diabetes Mellitus (T1DM) should be considered in individuals that present with acute symptoms of diabetes and cycling between markedly elevated blood glucose levels and severe low blood sugars. Diabetic ketoacidosis may also be part of their past medical history. If diagnosis is uncertain or ambiguous, consider ordering a random C-peptide serum test with concurrent glucose level. Normal range is 0.8-3.5 ng/mL. A low serum c-peptide level is generally indicative of insulin depletion and T1DM. A high c-peptide level is generally indicative of insulin resistance and type 2 diabetes mellitus (T2DM). Results should be interpreted in context of disease duration, comorbidities and family history. Note: if the concurrent glucose is <70 mg/dL or if the patient may have been fasting, consider repeating the test. If results show levels <0.24 ng/mL, repeat lab is not needed. Serum c-peptide level may be falsely elevated in patients with renal disease. Consult with specialist may also be considered to interpret results.

3. Type 2 Diabetes Mellitus
   a) Asymptomatic patients who are overweight or obese (BMI ≥ 25 kg/m² or BMI ≥ 23kg/m² in Asian Americans) and who have one or more additional risk factors:
      i. Physical inactivity
      ii. First-degree relative with diabetes
      iii. Member of high-risk ethnic population (e.g., African-American, Latino, Native American, Asian American, Pacific Islander) Hypertension (≥ 140/90) or on therapy for hypertension
      iv. HDL Cholesterol level ≤ 35 mg/dl and/or a triglyceride level > 250 mg/dl
      v. History of cardiovascular disease
      vi. Other clinical conditions associated with insulin resistance (e.g., PCOS or acanthosis nigricans)
      vii. Medications to consider: glucocorticoids, some HIV medications (ex. protease inhibitors) and atypical antipsychotics are known to increase the risk of diabetes
         - In patients who are prescribed atypical antipsychotics, screen for prediabetes and diabetes at baseline, repeat at 4 months after medication initiation, and annually thereafter (see Psychosis DMG)
         - Table B. Risk for diabetes within atypical antipsychotics:

Low	Aripiprazole	Paliperidone	Lurasidone	Ziprasidone
Moderate	Quetiapine	Risperidone		
High	Clozapine	Olanzapine		

   a) Women who were diagnosed with gestational DM should have lifelong testing every 1-3 years. Please refer to the Pregnancy Wellness DMG for further information.
   b) For all other patients, testing should begin at age 35.
   c) If tests are normal, repeat every 3 years.

DIABETES DISEASE MANAGEMENT GUIDELINES

I. Assessment (*continued*)

A. Diagnostic tests – in the absence of unequivocal hyperglycemia (ex. hyperglycemic crisis), a second confirmatory test is required. Different tests may be obtained at the same time or the same test can be conducted at 2 different time points for diagnosis.
   1. Fasting Plasma Glucose (FPG). Fasting is defined as no caloric intake for at least 8 hours.
   2. 2-hour Plasma Glucose (2-h PG) during an Oral Glucose Tolerance Test (OGTT). Preferred test in pregnancy.
   3. HbA1c (A1c) – test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.
   4. Random Plasma Glucose (PG) plus classic symptoms of hyperglycemia or hyperglycemic crisis.
      a) Symptoms of hyperglycemia
         i. Polyuria
         ii. Weight loss with polyphagia
         iii. Polydipsia
         iv. Fatigue
         v. Blurred vision
         vi. Vaginitis or balanitis
         vii. Extremity numbness/paresthesia
         viii. Acanthosis nigricans

B. Diagnosis

Table 1.

CRITERIA FOR DIABETES MELLITUS DIAGNOSIS			
Lab:	Normal:	Pre-diabetes:	Diabetes:
Fasting Plasma Glucose (FPG)	< 100 mg/dL	100 to 125 mg/dL	≥ 126 mg/dL
Two-hour plasma glucose following oral glucose tolerance test (OGTT)	< 140 mg/dL	140 to 199 mg/dL	≥ 200 mg/dL
HbA1c (A1c)	< 5.7%	5.7 to 6.4%	≥ 6.5%
Random Plasma Glucose (PG)	<140 mg/dL	n/a	≥ 200 mg/dL+ classic symptoms of hyperglycemia

D. Medical history
   1. Age and characteristics of onset of diabetes (e.g., diabetic ketoacidosis, asymptomatic laboratory finding)
   2. Physical activity habits and eating patterns (frequency of going to chow and/or eating out of commissary)
   3. Presence of common comorbidities, psychosocial problems, and periodontal disease
   4. History of smoking, alcohol consumption and substance abuse
   5. Diabetes education, self-management and support history and needs
   6. Review of previous treatment regimens and response to therapy (A1c records)
   7. Review of AM and PM finger sticks *(FSBS*)
   8. Diabetic ketoacidosis and frequency, severity and cause
   9. Hypoglycemia episodes, awareness and frequency and causes
   10. History of blood pressure and lipids
   11. Microvascular complications: retinopathy, nephropathy, neuropathy (sensory and autonomic e.g., sexual dysfunction and gastroparesis)
   12. Macrovascular complications: coronary heart disease, cerebrovascular disease and peripheral arterial disease

E. Physical Examination: Initial visit and CCC
   1. Vitals: blood pressure, height and weight
   2. Thyroid palpitation
   3. Skin examination (e.g., for acanthosis nigricans, insulin injection site reactions, fungal infections)
   4. Comprehensive foot examination, including monofilament exam on feet
   5. Cardiac exam, peripheral vascular exam to include pedal pulses

F. Lab Evaluation
   1. Complete Metabolic Panel (CMP) – obtain annually
   2. Fasting lipid panel – obtain annually
   3. Urinary albumin-to-creatinine ratio (ACR) *Note*: false positives may occur; clinical microalbuminuria is defined as the occurrence of elevated urine ACR for two of three tests within a three-to-six-month period. Measurement of spot urine for albumin only is **not** recommended**.** – obtain annually
   4. A1c – obtain every 3 months, once at goal obtain every 6 months
   5. Thyroid-stimulating hormone (TSH) – obtain every 1-2 years in type 1 diabetes

G. Verify annual dilated eye exam was conducted.

H. Referrals
   1. Dental for comprehensive dental and periodontal examination
   2. Mental health, if indicated

II. Plan/Treatment

A. Diet: Diet For Health is recommended. Patient should be counseled to increase carbohydrate intake from whole grains, vegetables, legumes and dairy products with an emphasis on foods higher in fiber and lower in glycemic load. Refined carbohydrates should be limited, and sugar sweetened beverages and sucrose-containing foods should be avoided.

B. Exercise: If there are no medical contraindications, at least 150 min/week of moderate-intensity aerobic physical activity (50-70% of maximum heart rate), spread over at least 3 days/week with no more than 2 consecutive days without exercise if not contraindicated, T2DM patients should be encouraged to perform resistance training at least twice per week

C. Weight loss: In overweight and obese patient, encourage moderate weight loss (5% of initial body weight)

D. Pharmacologic Therapy:
   1. See Treatment Algorithms and Tables 1 and 2.
   2. Glycemic goals should be individualized by the provider
      a. A reasonable A1c goal for many adults is <7%.
      b. Consider a less stringent A1C goal (<8%) in patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions or long-standing diabetes.
      c. Consider a more stringent A1c goal in patients with a short duration of diabetes mellitus, long life expectancy or no significant cardiovascular disease.
      d. AM fingerstick 90-130 mg/dL and PM fingerstick <180 mg/dL.

E. Control of Co-morbid disease states such as:
   1. HTN – BP goal < 140/90; BP goal of <130/80 in patients with albuminuria. See Hypertension DMG.
   2. Lipid management – Initiate statin therapy, as appropriate. See Hyperlipidemia DMG

F. Vaccinations:
   1. Pneumococcal vaccine
   2. Annual influenza
   3. Covid-19 vaccine vaccine

III. Classification

A. <u>HSM-18 Restrictions</u>: Should be an individualized assessment commiserate with the patient's severity of disease.
   1. Unit of Assignment: If a patient is a brittle Type 1 Diabetic, for example, the patient should be assigned to a unit with 24 hours nursing coverage. Patients with severe diabetes and multi-system end organ disease would be more appropriately monitored at a 24-hour nursing unit or RMF. Diabetics that require BID insulin dosing should be housed at units with at least 12-hour nursing service.
   2. Housing Assignment: For most diabetics, who are stable, no restrictions. However, a severe diabetic should not be assigned to a single cell. Diabetics, who are prone to hypoglycemia or ketoacidosis, should also be restricted to a lower bunk, ground floor and restricted from climbing.
   3. Work Assignment: For patients prone to hypoglycemia or severe hyperglycemic, consideration should be given to restriction from temperature and humidity extremes. Patients with documented peripheral vascular disease and/or neuropathy should not wear steel toed boots and should limit squatting.
   4. ITP: No restrictions unless severe diabetic, then as needed.
   5. Transportation: No restriction unless severe/brittle diabetic that would necessitate nursing/EMS care/monitoring during transport.

PHARMACOLOGIC THERAPY

Table 2. Dosing/Precautions/Contraindications to medications commonly used in Diabetes Management

Medication	Drug Class	Dosing/Precautions/Contraindications
Metformin (Glucophage®) (Formulary)	Biguanide	• Medication of choice for initial treatment of T2DM • Clinical trials have demonstrated efficacy in the use of metformin for the prevention of progression of prediabetes to T2DM in adults, especially those age 25-59 years of age ~~and~~ with BMI of ≥35, higher FBG (ex. ≥110mg/dL), and higher A1c (ex. ≥6.0%), and in women with history of gestational diabetes. For patients who do not meet this criteria, consider assessing risks vs benefits of starting pharmacotherapy. Note: there is currently no FDA approved medication to prevent T2DM in patients with prediabetes. • Before starting metformin, obtain patient's eGFR. o eGFR <30 mL/min/1.73m^2- metformin is contraindicated. If it falls below this level after initiation, discontinue treatment. o eGFR 30 to 45 mL/min/1.73m^2 – initiation of metformin is not recommended. If patient is already on it, assess the benefits and risks of continuing treatment. Continue at maximum dose of 500 mg BID with close monitoring if patient is deriving benefit from treatment. o eGFR >45 mL/min/1.73m^2 – initiate metformin • Dosing: Initiate metformin at 500 mg daily-BID. Titrate up to 1000 mg BID over 2-4 weeks to prevent gastrointestinal intolerance. Once initiated, continue metformin for as long as it is tolerated and not contraindicated. Other agents, including insulin, should be added to metformin. • Discontinue metformin at the time of or before an iodinated contrast imaging procedure in the following patients. Re-evaluate eGFR 48 hours after the imaging procedure. Restart metformin if renal function is stable. o In patient with eGFR 30 to 60 mL/min/1.73m2 o In patients with a history of liver disease, alcoholism, or heart failure o In patients who will be administered intra-arterial iodinated contrast • Caution: o Should be avoided in patients with hepatic insufficiency o Conservative doses should be used in patients aged 80 years or older due to decreased renal function • Contraindications: o Metabolic acidosis, acute or chronic, including ketoacidosis o Hypersensitivity to metformin • Associated with vitamin B12 deficiency. Consider periodic monitoring of vitamin B12 if patient is symptomatic of worsening neuropathy • Beneficial cardiovascular effects • A1c reduction ~1% as monotherapy
Glipizide (Glucotrol®) (Formulary)	Sulfonylurea	• Additional treatment option for T2DM • Dosing: Initiate glipizide at 5 mg daily. Titrate up to 10 mg BID in 5 mg increments over 2-4 weeks as tolerated. (Maximum recommended effective dose: 20 mg/day. Note: labeled maximum dose of 40 mg/day may be appropriate in some patients but can increase risk for hypoglycemia) • Caution: o Weight gain o Hypoglycemia - Counsel patient to take within half an hour prior to eating to avoid hypoglycemia. o Elderly • Contraindications: o Diabetic ketoacidosis o Hypersensitivity to glipizide o Type 1 DM • Avoid use with Regular insulin to reduce risk of hypoglycemia. May be used in conjunction with basal insulin. • Limited efficacy: sulfonylureas' action site are the beta cells of the pancreas. Diabetics have typically depleted their beta cells by year 10, thus making sulfonylureas ineffective. Discontinue glipizide and initiate Intensive Insulin regimen if A1c is not at goal and patient has been diabetic for over 10 years. • Neutral cardiovascular effects • A1c reduction 0.7 to 1.3% as monotherapy

Medication	Drug Class	Dosing/Precautions/Contraindications
Empagliflozin (Jardiance®) (Non-Formulary)	Sodium-Glucose Cotransporter 2 Inhibitor (SGLTI2i)	• Additional treatment option for T2DM with CKD, Heart Failure (HFrEF or HFpEF) or established ASCVD • Dosing: Initiate dose at 10 mg once a day. There appears to be little difference in efficacy between the 10 mg dose and 25 mg dose. The difference in mean A1c reduction between the two doses is generally <0.2%. • T2DM + CKD criteria o eGFR 20 to 59 mL/min/1.73m2. Continue until initiation of dialysis. Note: glucose-lowering efficacy is reduced with GFR <45 mL/min/1.73m2. o Urinary Albumin Creatinine Ratio (UACR) >30mg/g, particularly >300mg/g • Heart failure criteria – reduced ejection fraction or preserved ejection fraction • ASCVD criteria o History of MI o Evidence of multi-vessel CAD (coronary artery disease) in >/= 2 major coronary arteries or the left main artery o Unstable angina with evidence of single or multi-vessel CAD o History of stroke (ischemic or hemorrhagic) o Peripheral artery disease (PAD), documented by limb angioplasty, stenting, bypass surgery, limb or foot amputation, evidence of PAD (>50% on angiography), ankle brachial index <0.9 in ≥ 1 ankle • Caution: o Hypotension – SGLT2i cause intravascular volume contraction. Symptomatic hypotension may occur after initiation. Monitor for signs and symptoms, particularly in patients with eGFR <60 mL/min/1.73m^2, the elderly, those taking diuretics (may need to be adjusted) or have low systolic blood pressure (blood pressure meds may need to be adjusted). Volume status should be assessed and corrected before initiation in patients with these characteristics. o Hypoglycemia – There is an increased risk of hypoglycemia when used with insulin or glipizide. Dose reductions in insulin or glipizide may be required. o Ketoacidosis – Do not use SGLT2i in T1DM. Assess patients who present with signs and symptoms of metabolic acidosis for ketoacidosis, regardless of blood glucose levels. Monitor and possibly temporarily discontinue SGLT2i during periods of prolonged fasting due to illness or surgery. o Acute kidney injury (AKI) and impairment in renal function – SGLT2i can increase serum creatinine and decrease eGFR. Baseline and periodic monitoring of renal function is recommended. o Urosepsis and Pyelonephritis – SGLT2i increase the risk of urinary tract infections. Counsel patient to have adequate fluid intake. Evaluate patients for signs and symptoms of urinary tract infections and treat promptly. o Genetic mycotic infections: SGLT2i increase the risk of genital mycotic infections. Uncircumcised males and patients with history of genital mycotic injections are at higher risk. o Fournier's Gangrene (rare adverse event) - Patient should seek immediate attention if they experience any symptoms of tenderness, erythema, or swelling in the genital or perineal area, fever, or malaise o Hypersensitivity reactions – Hypersensitivity reactions including serious reactions (e.g., angioedema) have been reported . If a hypersensitivity reaction occurs, discontinue use and treat per standard of care. If serious reaction occurs, the SGLT2i should not be restarted. o Amputation – No increase in lower extremity amputation has been reported for empagliflozin. Additional studies are needed to assess if amputations are a class effect or limited to canagliflozin. Before initiating, consider factors that may increase the risk of amputation, such as history of prior amputation, peripheral vascular disease, neuropathy, and diabetic foot ulcers. Instruct patient to seek medical attention if they notice any new pain or tenderness, sores or ulcers, or infections in his/her legs or feet. o Increased LDL - Increases in LDL may occur. Monitor LDL and treat per standard of care. o Pregnancy Category C – Empagliflozin is not recommended during the 2nd and 3rd trimesters. • Contraindications: o History of hypersensitivity to empagliflozin o Dialysis o End stage renal disease • Beneficial cardiovascular effects • Beneficial renal effects • A1c reduction 0.4% to 0.7%

Table 2. Dosing/Precautions/Contraindications to medications commonly used in Diabetes Management

<table>
<tr><th>Medication</th><th>Drug Class</th><th>Dosing/Precautions/Contraindications</th></tr>
<tr><td>Regular, Novolin R® – prandial insulin (Formulary)

NPH, Novolin N® – basal insulin (Formulary)

Insulin glargine, Lantus® - basal insulin (Formulary)</td><td>Insulin</td><td>
• Reduced symptomatic awareness of hypoglycemia may occur in those with long-standing diabetes, recurrent hypoglycemia, or beta blocker use; increased monitoring is recommended.
• Infection, fever, dehydration, trauma, surgery or stress can increase the risk of hyperglycemia; monitoring and dose adjustment may be necessary.
• Caution:
o Hypoglycemia
o Weight gain
• Contraindicated in hypersensitivity to any component of the formulation
• When to use Regular Insulin Sliding Scale:
o Insulin regular sliding scale may be used temporarily, <u>in addition</u> to fixed dose regular insulin when initiating insulin and during dose titration to achieve fingerstick goals.
o Reassess regular insulin needs after 2-4 weeks. Adjust the fixed dose of regular insulin and discontinue the regular insulin sliding scale.
o Regular sliding scale should not be used long-term or in place of fixed regular insulin for glycemic control as it treats hyperglycemia after it occurs. “The American Association of Clinical Endocrinologists (AACE), the American Diabetes Association (ADA), and the Endocrine Society all discourage the use of sliding scale insulin alone as the sole method for controlling inpatient blood glucose levels. Scheduled subcutaneous administration of insulin is the preferred method for achieving and maintaining glucose control in non-critically ill patients with diabetes or stress hyperglycemia. In fact, prolonged use of CORRECTIONAL sliding scale insulin without a scheduled dose is ineffective for most patients with diabetes and can be dangerous in patients with type 1 diabetes. A number of published articles have also focused on the problems associated with sliding scale insulin, primarily related to the heightened risk of errors with this dosing method and the “roller coaster” effect on blood glucose levels that often results. Authors of a literature review concluded that fluctuating glucose levels are more harmful physiologically than levels that are continuously elevated.”
• Overbasalization is defined as the titration of basal insulin beyond clinically necessary in attempt to achieve glycemic targets. This may occur due to high doses of basal insulin and insufficient mealtime insulin. Overbasalization can be identified by basal insulin dose >0.5 units/kg/day, A1c not at goal despite FBG at target, or recurrent complaints of hypoglycemia. Post-prandial hyperglycemia should be targeted with Novolin R insulin dose administration.
• Avoid therapeutic inertia. Delaying insulin initiation or titrations for patients not at glycemic goals can lead to lack of optimal diabetes care.
• Glargine (Lantus®, Semglee) – formulary long-acting basal insulin.
o Preferred in patients with frequent hypoglycemia with NPH insulin or T1DM patients
• A1c reduction 1.5% to 3.5%
• Avoid combination of NPH and insulin glargine (Lantus, Semglee) as this is duplication of basal insulin, increasing risk for
hypoglycemia

Table C. Pharmacokinetics of Insulin:
<table>
<tr><td>Insulin</td><td>Onset of action</td><td>Peak Action</td><td>Effective duration</td></tr>
<tr><td>Regular Insulin (Novolin R®)</td><td>30 to 60 min</td><td>2 to 3 hours</td><td>8 to 10 hour</td></tr>
<tr><td>NPH Insulin (Novolin N®)</td><td>2 to 4 hours</td><td>4 to 10 hours</td><td>14 to 24* hours</td></tr>
<tr><td>Glargine (Lantus®, Semglee)</td><td>2 to 4 hours</td><td>No peak</td><td>22** to 24 hours</td></tr>
</table>
*Due to the variability in duration of action, NPH is most often dosed twice daily to achieve sustained control over 24 hours

**Some patients with type 1 diabetes may experience reduced duration of action, consider administering Lantus twice daily. May also consider splitting regimen to twice daily in patients on higher doses (ex. >50 units/day) where impaired absorption may be suspected.

The pharmacokinetics of insulin preparations may be used to determine which insulin to adjust <u>when</u> a patient is experiencing symptoms of low or high blood glucose.

Examples:

1. If patient is symptomatic of hypoglycemia around 9am and he or she injected NPH and Regular insulin at 4am, most likely it is the NPH that needs to be adjusted as it is peaking 5 hours after injection.

2. If patient is symptomatic of hypoglycemia or hyperglycemia roughly an hour after a meal, the Regular insulin will need to be adjusted as its onset of action is faster than the NPH.
</td></tr>
</table>

Table 2. Dosing/Precautions/Contraindications to medications commonly used in Diabetes Management

Insulin Dosing and Conversion	• **Starting NPH/Regular insulin** o Total Daily Dose (TDD) = 0.5 units/kg/day o Designate 66% of TDD to the NPH insulin and 33% of TDD to the Regular insulin (can also consider 50%/50% for a more conservative regimen; proportion may depend on several factors including but not limited to diagnosis of T2DM vs T1DM, carbohydrate consumption, age, pregnancy status, and puberty stage) o Administer 2/3 of NPH dose in the AM and 1/3 of NPH dose in the PM o Divide the Regular insulin portion into 2 equal parts to give in the AM and in the PM o Example: 40kg patient needs to be started on NPH and Regular insulin 40kg x 0.5 units/kg/day = 20 units TDD 66% of 20 units = 13 units of NPH; 33% of 20 units = 7 units of Regular Insulin 2/3 of 13 units = 9 units of NPH qAM, 1/3 of 13 units = 4 units NPH qPM 7 units/2 = ~4 units of Regular Insulin qAM and qPM • Notes: o NPH is cloudy, Regular insulin is clear. o Patient receives 2 injections/day because insulins may be mixed and administered in the same syringe. o Converting from long-acting basal insulins to NPH ▪ Reduce dose by 20% (administer 80% of total basal insulin dose) ▪ Administer NPH twice daily: 2/3 in the AM and 1/3 in the PM • **Starting Glargine (Lantus®, Semglee)/ Regular insulin** o Total Daily Dose (TDD) – 0.5 units/kg/day o Designate 50% of TDD to the glargine in the AM or PM. In some instances (ex. doses >50 units/day, patients with type 1, suspicion of impaired absorption despite adherence) , splitting the dose twice daily may exhibit better control. o Administer half of the glargine insulin in the morning and the other half in the evening o Split the regular insulin into three portions to be taken before breakfast, lunch and dinner (if patient is eating all 3 meal). Note: Lantus and Novolin R cannot be mixed; Lantus regimen may consist of up to 5 injections per day. If a patient is routinely skipping a meal, consider not ordering scheduled insulin for that mealtime. o Example: 40kg T1DM patient needs to be started on glargine 40kg x 0.5 units/kg/day = 20 units TDD 50% of 20 units = 10 units of glargine insulin, 10 units (remaining 50%) of Regular Insulin 10 units of glargine can be administered once a day, or 5 units can be administered twice a day. 10/3 = 3 units of regular insulin before breakfast, lunch and dinner. • Notes: o Do not mix glargine with other insulins (ex. Novolin R). If mixed, the properties of Lantus will be altered. o Patient receives 4-5 injections/day and needs to come to medical three times a day o NPH to glargine conversion: administer 80% of total NPH total daily dose and administer glargine once a day • **Switching from NPH + Regular insulin regimen to insulin glargine (Lantus®, Semglee) + Regular insulin** o Example: Current regimen of NPH 32 units qAM + 16 units qPM and Regular insulin 6 units BID o Total daily dose of basal= 48 units & total bolus daily dose= 12 units o To switch to insulin glargine once daily, administer 80% of the total daily basal dose to prevent hypoglycemia =38 units daily (administered AM or PM) o Since insulin glargine is relatively peakless, it is needed to change prandial insulin from Regular twice daily to three times daily before each meal (*Note*: if a patient is routinely skipping a meal, consider not ordering scheduled insulin for that mealtime). With NPH twice daily regimen, there is peak activity which covers lunch time blood glucose without need of Regular insulin qNOON. o Split bolus daily dose to three times daily (before each meal): 12/3= 4 units before breakfast, lunch, and dinner (if eating all 3 meals) • Notes: o Do not mix glargine with other insulins (ex. Novolin R). If mixed, the properties of Lantus will be altered. o Patient receives 4-5 injections/day and needs to come to medical three times a day o NPH to glargine conversion: administer 80% of total NPH total daily dose and administer glargine once (or twice) daily (see Table C, page 10) • **Switching from Glargine (Lantus®, Semglee) + Regular insulin to NPH twice daily + Regular insulin regimen** o Example: Current regimen of Lantus 40 units qPM and Regular insulin 4 units TID before meals o Total daily dose of basal= 40 units & total bolus daily dose= 12 units o To switch to twice daily NPH from once daily insulin glargine dose, administer 80% of the total daily basal dose to prevent hypoglycemia = 32 units total basal regimen should be split & administered as 2/3 in the AM & 1/3 in the PM. New NPH regimen should consists of 21 units qAM + 11 units qPM o The total bolus daily dose (12 units) should be split by half and administered twice daily before breakfast and dinner= 6 units BID o Note: With NPH twice daily regimen, there is peak activity which covers lunch time blood glucose without the need of Regular insulin at NOON. • Notes: o NPH is cloudy, Regular insulin is clear. o Patient receives 2 injections/day because insulins may be mixed and administered in the same syringe. o Converting from long-acting basal insulins to NPH ▪ Reduce dose by 20% (administer 80% of total basal insulin dose) ▪ Administer NPH twice daily: 2/3 in the AM and 1/3 in the PM

Table 2. Dosing/Precautions/Contraindications to medications commonly used in Diabetes Management

Medication	Drug Class	Dosing/Precautions/Contraindications
Lisinopril (Prinivil®, Zestril®) (Formulary)	Ace-Inhibitor (ACE-I)	• Dosing: Lisinopril 5 mg to 40 mg daily • First-line option for blood pressure control in patients with diabetes and albuminuria • Not recommended to be used as a nephroprotective drug in diabetic patients without hypertension • Avoid concomitant use of ACE inhibitors with angiotensin receptor blockers: dual renin-angiotensin system blockers do not provider additional benefit in comparison to monotherapy • Caution: Hyperkalemia; increased risk in patients with renal impairment, diabetes mellitus, or with concomitant use of potassium-sparing diuretics or potassium supplement. Serum creatinine and serum potassium monitoring is recommended. • Contraindications: o ACE-inhibitor induced angioedema o Hereditary or idiopathic angioedema o Pregnancy o Hypersensitivity to lisinopril or other ACE inhibitors
Losartan (Cozaar®) (Formulary)	Angiotensin Receptor Blocker (ARB)	• Dosing: Losartan 25 mg to 100 mg daily • First-line option for blood pressure control in patients with diabetes and albuminuria • Not recommended to be used as a nephroprotective drug in diabetic patients without hypertension • Avoid concomitant use of angiotensin receptor blockers with ACE inhibitors: dual renin-angiotensin system blockers do not provider additional benefit in comparison to monotherapy • Caution: Hyperkalemia; increased risk in patients with renal impairment, diabetes mellitus, or with concomitant use of potassium-sparing diuretics or potassium supplement. Serum creatinine and serum potassium monitoring is recommended. • Other warnings: o ARB induced angioedema o Hereditary or idiopathic angioedema • Contraindication: o Pregnancy
Aspirin (Ecotrin®) (Formulary)	Anti-platelet	• Dosing: Aspirin 81 mg daily for secondary prevention in diabetics with history of ASCVD • For patients with atherosclerotic cardiovascular disease and documented aspirin allergy, clopidogrel (75 mg/day) may be considered. • Consider low dose aspirin for primary prevention in patients with diabetes and increased cardiovascular risk (e.g., patients ≥50 years of age with at least one additional major risk factor: family history of premature atherosclerotic cardiovascular disease, hypertension, dyslipidemia, smoking or albuminuria) who are not at increased risk of bleeding. • Contraindications: o Syndrome of asthma, nasal polyps and rhinitis o Inherited or acquired bleeding disorders (including factor VII and factor IX deficiency o Pregnancy (3rd trimester) o Hypersensitivity to salicylates, other NSAIDs, or any component of the formulation
Pravastatin (Pravachol®) and Atorvastatin, Lipitor®) (Formulary)	Anti-hyperlipidemic (Statin)	• Dosing: Atorvastatin 10-20 mg (moderate intensity) or 40 -80 mg daily (high intensity), Pravastatin 40 mg qHS (moderate intensity) • High intensity statin is recommended: o Secondary prevention o Clinical ASCVD risk score of 20% or over o LDL >190 mg/dL and ≥20 years old o Age 40-75 and LDL 70-189 mg/dL with multiple risk enhancers* • Moderate intensity statin is recommended: o Age 20-39 with risk enhancers* o Age 40-75 with ≤ 1 risk enhancer* • Caution: Myopathy and rhabdomyolysis is a risk; monitoring is recommended and discontinue statin immediately if myopathy is suspected or diagnosed. • Contraindications: o Active liver disease o Unexplained persistent elevations of serum transaminases o Pregnancy and in breastfeeding o Hypersensitivity to statins or any component of the formulation *Risk enhancers: long history of diabetes (≥10 years T2DM,≥20 years T1DM), albuminuria, eGFR <60 mL/min, retinopathy, neuropathy, ankle-brachial index (ABI) <0.9

EDUCATION FOR PATIENTS AND PRACTITIONERS

I. Who is educated?
   A. Unit Practitioners – updated on diabetes so accurate and easy to understand information is provided to patients.
   B. All patients with diabetes or prediabetes
      1. Type 1 diabetics - absolute deficiency in insulin secretion.
      2. Type 2 diabetics - a combination of resistance to insulin action and inadequate compensatory insulin secretory response.
      3. Prediabetic – precursor before the diagnosis of type 2 diabetes; at risk for developing resistance to insulin action and inadequate compensatory insulin secretory response.

II. Who educates?
   A. The Unit Team will delegate educational responsibility
      1. Educator must document date and time of education in patient's chart.
      2. Physician, Mid-level Provider, or Clinical Pharmacist have final responsibility to ensure education occurs (if not documented on chart as completed by some other designated education provider, must provide diabetes education at clinic visit).

III. The unit medical staff will provide counseling on diet and how to choose the correct foods from the meal line.

IV. When does education take place? At every clinic visit.

V. What is included in diabetes education? (to include health services personnel and diabetic patients)
   A. Pathophysiology of Type 1 versus Type 2 diabetes, risk for developing type 2 if prediabetic
   B. Non-pharmacologic treatment plan & importance of lifestyle modifications
   C. Signs, symptoms, and treatment for acute complications of diabetes mellitus
      1. Hypoglycemia
         a. Signs and symptoms – dizziness, lightheadedness, shakiness, blurry vision
         b. Treatment - Counsel patient to ingest 15 grams of carbohydrates (i.e., 1 slice of bread, 4-5 small pieces of candy, ½ can of soda, 4oz of orange juice). Have the patient wait 15 minutes for blood glucose to rise. If patient continues to be symptomatic, counsel patient to have another 15 grams of carbohydrates or to seek medical attention.
      2. Hyperglycemia
         a. Signs and symptoms – polyuria, polyphagia, polydipsia, blurry vision
         b. Treatment – exercise, hydration, diet counseling and pharmacotherapy
      3. Diabetic Ketoacidosis
         a. Signs and symptoms – Polyuria, polyphagia, polydipsia, acute abdominal pain, nausea, shortness of breath, altered mental status, sinus tachycardia, ketotic breath
         b. Labs – serum ketones, anion gap/metabolic acidosis
         c. Treatment – manage as inpatient or as an emergent issue
   D. Monitoring parameters – frequency and importance
      1. A1c – Done every 3 months (if not at goal) or every 6 months (if at goal). A1c signifies overall control of patient's diabetes. If prediabetic, repeat at least annually.
      2. Finger sticks – Ordered at the provider's discretion. This depicts a snapshot of patients' blood glucose at the current time. The patient should be counseled to take the finger stick before the meal (i.e., breakfast and supper). They should know what his or her goals are and should be encouraged to self record his or her finger sticks and bring the log to his or her clinic appointments.
   E. The importance of insulin – Patients should be counseled that diabetes is a progressive disease and that eventually he or she may be started on insulin. Insulin should be presented in a positive light, as the most effective measure to control blood sugars. It should not be viewed as a threat or retaliation in response to uncontrolled blood sugars. Thoroughly counsel patient on potential side effects (i.e., hypoglycemia and possible weight gain), and how to manage them. Counsel patient to administer insulin before meals and that it is important not to skip meals when on insulin.
   F. Proper techniques of administering insulin for all patients on insulin (i.e., proper self-administration, insulin preparation, mixing, and administration sites)
   G. Chronic complications of diabetes (i.e., retinopathy, neuropathy, nephropathy, cardiovascular, cerebrovascular, and peripheral vascular disease) and means for prevention
   H. Patient self monitoring to include foot, skin, and wound care
      Foot/skin care tips:
      1. Watch for pain, numbness, and/or wounds that will not heal
      2. Keep skin supple by drinking plenty of water. Never put lotion or moisturizers between the toes.
      3. Wash feet daily with lukewarm water and soap
      4. Dry feet well, especially between the toes
      5. Check feet daily (including bottoms and between toes) for sores, redness, and swelling
      6. Change into clean socks daily
      7. Keep feet warm and dry
      8. Never walk barefoot
      9. Keep toenails trimmed
      10. Examine shoes daily for things that could hurt your feet such as rocks or debris
   I. Dental hygiene to include daily brushing in the morning and evening and flossing once daily.

Initial Assessment of Suspected Overdose
Management of Diphenhydramine, Benztropine, & Anticonvulsant Overdose

1

ASSESSMENT FOR SUSPECTED OVERDOSE

Patient presents stating he/she has taken an overdose of pills:

1. Obtain print pass
2. Document - WHAT, HOW MANY, TIME THEY TOOK IF AVAILABLE (Patient may have taken another patient's medication).
3. Initiate patient evaluation and assess level of consciousness. Monitor vital signs, oxygen saturation, & EKG. Initiate basic life support as indicated.
4. Monitor for side effects:
   a. Common (mild-moderate poisoning): Somnolence, anticholinergic effects (mydriasis, blurred vision, flushing, fever, dry mouth, urinary retention, decreased bowel sounds), tachycardia, nausea, and vomiting are common after overdose
   b. Moderate poisoning: Agitation, confusion, and hallucinations
   c. Severe poisoning: Delirium, psychosis, seizures, coma, respiratory depression, and ventricular dysrhythmias including torsades de pointe
5. Call Poison Center 1-800-222-1222 to report incident.

2 Suspected overdose of Diphenhydramine, Benztropine, or Anticonvulsants?

Yes

3 OBTAIN APPROPRIATE LAB STUDIES

Patient presents early and
- is fully conscious,
- has protected airway,
- is not at risk for GI perforation or hemorrhage and
- has not also ingested corrosives?

No

4 Consider patient medical history and exposure to other poisons. If patient is symptomatic transfer to ER.

The pathways do not replace sound clinical judgment nor are they intended to apply to all patients.

No

5 Stabilize patient and provide general and supportive care, provide airway management if indicated. Transfer to ER.

Yes

6 Does the suspected overdose exceed the maximum daily dose?

(See Dosing Table page 2)

No

8 Administer 8 ounces of Activated Charcoal slurry (Actidose®)

9 Observe 4-6 hours in the medical department.

- Consider additional courses of charcoal as clinically indicated.
- Consider repeat EKG to monitor for QT prolongation, ventricular arrhythmia, or heart block as clinically indicated.
- Obtain report and if asymptomatic release patient.
- Schedule follow up appointment next day and consider Mental Health referral.

Yes

7 Administer 8 ounces of Activated Charcoal slurry (Actidose®)

AND

Transfer to the nearest Emergency Room

Call 911 and follow unit protocol. For UTMB, if ambulance is not immediately available, call 911.

Call Utilization Review/ Utilization Management

Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee.
Approved March 2011. Reviewed November 2014, March 2019, Nov 2023

Therapeutic and Toxic Doses

Diphenhydramine, and Benztropine Therapeutic and Toxic Doses		
Drug	**Usual Therapeutic Dosing**	**Maximum Daily Dose**
Benztropine	0.5-6 mg/day	6 mg/day
Diphenhydramine	25-50 mg q 4-8h	400 mg divided

Divalproex Therapeutic and Toxic Doses			
Drug	**Usual Therapeutic Dosing**	**Maximum Daily Dose**	**Usual Toxic Serum Level**
Valproic Acid	1500-2500 mg/day	60 mg/kg	>150 mcg/mL

Phenytoin Therapeutic and Toxic Doses			
Drug	**Usual Therapeutic Dosing**	**Maximum Daily Dose**	**Usual Toxic Serum Level**
Phenytoin	300-400 mg/day	1,200 mg divided	>20 mcg/mL

Carbamazepine Therapeutic and Toxic Doses			
Drug	**Usual Therapeutic Dosing**	**Maximum Daily Dose**	**Usual Toxic Serum Level**
Carbamazepine	200-1200 mg/day	1600 mg divided	>15 mcg/mL

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider**.

Gastrointestinal Pathways

The protocol does not replace sound clinical judgment nor is it intended to strictly apply to all patients.

Present?	Symptom / Disease
☐ Yes ☐ No	Acute GI Bleed → Refer to Acute GI Bleed algorithm
☐ Yes ☐ No	Epigastric discomfort, early satiety, postprandial fullness/bloating → Refer to Dyspepsia algorithm
☐ Yes ☐ No	Heartburn and regurgitation (with or without dyspepsia symptoms) → Refer to GERD algorithm
☐ Yes ☐ No	H. Pylori Positive → Refer to H. Pylori algorithm
☐ Yes ☐ No	Ulcer → Refer to Peptic Ulcer Disease algorithm

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ACUTE GI BLEED TRIAGE

1

Obtain patient history

- Medical history – prior GI bleed, hemorrhoids, hepatic disease, peptic ulcer disease, malignancy, comorbidities (esp. heart, respiratory, or renal disease)?
- Medication history – NSAID, steroid, iron, ASA, anticoagulant or antiplatelet agents?
- Associated symptoms – bleeding, dizziness, confusion, angina, palpitations, cold/clammy extremities, weakness, epigastric pain, dysphagia, GERD, anorexia, abdominal pain, changes in bowel movements?

Complete physical exam

- Signs of hypovolemia – resting tachycardia (HR > 100 bpm), tachypnea (RR > 20/min), orthostatic hypotension (SBP decrease > 20 mmHg, DBP decrease > 10 mmHg, or HR increase > 20 bpm), supine hypotension (SBP < 80 mmHg), cold extremities, poor mentation. (Note: hematocrit is a poor early indicator of blood loss)
- Assess for acute abdomen (guarding, rebound tenderness, rigidness)
- Perform rectal exam
- Assess for physical signs of liver disease
- Assess for active bleeding – hematemesis, hematochezia, melena

2

Signs of hypovolemia?
(SBP < 100, RR > 20/min, HR > 100 bpm, orthostatic hypotension)
OR
Evidence of active hemorrhage?
Consider significant history or associated symptoms placing patient at high risk of severe GI bleeding. Note: age > 60, liver disease, and comorbid conditions (heart, respiratory, or renal disease) are associated with higher risk of severe GI bleeding.

Yes

No

3

Unstable patient and/or apparent GI bleed

- Activate EMS/911 system
- Establish IV access and NS infusion
- Administer oxygen by nasal cannula or mask

4

Stable patient with possible GI bleed

Based on clinical presentation, further evaluation and/or observation may be indicated as follows:

- Consider close monitoring for new signs of GI hemorrhage or loss of hemodynamic stability (see Box 3)
- Consider transfer to nearby 24 hr unit or Emergency Room for evaluation / monitoring
- Consider laboratory studies (CBC, CMP, PT/PTT)
- Consider urgent or expedited referral to GI or tele-consult
- Consider risks associated with continuation versus cessation of antiplatelets, anticoagulants, and NSAIDs (CV risk vs. bleeding risk)
- Provide clinical education to patient based on presumptive diagnosis

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients

Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee, Approved May 2012; Reviewed 11/2015, 5/2020, 5/2025, 11/2025. Revised 3/2025.

DYSPEPSIA

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1 Dyspeptic symptoms defined as predominant epigastric pain/discomfort (postprandial bloating/fullness or early satiety) lasting for greater than 1 month

2 Heartburn and/or regurgitation are presenting complaint, predominant or frequent (more than once a week)?

Yes → 3 Manage as GERD ***See GERD Algorithm***

4 Chronic NSAID use?

5 Discontinue NSAID if possible. If not, consider lower dose and/or change to PRN.

6 Evaluate Patient Characteristics

7 Age ≥ 60 or alarm features (First degree relative with upper GI malignancy, unintended weight loss, iron-deficiency anemia, odynophagia, persistent vomiting)

7 → 9 Refer for GI Endoscopy Clinic for Endoscopy

Abnormal Pathology → 10 Manage based on pathology causing dyspepsia.

If Peptic Ulcer Disease, refer to **Peptic Ulcer Disease algorithm**

Normal (no other cause found) → 11 Functional Dyspepsia

8 Age < 60 years without alarm features

12 Test and, if positive, treat for H. pylori See **H. pylori Algorithm** **When treated, or if negative, continue to Box #13**

13 Symptoms Resolved?

Yes → 14 Discontinue therapy. Follow PRN.

No → 15 Initiate Proton Pump Inhibitor (PPI) trial x 8 weeks Omeprazole 20 mg daily

16 Symptoms Resolved?

No → 17 Stop PPI and begin metoclopramide 10 mg TID x 8 weeks

19 Symptoms resolved?

Yes → 20 Discontinue therapy. Follow PRN. If patient relapses after medication discontinuation, consider specialty referral

No → 21 Reassess diagnosis. Consider specialty referral.

Yes → 18 Discontinue therapy. Follow PRN.

22 Symptoms recurred?

Yes → 23 Repeat 8-week course of Omeprazole 20 mg daily. Go to Box #16

Alternate: Famotidine 20 mg daily or twice daily

*Metoclopramide

- Cautions/contraindications: Patients with increased risk for extrapyramidal symptoms, GI obstruction, perforation or hemorrhage, pheochromocytoma, depression or epilepsy.
- Chronic treatment with metoclopramide can cause tardive dyskinesia, a serious movement disorder that is often irreversible. The risk of developing tardive dyskinesia increases with the duration of treatment and the total cumulative dose. The elderly, especially elderly women, are most likely to develop this condition.

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GASTROESOPHAGEAL REFLUX DISEASE

1 Alarm features/symptoms present (i.e., unexplained weight loss, GI bleeding, dysphagia, vomiting, anemia, odynophagia, aspiration pneumonia, dysphonia, recurrent/persistent cough, persistent pain, lymphadenopathy, epigastric mass, new onset symptom at age 45 to 55 years, family history of esophageal/gastric cancer)?

Yes → 2 Consider specialty referral.

No ↓

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3 **IMPLEMENT LIFESTYLE MODIFICATIONS AND ELIMINATE MODIFIABLE RISK FACTORS WHEN POSSIBLE**

1. Weight loss.
2. No eating 2-3 hours prior to bed.
3. No reclining after eating.
4. Avoid known irritants.
5. Rule out drug induced problems, such as agents that reduce LES tone (e.g., theophylline, estrogens, opiates, NSAIDs, calcium channel antagonists) and agents that may cause upper gastrointestinal tract injury and exacerbate reflux-like symptoms (e.g., potassium supplements, tetracyclines, bisphosphonates, and anticholinergics).
6. Discontinue NSAID usage when possible. If not, consider lower dose and/or change to PRN.
7. Smaller meal size especially the last meal of the day.
8. Sleep on left side

OTHER FACTORS NOT APPLICABLE OR FEASIBLE AT TDCJ

1. Avoid alcohol.
2. Smoking cessation.
3. Elevation of the head of the bed (do not approve extra mattress).
4. Small frequent meals (do not approve AM & HS snacks).
5. Avoid late meals.

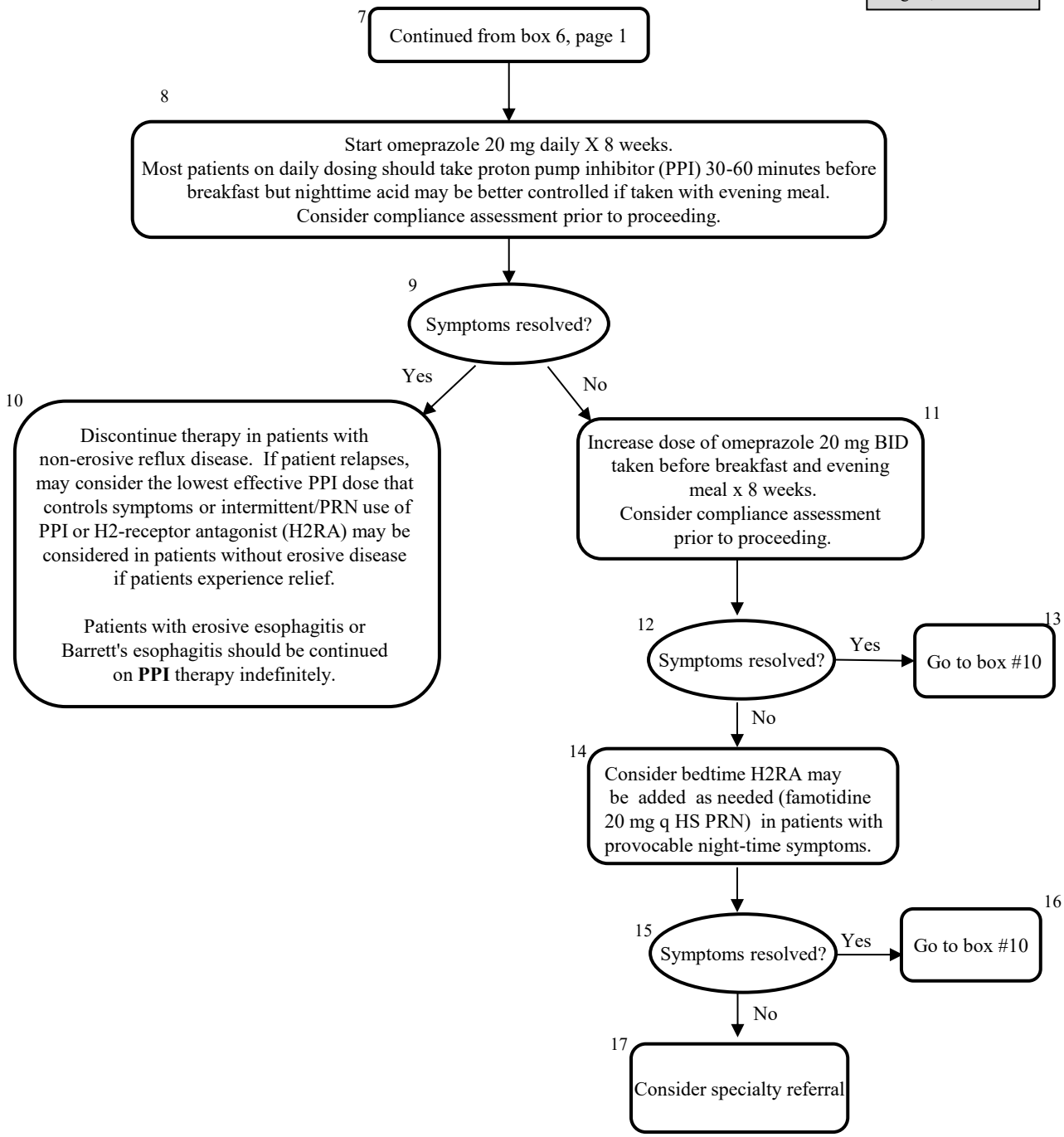
↓

4 Symptoms resolved with lifestyle modifications?

Yes → 5 Continue lifestyle modifications

No ↓

6 Go to Box #7, Page 2



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H. Pylori Treatment

1

Test (using the Fecal Antigen Test) for *H. Pylori* infection in the following patients:

1. Active Peptic Ulcer Disease (PUD) or History of PUD if cure for H. pylori has not been documented
2. Functional dyspepsia, or dyspepsia symptoms with risk factors. Risk factors may include:
    a. Patients taking long-term NSAIDS or starting long-term treatment with low-dose aspirin
    b. Patients with unexplained iron-deficiency anemia (can consider after evaluation of other causes and lack of sufficient response after treatment with oral iron)
    c. Patients with secondary idiopathic thrombocytopenic purpura
3. Patients who are at high risk of gastric adenocarcinoma:
    a. Patients who have autoimmune gastritis OR current or a history of gastric premalignant conditions, early gastric cancer resection, or gastric adenocarcinomas OR a first degree relative with gastric cancer

2 *H.pylori* positive?

No → 3 Consider other diagnosis (e.g., GERD, nonulcer dyspepsia)

Yes

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4

Consider *Helicobacter pylori* Infection treatment with combination therapy for 14 days

First-Line Regimens:

- **Bismuth Quadruple Therapy (BQT):**
    - Metronidazole 500 mg QID
    - Omeprazole 20 mg BID
    - Bismuth Subsalicylate 262 mg 2 tabs QID
    - Tetracycline 500 mg QID*

Alternative Regimens: ***(See text for further information)***

- **Rifabutin Triple Therapy:**
    - Amoxicillin 1000 mg TID
    - Rifabutin 150 mg BID
    - Omeprazole 40 mg TID

Consider a GI consult or Pharmacotherapy consult for other alternative suggestions.

Educate patients on the importance of medication adherence and completion of all 14 days therapy to prevent the likelihood of resistance and ensure the resolution of H pylori infection.

*= Requires a nonformulary request

Go to Box #5, Page 2

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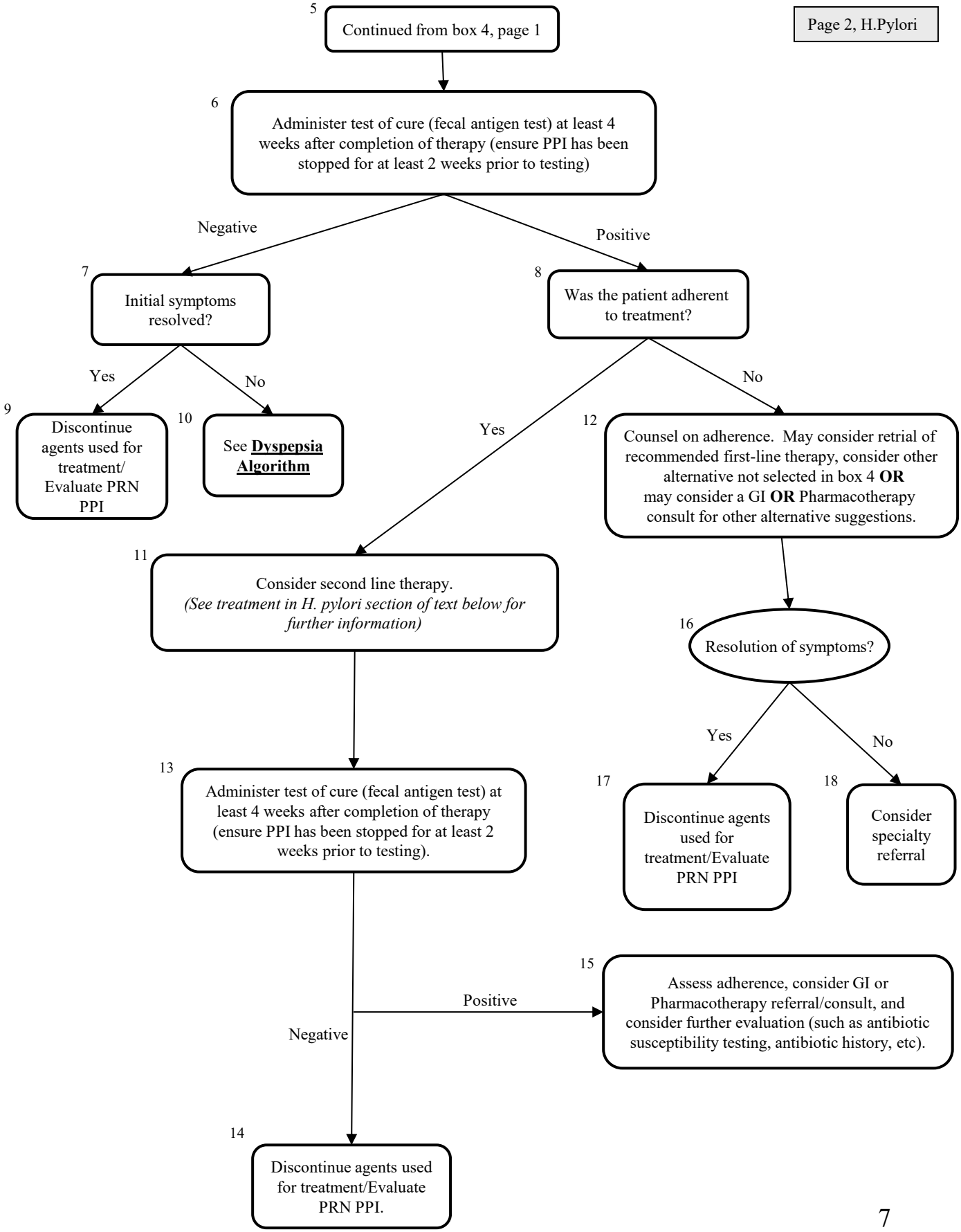

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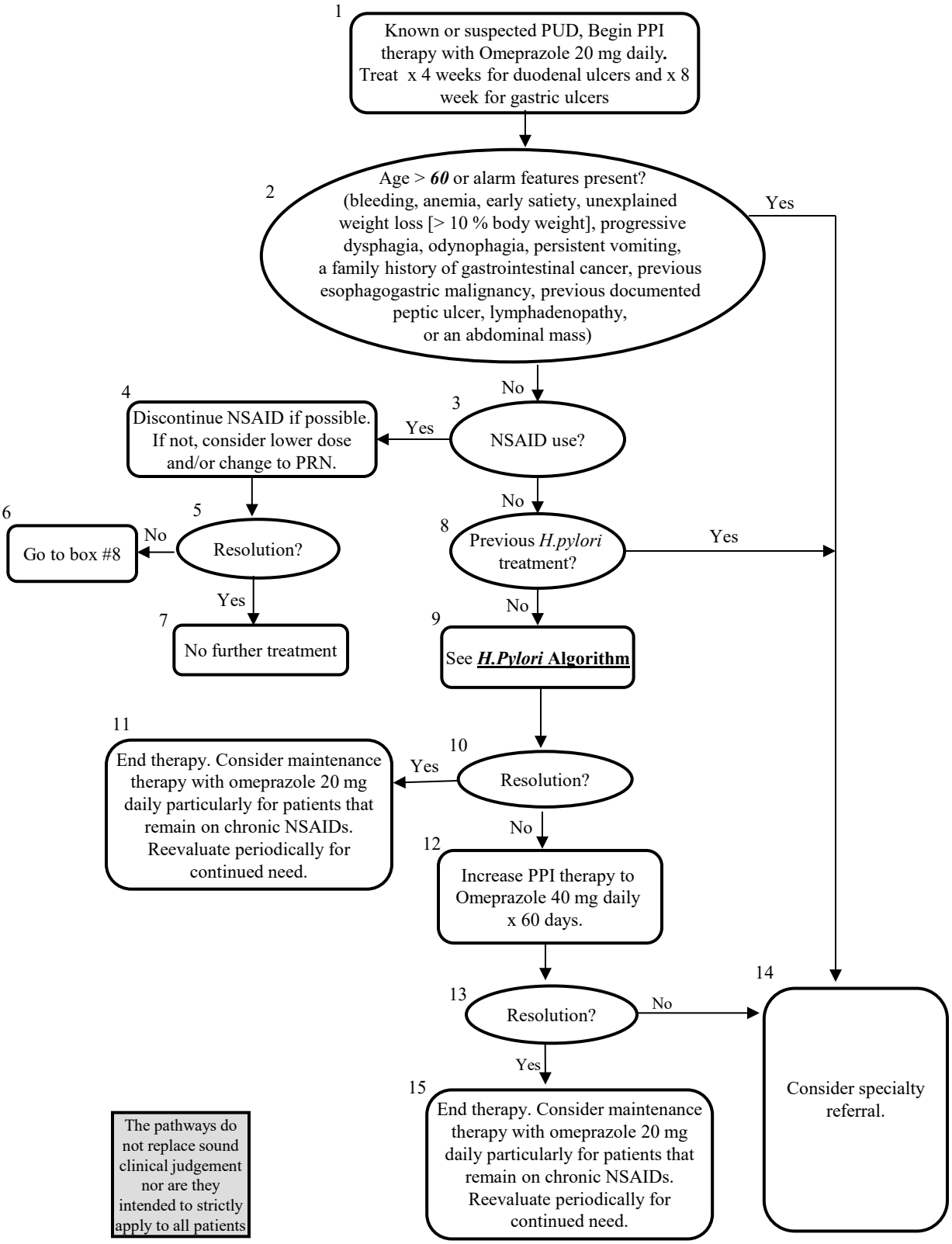
Peptic Ulcer Disease (PUD)



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I. Acute Gastrointestinal Bleed (GIB)

a. Definition - GIB refers to bleeding from the gastrointestinal tract. The bleeding may come from any site along the gastrointestinal tract and is usually divided into:
   i. Upper GIB: Includes bleeding from the esophagus, stomach, and duodenum, and
   ii. Lower GIB: Includes bleeding from the large intestines, rectum, and anus

b. Causes:
   i. Peptic ulcers: accounts for up to 50% of cases
   ii. Esophageal varices
   iii. Hemorrhoids
   iv. Gastrointestinal cancers
   v. Mallory-Weiss tears
   vi. Gastroduodenal erosions
   vii. Erosive esophagitis (due to non-steroidal anti- inflammatory drugs (NSAIDs) or alcohol use)
   viii. Medications such as anticoagulants, antiplatelets, and NSAIDs

c. Common clinical presentations:
   i. Hematemesis
   ii. Hematochezia
   iii. Melena

d. Diagnosis:
   i. History of symptoms:
      1. Peptic ulcer: abdominal pain
      2. Esophageal ulcer: odynophagia, gastroesophageal reflux, dysphagia
      3. Mallory-Weiss tear: emesis, retching, hematemesis, melena, hematochezia
   ii. Drug history: NSAID, aspirin, antiplatelet and anticoagulant use
   iii. Past medical history: previous episodes of upper GIB, varices or portal hypertension, peptic ulcer disease, GI malignancy, alcohol abuse, Helicobacter pylori (H. pylori) infection
   iv. Past surgical history: previous abdominal surgery
   v. Physical examination:
      1. Vitals: pulse (assess for tachycardia), blood pressure (assess for orthostatic/supine hypotension)
      2. Signs of shock: cold extremities, tachycardia, tachypnea, hypotension, confusion, delirium, oliguria
   vi. Lab monitoring: CBC, CMP, PT/INR
   vii. Upper endoscopy for upper GIB

e. Management:
   i. Hemodynamically unstable patients: activate the emergency response system
   ii. Hemodynamically stable patients: consider transfer to nearby 24-hour facility or ER for further evaluation/monitoring or consider urgent or expedited referral to GI or tele-consult
   iii. Stop NSAIDs, antiplatelets, anticoagulants if feasible

II. Dyspepsia

a. Definition - Dyspepsia is defined as predominant epigastric pain lasting for at least 1 month. Approximately 25% of patients with dyspepsia are found to have an underlying organic disease on diagnostic evaluation; however, about 75% of patients have functional (idiopathic or non-ulcer) dyspepsia.

b. Causes - Most causes of functional dyspepsia are from:
   i. Gastroesophageal reflux disease (GERD)
   ii. Peptic ulcer disease (PUD)
   iii. Helicobacter pylori (H. pylori)
   iv. Anti-inflammatory drugs like NSAIDs and steroids
   v. Gastrointestinal malignancy (increased risk for those over 60 years old)

c. Symptoms:
   i. Dyspepsia also causes other upper gastrointestinal (GI) symptoms such as:
      - Heartburn
      - Nausea
      - Vomiting
      - Fullness
      - Bloating
      - Epigastric discomfort

II. Dyspepsia

a. Symptoms:

ii. Alarm features/symptoms –Consider specialty referral for patients presenting with any of the following:

- New onset dyspepsia in patients > 60 years old
- Significant weight loss (>10% of usual body weight over 6 to 12 months)
- Overt gastrointestinal bleeding
- Unexplained anemia
- Dysphagia
- Odynophagia
- Persistent vomiting
- First-degree relative with gastrointestinal cancer
- Rapidly progressive alarm features
- Not responding to first and second-line recommended therapies

b. Diagnosis:

i. Patient's current symptoms (e.g., upper abdominal pain, nausea, vomiting, early satiety, bloating)

ii. Upper endoscopy:

1. Patients who have an endoscopy may be identified to have an abnormal pathological cause for their dyspepsia, including malignancy, peptic ulcer disease, or esophagitis
2. Patients who have an endoscopy with normal findings and predominant epigastric pain are considered to have functional dyspepsia.

c. Treatment:

i. Non-pharmacological management

1. Eat smaller meals
2. Refrain from smoking and drinking alcohol (not applicable to TDCJ patients)
3. Abstain from consuming coffee and carbonated beverage
4. Stop medications that may irritate the stomach lining (such as aspirin or anti-inflammatory drugs)
5. Find ways to reduce stress such as getting adequate rest and meditation

ii. Pharmacological management

1. All patients under the age of 60 years old with dyspepsia symptoms should be tested for H.pylori through a non-invasive test. See the **H. pylori Treatment Algorithm and Text** for more information.
2. Proton pump inhibitors (PPIs) (e.g., omeprazole (Prilosec®)): PPIs are the most effective agents in treating symptoms of dyspepsia.
3. Long term risks associated with PPI therapy
    a. Fractures: Increased incidence of osteoporosis-related bone fractures of the hip, spine, or wrist may occur with long term PPI therapy (>1 year); however, osteoporosis should not affect the decision to use PPI long-term except in patients with other risk factors for hip fracture. Consider formulary calcium + vitamin D supplementation in patients at risk of osteoporosis.
    b. Clostridium difficile (C. diff): Use of PPIs long term may increase the risk of C. diff associated diarrhea.
    c. Vitamin B_{12} deficiency: Prolonged treatment (>3 years) may lead to vitamin B_{12} malabsorption and subsequent vitamin B_{12} deficiency. The magnitude of the deficiency is dose-related, and prevalence is decreased after discontinuation of therapy.
    d. Recommended to avoid scheduled use of PPIs for more than 8 weeks or dose reduce in older adults unless patients are high-risk (eosinophilic esophagitis or Barrett's esophagus)
    e. Prokinetic agents (e.g., metoclopramide (Reglan®)): Metoclopramide may be a helpful second line agent for patients who fail first line PPI therapy. Metoclopramide can be trialed for a maximum of 12 weeks for symptom resolution.
    f. Prokinetics have frequent side effects that limit their usefulness, including fatigue, drowsiness, restlessness, headaches, dystonic reactions, seizures, suicidal ideations, and tardive dyskinesia. Metoclopramide has a black box warning to avoid use for more than 12 weeks to prevent the occurrence of tardive dyskinesia which is associated with long term use

III. Gastroesophageal Reflux Disease (GERD)

a. Definitions: GERD is defined as symptoms or complications resulting from the reflux of gastric contents back into the esophagus or beyond. It is the most common GI disorder, which is often chronic and relapsing. GERD is classified further as symptoms without erosions, also known as Nonerosive reflux disease (NERD) or symptoms with erosions, also known as Erosive esophagitis (EE). NERD is present in about 50-70% of the US population with GERD and may progress to EE in ~10% of these patients.

b. Causes:
   i. Reduced lower esophageal sphincter pressure (muscle tone)
   ii. Delayed gastric emptying

c. Symptoms:
   i. Typical symptoms
      1. Regurgitation
      2. Heartburn (daytime or nocturnal)
   ii. Alarm features/symptoms

Table 1. Alarm Features and Symptoms Requiring Further Endoscopy and Referral

Dysphagia	Odynophagia	Iron-deficiency anemia
Dysphonia	Early Satiety	Persistent epigastric pain
GI Tract Bleeding	Epigastric mass	Progressive, unintentional weight loss
Hypersalivation	Extraesophageal symptoms (ie. Chronic cough, hoarseness, wheezing, aspiration pneumonia)	Frequent nausea and/or vomiting
Lymphadenopathy		Gastrointestinal cancer in first degree relative

d. Diagnosis:
   i. Patient reported symptoms of heartburn and regurgitation
   ii. Upper endoscopy: recommended only in the presence of alarm symptoms
   iii. Patients with reported chest pain should have diagnostic evaluation before institution of therapy

e. Treatment:
   i. Non-pharmacological management:
      1. Weight loss for overweight patients
      2. Avoid high fat meals 2-3 hours before bedtime for patients with nocturnal GERD
      3. Abstain from foods that trigger reflux (including chocolate, caffeine, alcohol, acidic and/or spicy foods)
   ii. Pharmacological management:
      1. When choosing medications for GERD, it is reasonable to choose the lowest effective dose of the medication and consider stepping up therapy in patients with poor response.
      2. The efficacy of PPIs is maximized when PPIs are taken 30 to 60 minutes before breakfast, for patients taking it once daily, and 30- 60 minutes before the last meal of the day as well, for patients taking it twice daily due to partial response to once daily therapy.
      3. Overall, PPIs have been associated with superior healing rates and decreased relapse rates compared with H2 receptor antagonists and placebo, in patients with EE. Maintenance PPI therapy should be administered for GERD patients who continue to have symptoms after PPI is discontinued, especially in patients with complications including EE.
      4. H2 receptor antagonist (H2RA) therapy may be considered for maintenance therapy in patients without erosive disease (NERD) if patients experience relief (Conditional recommendation, moderate level of evidence). Note that tachyphylaxis may develop after one or more weeks of continued use. Bedtime H2RA therapy has also been recommended with daytime PPI therapy in select patients that remain symptomatic with provocable night-time symptoms (Conditional recommendation, low level of evidence). If clinical tolerance develops, may consider intermittent use.
      5. About two-thirds of NERD patients will have a symptomatic relapse upon discontinuation of PPIs over time. For these patients, the guidelines recommend considering intermittent antacid or PPI therapy (on-demand therapy).
      6. It has been estimated that about 70-80% of patients with EE and about 60% of patients with NERD will demonstrate complete response from PPI therapy after a standard 8-week course of PPI therapy, taken once or twice daily.

ii. Pharmacological management (continued)

6. Failure to respond to PPI therapy is typically seen in patients who have atypical symptoms, presence of hiatal hernia, extraesophageal symptoms, longer disease duration, poor compliance, and obesity.
7. Refractory GERD can be managed by confirming compliance and ensuring appropriate dosing. Consider specialist referral for patients who do not respond to twice daily PPI dosing.

f. Complications of GERD:

i. Erosive esophagitis: This is one of the most common complications of GERD. It is also called reflux esophagitis. It occurs when the lining of the esophagus has been inflamed due to damage from the abnormal reflux of gastric acid.
ii. Peptic Stricture: This results from chronic acid injury and scarring of the lower esophagus.
iii. Barrett's Esophagus: This is a serious complication of chronic GERD where the lining of the esophagus changes to resemble the intestine. This is a precancerous condition. Patients with Barrett's esophagus have approximately a 30-fold increased risk of developing esophageal cancer.
iv. Esophageal Cancer

Table 2. Formulary GERD Medications

Drug class	Formulary medication (s)	Mechanism of action	Drug properties	Adult dosing	Side effects
Antacids	Calcium carbonate chewable ($CaCO_3$), 420 mg (NP); 500 mg Magnesium hydroxide suspension, ($Mg(OH)_2$) 30 mL (NP)	Antacids work by neutralizing gastric acid, thus increasing gastric pH	Provides relief within minutes, but the duration of relief is short (30 – 60 minutes). Good for use in intermittent GERD or for relief of mild, infrequent GERD symptoms	$CaCO_3$ 420mg: 1-6 tablets TID x 3 days; maximum: 8 g (19 tabs)/day $CaCO_3$ 500mg: 1-3 tablets TID x 2 weeks; maximum: (10 tabs)/day $Mg(OH)_2$: 1 UD (30 mL) daily as needed at bedtime x 3 days; take with 8 oz of liquid. Do not exceed 60 mL in 24 hours.	Unpleasant taste Calcium: constipation, bloating, belching Magnesium: loose stools
H2-antagonists	Famotidine 20 mg	H2RAs reversibly bind to histamine at the gastric parietal cells and block gastric acid secretion	Provides relief within 60 minutes; duration of relief is 10-12 hours Good for use in intermittent GERD or for relief of mild, infrequent GERD symptoms. May also be used for residual acid reflux despite maximal PPI therapy. Recommended to be taken 10-60 minutes before eating foods or drinking beverages known to cause heartburn.	20 mg BID x 2 weeks 20 mg once daily at bedtime for residual acid reflux despite maximum PPI therapy	Constipation, diarrhea, dizziness, headaches.
PPIs	Omeprazole 20 mg	PPIs work by irreversibly binding to the gastric parietal cells and blocking gastric acid secretion	The duration of relief is for up to 3 days. Considered most effective agents for GERD. Recommended for maintenance therapy in patients with erosive esophagitis, strictures, and Barrett's esophagus. Recommended to be taken 30-60 minutes before meals for maximal pH control.	20 mg daily **x 8 weeks** Increase to 20 mg BID x 8 weeks if no symptom resolution with once daily therapy.	Headache, dizziness, abdominal pain, gas, nausea, vomiting, *C.diff* diarrhea, osteoporosis related fractures, hypomagnesemia, vitamin B12 deficiency with prolonged use

IV. H. pylori

a. Definition - *H. pylori* infection is one of the most common chronic gastrointestinal bacterial infections in the world (affects two-thirds of the world's population). *H. pylori* bacteria is a key constituent of the human microbiome, associated with PUD, chronic gastritis, gastric adenocarcinoma, and gastric mucosa associated lymphoid tissue (MALT) lymphoma.

b. Causes - *H. pylori* infection is usually acquired during childhood (unclear mechanism of action), or through contaminated water or food. It may be passed from person to person through direct contact with vomit, fecal matter, or saliva.

c. Symptoms - Most people with *H. pylori* infection will not show any signs or symptoms. Other patients will show gastrointestinal symptoms from complications of *H. pylori* (PUD, dyspepsia). Refer to GERD (Section III.C.2) for a list of alarm features which may be suggestive of a gastrointestinal malignancy.

d. Diagnostic tests:

   i. Fecal Antigen Test (also used for testing for H. pylori eradication). Preferred for diagnosis of acute disease at UTMB units.

   ii. Urea Breath Test (also used for testing for H. pylori eradication).

   iii. Antibody Serologic Test (detects IgG antibodies). Does not distinguish between recent and past infection, or between disease and colonization. In low prevalence areas, as in much of the United States, a positive serologic test is more likely to be a false positive. Secondary testing with a stool or breath test to confirm the initial result is appropriate before initiating treatment. However, a negative test may help exclude infection in a patient with a low pretest probability of infection. Serologic testing is also considered acceptable in patients with documented active PUD because of higher pretest probability of infection.

e. Testing for *H. pylori* infection:

   i. Patients who should be tested for *H. pylori* infection include:

      1. Patients with active or a history of peptic ulcer disease
      2. Patients with persistent dyspeptic symptoms (not previously treated for *H. pylori*) or with uninvestigated dyspepsia, under the age of 60 years old
      3. Patients with *H. pylori*-associated Mucosa Associated Lymphoid Tissue lymphoma
      4. Patients who require primary or secondary prevention of gastric adenocarcinoma because they are high risk

   ii. Prior to testing for infection, all antibiotics, bismuth, and PPI therapy should be withheld for at least 2 weeks.

f. Treatment:

   i. All patients with an indication for testing should be offered treatment if confirmed to have active infection.

   ii. Pharmacologic therapies typically consist of a combination of antibiotics and gastrointestinal agents for **14 days** (refer to *H. pylori* treatment algorithm). See Table 3 for details on regimens for patients who have not been treated before (treatment naïve patients).

      1. Rifabutin Triple Therapy and Bismuth Quadruple Therapy are recommended first line agents.
      2. The American College of Gastroenterology discusses lower rates of eradication from substituting doxycycline 100 mg BID for tetracycline 500 mg QID for Bismuth Quadruple Therapy. It is highly encouraged that providers speak with a Clinical Pharmacist (PCPS) if doxycycline or an alternate regimen is being considered.

   iii. If patients fail first line therapy, providers can provide an alternate regimen as outlined in Table 3 that was not provided previously. If the patient received a modified version of Bismuth Quadruple Therapy or Rifabutin Triple Therapy, Bismuth Quadruple Therapy can be provided again, but using tetracycline 500 mg QID. A non-formulary request will be required. If Bismuth Quadruple Therapy with tetracycline was provided initially, Rifabutin Triple Therapy can be provided.

g. H. pylori eradication testing:

   i. It is recommended to test all patients for eradication upon completion of *H. pylori* treatment to ensure prevention of downstream sequelae of *H. pylori* infection

   ii. If eradication testing is performed, it is recommended after 4 weeks of therapy completion and after withholding of all antibiotics, bismuth, and PPI therapy for at least 2 weeks.

   iii. Testing 4 weeks after treatment will allow any surviving *H. pylori* to regrow to detectable levels. This will also avoid false negative results.

   iv. Ensure patients are followed up at least 2 weeks after therapy completion. In general, if symptoms are persistent or recurrent 2 weeks after treatment completion, this could imply treatment failure.

h. Factors that cause medication non-adherence:

   i. Therapy duration
   ii. Complexity of medication regimen
   iii. Adverse effects or fears about adverse effects
   iv. Misunderstanding or lack of information
   v. Poor communication
   vi. Inappropriate expectations

g. Importance of medication adherence:
   i. Medication adherence is one of the best ways to predict successful *H. pylori* eradication.
   ii. Failure to take at least 80% of the prescribed medicine is strongly predictive of treatment failure.
   iii. Failure of eradication often leads to antibiotic-resistant strains of the bacteria.
   iv. Educate patients that it is better not to treat than to treat inadequately because that could resistant strains.

Table 3. First-Line Regimens and Clinical and Logistical Pearls
(All treatment regimens must be taken for14 days)

Regimen Name and Agents to Order	Clinical and Logistical Pearls
Bismuth Quadruple Therapy • Tetracycline 500 mg 1 cap QID • Metronidazole 500 mg 1 cap QID • Bismuth Subsalicylate 262 mg 2 tab QID • Omeprazole 20 mg 2 cap BID	• Recommended as a first line therapy by American College of Gastroenterology • Consider alternative therapy in patients with penicillin allergy. • **Tetracycline is a nonformulary agent, and a request will need to be placed prior to prescribing.** • Note that tetracycline may be associated with more gastrointestinal side effects.
Rifabutin Triple Therapy • Amoxicillin 500 mg 2 cap TID • RifaBUTin (Mycobutin®) 150 mg 1 cap BID • Omeprazole 20 mg 2 cap TID	• Recommended as a first line therapy by American College of Gastroenterology • Consider alternative therapy in patients with penicillin allergy. • RifaBUTin interacts with medications such as cobicistat- and ritonavir-based HIV regimens, protease inhibitors, and bictegravir – not dolutegravir. It will also interact with CYP3A4 inducers (phenytoin, carbamazepine, etc), inhibitors, and substrates (ie. Warfarin). Please consider consulting a pharmacist before prescribing.

V. Peptic Ulcer Disease (PUD)

a. Definition - Peptic ulcers are open gastrointestinal (GI) sores that may line the inside of the stomach or small intestine. The word "peptic" implies the cause of the ulcer is due to stomach acid. The two types of peptic ulcers are gastric ulcers and duodenal ulcers.

Table 4: Differences in Symptoms between Gastric and Duodenal Ulcers in Peptic Ulcer Disease

Gastric ulcer	Duodenal ulcer (Most common)
Ulcer forms in the lining of the stomach	Ulcer forms in the lining of the small intestine
Forms due to normal secretion of stomach acid	Forms due to hypersecretion of stomach acid
Pain occurs 1-2 hours after a meal	Pain occurs 2-3 hours after a meal
Ingestion of food does not relieve pain/sometimes increases pain	Ingestion of food relieves pain
Vomiting co-occurs	Dark, tarry stools (Melena) occurs
Peak age is 50-60 years	Peak age is 35-45 years

b. Causes and risk factors:
   i. *H. pylori*
   ii. NSAIDs:
      1. NSAIDs cause ulcers by interrupting the natural ability of the stomach and the duodenum to protect against stomach acid.
      2. NSAIDs can also interfere with blood clotting, which is important for bleeding ulcers
      3. People who take NSAIDs for a long time and/or at high doses, have a higher risk of developing ulcers.

c. Symptoms:
   i. About 70% of patients have no symptoms. However, the most prominent symptom is upper abdominal pain.
   ii. Atypical symptoms: Weight loss, Nausea/vomiting, Epigastric fullness, Dark, tarry stools/ bleeding, Diarrhea, Trouble sleeping, Burping

d. Diagnosis:
   i. PUD may be suspected in patients with dyspepsia, especially in the setting of NSAID use or a history of *H. pylori* infection
   ii. Upper endoscopy (should be reserved for patients with alarm symptoms)

e. Treatment:
    i. Goals: Relieve pain, Heal the ulcer, Prevent ulcer recurrence, Reduce ulcer-related complications
    ii. Drug therapy and duration
        1. PPIs are preferred to H2 receptor antagonists for treating ulcers due to their rapid symptom relief and ulcer healing properties.
        2. PPIs are more effective in preventing NSAID-induced gastroduodenal toxicity and in healing gastroduodenal ulcers associated with NSAIDs when they cannot be discontinued.
        3. The overall duration of treatment should be between 4 – 8 weeks, depending on location/severity of ulcer. Treat for 4 weeks for uncomplicated duodenal ulcers and for 8 weeks for gastric ulcers or any complicated ulcer

f. Prevention:
    i. Avoid NSAIDs and consider using alternative formulary pain medications such as Acetaminophen (Tylenol®) if possible or only use NSAIDs PRN.
    ii. Consider prophylactic PPI therapy for the following patients:
    iii. Patients with a history of NSAID-induced ulcers who require daily NSAID therapy
    iv. Patients with active bleeding peptic ulcers
    v. Patients > 60 years taking long term steroids or anticoagulants

Gender Dysphoria Hormone Monitoring Guideline

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

Terms:
GD: Gender Dysphoria
GDC: Gender Dysphoria Clinic

1

Patient presents to the medical department and requests GD evaluation or treatment

2

Initial Assessment:

1. Obtain Past Medical History: prior history of GD treatment or work-up and assess for possible contraindications to therapy (refer to page 4, section IV.B)
2. Prior GD medical and mental health records from the free world providers who diagnosed and/or treated the offender should be requested
3. Perform complete physical exam
4. Obtain Baseline Labs: CBC, lipid profile, CMP, prolactin, testosterone, estradiol, A1c, LH, FSH
5. Complete referral to GDC or expedite referral if patient is already on hormone therapy at intake
6. Documentation of patient education and written consent only if continuing hormone at intake
7. Inform patient that evaluation is required by GDC prior to starting treatment in patients not currently receiving GD treatment. If the patient is receiving GD treatment at intake, they should be continued on the same documented hormone regimen, unless medically contraindicated, until they are evaluated by GDC (refer to page 2, section II.A).

3

Was a GD diagnosis confirmed by GDC?

Yes

No

4

Was the decision made to start hormone therapy?

No

5

Pt will be informed by GDC

Yes

6

The patient will be scheduled for chronic care clinic after initiation of hormone therapy and the unit provider will be notified if spironolactone is ordered, to facilitate monitoring of potassium levels and renal function. Avoid concomitant use of potassium sparing medications (see Table 1).

7

Medical Treatment Plan:

- Evaluate the patient at least every 3 months in the first year and then 1-2 times per year to monitor for development of adverse reactions, comorbid disease states, drug-drug interactions, and risks associated with hormone therapy.
- Refer to Tables 5 & 6 for evaluation of labs and management of laboratory abnormalities.
- Refer to Table 3 for risks associated with hormone therapy.

Nurses: DMGs are to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.**

I. Terms
- A. Gender Dysphoria (GD) – is defined as the clinically significant distress or impairment that is associated with the marked incongruence between one's experienced or expressed gender and one's assigned gender for a specific time (e.g., of at least 6 months duration). The diagnosis can be made with a concurrent disorder of sex development.
- B. Intersex – a person whose sexual or reproductive anatomy or chromosomal pattern does not seem to fit typical definitions of male or female. Intersex medical conditions are sometimes referred to as sex development disorders.
- C. Transgender – a person whose gender identity (i.e., internal sense of feeling male or female) is different from the person's assigned sex at birth.
- D. Male-to-female (MtF) – transgender person who is born as a male (male sex by birth) but whose gender identity is a woman (or in-between man and woman). Also known as transgender woman or trans woman.
- E. Female-to-male (FtM) – transgender person who is born as a female (female sex by birth) but whose gender identity is a man (or in-between woman and man). Also known as transgender man or trans man.

II. Initial Assessment
- A. Screening
  1. At intake, a patient with a reported history of GD prior to incarceration will receive thorough medical and mental health evaluations.
  2. The patient will be continued on the same documented hormone regimen, if any, upon arrival into TDCJ, unless medically contraindicated. Hormone therapy will be ordered as prior authorization medications by the unit provider to ensure that continuity of care is maintained during the initial evaluation process. Prior authorization criteria must be met and noted in the special instructions field of the order. Criteria include: GD.
  3. If continuing hormones at intake, obtain documentation of patient education and written consent which are required prior to ordering the medications. For this documentation, refer to the Treatment of Offenders with Intersex Conditions, or Gender Dysphoria, Formerly Known as Gender Identify Disorder Policy (Number: G-51.11) located in the Correctional Managed Health Care Policy Manual.
- B. Past Medical history
  1. Prior history of GD treatment or work-up
  2. Assessment for possible contraindications to therapy
  3. Prior medical and mental health records from the free world providers who diagnosed and/or treated the patient should be requested
- C. Physical Exam
  1. Perform complete physical exam
- D. Baseline Labs
  1. CBC
  2. Lipid profile
  3. CMP
  4. Prolactin
  5. Testosterone
  6. Estradiol
  7. A1c
  8. LH
  9. FSH
- E. Complete referral to GDC for GD evaluation and documentation of patient education and written consent

III. Treatment options
- A. Pharmacologic therapy: a treatment plan MtF or FtM will be selected and managed by GDC. Unit providers should not initiate hormone treatment regimens, except for continuation at intake (pending **GDC** evaluation). Refer to Table 1 for hormone treatment options.
- B. Physical changes anticipated during treatment
  1. FtM: Refer to table 2 for masculinizing effects in FtM transgender persons.
     a. Potentially irreversible changes include, but are not limited to: deepening of voice, development of facial and body hair, fat redistribution, genital changes, infertility, male pattern baldness.
  2. MtF: Refer to table 3 for feminizing effects in MtF transgender persons.
     a. Potentially irreversible changes include, but are not limited to: breast growth, fat redistribution, genital changes, infertility.

Table 1. Hormonal Therapy in Patients with Gender Dysphoria

	Dosing*	Formulary Status	Comments
MtF Transgender Persons			
ESTROGEN			
Oral estradiol	2-6 mg PO per day	Prior authorization: GD diagnosis	
Parenteral estradiol cypionate	5-30 mg IM every 2 weeks 2-10 mg IM every week	Prior authorization: GD diagnosis	When possible, test hormone level midway between injections.
ANTI-ANDROGENS			
Spironolactone	50 mg PO BID – 200 mg PO BID	Formulary	Contraindicated to remain on therapy with renal insufficiency and/or potassium > 5.5 mmol/L. Use cautiously in patients who are receiving digoxin, ACE inhibitors and potassium sparing diuretics.
Finasteride	5 mg PO daily	Prior authorization: GD diagnosis	May be an option for those unable to tolerate, or with contraindications to the use of spironolactone
FtM Transgender Persons			
TESTOSTERONE			
Parenteral testosterone cypionate	100-200 mg IM every 2 weeks	Prior authorization: GD diagnosis	When possible, test hormone level midway between injections. Approximately 15% of patients will experience elevations in liver enzymes.
PROGESTERONE			
Oral medroxyprogesterone	5-10 mg PO once daily	Prior authorization: GD diagnosis	Progesterone considered if menses persists. Weight gain and depression are side effects.
Parenteral medroxyprogesterone	150 mg IM once every 3 months	Prior authorization: GD diagnosis	Progesterone considered if menses persists. Weight gain and depression are side effects.

*Maximum dosing does not mean maximal effect. Furthermore, these dosage ranges do not necessarily represent a target or ideal dose. Dose increases should be based on patient response and/or monitored hormone levels. Some patients may require less than this amount, and some may require more.

Table 2. Masculinizing effects in FtM transgender persons

Effect	Onset	Maximum
Skin oiliness/ acne	1-6 months	1-2 years
Facial/ body hair growth	6-12 months	4-5 years
Scalp hair loss	6-12 months	
Increased muscle mass/ strength	6-12 months	2-5 years
Fat redistribution	1-6 months	2-5 years
Cessation of menses	1-6 months	
Clitoral enlargement	1-6 months	1-2 years
Vaginal Atrophy	1-6 months	1-2 years
Deeping of voice	6-12 months	1-2 years

Table adapted from Hembree et al. (2017).

Table 3. Feminizing effects in MtF transgender persons

Effect	Onset	Maximum
Redistribution of body fat	3-6 months	2-3 years
Decrease in muscle mass and strength	3-6 months	1-2 years
Softening of skin/ decreased oiliness	3-6 months	Unknown
Decreased libido	1-3 months	3-6 months
Male Sexual dysfunction	Variable	Variable
Breast growth	3-6 months	2-3 years
Decreased testicular volume	3-6 month	2-3 years
Decreased sperm production	Unknown	>3 years
Scalp hair	Variable	
Voice changes	None	

Table adapted from Hembree et al. (2017). Copyright 2017, The Endocrine Society

IV. Monitoring of treatment regimens
- A. Control of comorbid disease states
  1. History of or active venous thromboembolism: stop estrogen hormone therapy pending reassessment during next GDC.
  2. Cardiovascular disease (CVD) risk is increased in MtF due to higher rates of tobacco use, obesity, diabetes, lipid disorders and reduced physical activity. Cardiovascular disease risk is unclear in FtM.
     a. Refer to the Hyperlipidemia Disease Management Guideline (DMG) for management of hyperlipidemia.
        - Currently there is no guidance on whether to use risk calculators based on natal sex or affirmed gender. It may be reasonable to use natal sex-based calculators in transgender people who have transitioned later in life.
  3. Diabetes: The effect of gender-affirming hormone therapy on diabetes risk or disease course is unclear. Management of diabetes in transgender patients has not been specifically studied.
     a. Refer to the Diabetes DMG for management.
     b. Generally, diabetes should be reasonably well controlled prior to initiating hormone therapy; however, no absolute criteria on hormone initiation is recommended.
  4. Bone health and osteoporosis: MtF and FtM patients receiving hormone therapy may be at an increased risk of osteoporosis. Consider obtaining bone mineral density (BMD) measurements when risk factors for osteoporosis exist, specifically in those who stop hormone therapy after gonadectomy. Osteoporosis should be considered in acute bone fractures.
  5. General approach to cancer screening in transgender people: Follow current policy regarding routine cancer screening with the addition of an annual mammogram screening for patients >40 years of age on estrogen therapy. Transgender females should receive regular prostate examinations to screen for prostate cancer and monitor prostate growth.
- B. Assess for contraindications: hormonal therapy, antiandrogen, or medroxyprogesterone therapy should not be initiated or continued in the presence of absolute contraindications
  1. Absolute contraindications to estrogen therapy include:
     a. Active or history of breast or estrogen-sensitive cancer
     b. End stage chronic liver disease (refer to CMC Disease Management Guideline)
     c. Current or history of venous thrombotic event
     d. Protein C, protein S, or antithrombin deficiency, or other known thrombophilic disorders
     e. Cerebrovascular disease
     f. Active psychosis, suicidality, homicidality
     g. Ischemic cardiovascular disease
     h. Hyperprolactinemia (prolactin level >100 ng/mL)
     i. Inability to provide informed consent

2. Absolute contraindications to testosterone therapy include:
    a. Active or history of breast, prostate, or sex-hormone sensitive cancer
    b. End stage chronic liver disease (refer to CMC Disease Management Guideline)
    c. Pregnancy
    d. Unstable coronary artery disease
    e. Untreated polycythemia (hematocrit ≥ 55%)
    f. Active psychosis, suicidality, homicidality
    g. Inability to provide informed consent
3. Absolute contraindications to spironolactone therapy
    a. Renal insufficiency (refer to Table 6)
    b. Hyperkalemia (refer to Table 6)
4. Absolute contraindications to finasteride therapy
    a. Pregnancy, known or suspected
5. Absolute contraindications to medroxyprogesterone therapy
    a. Current or history of venous thrombotic event
    b. Current or history of arterial thromboembolic disease
    c. End stage chronic liver disease (refer to CMC Disease Management Guideline)
    d. Active estrogen or progesterone dependent tumor
    e. Known, suspected, or history of breast malignancy
    f. Pregnancy

C. Monitoring
1. Evaluate the patient every 3 months in the first year and then 1-2 times per year to monitor for development of adverse reactions, comorbid disease states, drug-drug interactions, and risks associated with hormone therapy. Also obtain potassium level at 1 week after initiation of spironolactone, at least monthly for the first 3 months of therapy, and every 3 months thereafter for the first year of treatment.
2. Monitoring for specific drug treatment regimens:
    a. Estrogen:
        - Monitoring: For injection therapy, when possible, test hormone level midway between injections. GDC to titrate estrogen dose to result in a physiologic range for young healthy females, not to exceed 200 pg/ml. Monitor for signs and symptoms of thrombotic disorders.
        - Adverse effects include, but are not limited to: increased risk of emotional lability/depression, thromboembolic disease, pituitary prolactinoma, hypertension, diabetes mellitus, liver disease, cholelithiasis, breast cancer, and cardiovascular disease
        - Estrogen therapy may exacerbate pre-existing thromboembolic diseases, macroprolactinoma, liver dysfunction, breast cancer, coronary artery disease, cerebrovascular disease, and migraine headaches
        - Drug interactions include, but are not limited to:
            - Estrogen levels or effects may be increased by: erythromycin, clarithromycin, azole antifungals, verapamil, diltiazem, isoniazid, fluoxetine, paroxetine, sertraline, fluvoxamine, nefazodone, efavirenz, indinavir, saquinavir, atazanavir, etravirine
            - Estrogen levels or effects may be decreased by: carbamazepine, oxcarbazepine, phenytoin, phenobarbital, topiramate, rifampin, rifapentine, cimetidine, dexamethasone, lopinavir/ritonavir, ritonavir, tipranavir, darunavir, nelfinavir, nevirapine
            - Estrogen may reduce levels or effects of: warfarin, fosamprenavir, levothyroxine
    b. Spironolactone:
        - Monitoring: blood pressure, serum electrolytes (potassium, sodium), renal function
        - Adverse effects include, but are not limited to: hyperkalemia, dehydration, hyponatremia
        - Drug Interactions include, but are not limited to: use cautiously with digoxin, ACE inhibitors, and potassium-sparing diuretics (avoid combination)

c. Finasteride:
- Adverse effects include, but are not limited to: orthostatic hypotension, dizziness, decreased libido, impotence, weakness
- Drug Interactions: There are no known significant interactions

d. Testosterone:
- Monitoring: For injection therapy, when possible, test hormone level midway between injections. GDC to titrate the testosterone dose to result in a serum testosterone level within normal physiologic range (400-700 ng/dL). The upper limit of normal for the normal physiologic range is 1,000 ng/dl.
- Adverse effects include, but are not limited to: increased risk of cardiovascular or cerebrovascular disease, hypertension, liver disease and increased LFTs, diabetes mellitus, thromboembolic disease, increased aggression or depression, and adverse changes in lipid profile
- Testosterone therapy may exacerbate pre-existing breast or uterine cancer, erythrocytosis, and liver dysfunction
- Drug interactions include, but are not limited to:
  - Testosterone increases levels or effects of: warfarin, cyclosporine

e. Medroxyprogesterone:
- Monitoring: signs and symptoms of thrombotic disorders
- Adverse effects include, but are not limited to: weight gain, abdominal pain, amenorrhea, deep vein thrombosis
- Drug interactions include, but are not limited to:
  - Avoid use with griseofulvin
  - Levels increased with use with mifepristone, voriconazole

Table 4. Risks Associated with Hormone Therapy

Risk Level	Feminizing hormones	Masculinizing hormones
Likely increased risk	Venous thromboembolic disease Gallstones Elevated liver enzymes Weight gain Hypertriglyceridemia	Polycythemia Weight gain Acne Androgenic alopecia Sleep apnea
Likely increased risk with increased age	Cardiovascular disease	
Possible increased risk	Hypertension Hyperprolactinemia or prolactinoma Emotional instability and depression	Elevated liver enzymes Hyperlipidemia
Possible increased risk with increase age	Cerebrovascular disease Type 2 diabetes	Cerebrovascular disease Destabilization of certain psychiatric disorders* Cardiovascular disease Hypertension Type 2 diabetes
No increased risk or inconclusive	Breast cancer	Loss of bone density Breast cancer Cervical cancer Ovarian cancer Uterine cancer

*Includes bipolar, schizoaffective, and other disorders that may include manic or psychotic symptoms. This adverse event appears to be associated with higher doses or supraphysiologic blood levels of testosterone.
Table adapted from Coleman et al. (2012).

Table 5. Laboratory Monitoring Frequencies for Hormonal Therapy in Patients with Gender Dysphoria

	Baseline	Every 3 Months for First Year of Treatment	Every 6-12 months after First Year of Treatment
Vitals	X	X	X
CMP*	X	X	X
CBC	X	X	X
BG/A1c¥	X	X	X
Lipid panel	X	X	X
Liver function tests	X	X	X
Prolactin♯	X		X
LH	X		
FSH	X		
Estradiol‡	X	X	X
Testosterone‡	X	X	X

CMP=comprehensive metabolic panel, CBC=complete blood count, BG= blood glucose, LH=luteinizing hormone, FSH=follicle-stimulating hormone

*Obtain potassium level at 1 week after initiation of spironolactone and every 3 months thereafter for the first year of treatment. Monitor regularly thereafter or more closely in patients with renal impairment or concomitant drugs that cause hyperkalemia.

¥A1c is indicated at baseline, and then again as recommended in the UTMB CMC Diabetes DMG if the patient is diabetic

♯Prolactin levels should be obtained at baseline and annually. Levels are also warranted when patients exhibit signs or symptoms of a prolactinoma (see Table 6)

‡Obtain levels every 3 months for the first year of treatment and continue monitoring every 3 months if hormone levels are not within the normal physiologic range for MtF (Male-to-Female) or FtM (Female-to-Male)

Table 6. Monitoring of Hormonal Therapy in Patients with Gender Dysphoria

	Action*
SCr	If there is a change in SCr by 30% from baseline or if GFR is <10, stop spironolactone pending reassessment at next GDC.
K+	Stop spironolactone if K+ rises above 5.5 mmol/L pending reassessment at next scheduled GDC.
Hematocrit	Stop testosterone therapy if HCt reaches ≥ 55% pending reassessment at next scheduled GDC.
Lipid panel	Refer to the CMC Hyperlipidemia DMG if age >40 yo, Low-density lipoprotein (LDL) ≥ 190 and ≥21yo, or if there is a history of clinical atherosclerotic cardiovascular disease.
ALT, AST	If LFTs are 3x the upper limit of normal stop hormone therapy pending reassessment at next scheduled GDC.
BG	For elevated fasting or random BG, refer to Diabetes DMG for management of patients with a diagnosis of diabetes.
A1c	For elevated A1c, refer to Diabetes DMG for management of patients with a diagnosis of diabetes.
Prolactin	Signs and symptoms of prolactinoma should be considered and consist of visual disturbances, excessive galactorrhea, and new onset headache. These signs or symptoms warrant reassessment of the prolactin level. Prolactin levels greater than 100 ng/mL may be suggestive of prolactinoma. Stop hormone therapy and expedite referral to endocrinology.

*For critical levels or symptomatic patients, treat as clinically indicated. If lab abnormalities persist, consider other causes. Monitor for labs to return to baseline.

GOUT

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients

1

Establish Diagnosis of Gout

Criteria for definitive diagnosis of gout:
Presence of monosodium urate crystals in the synovial fluid (examined using polarized light microscopy)

Criteria for clinical diagnosis of gout:
In the absence of the means to identify urate crystals or in the presence of a negative polarized light microscopy, a provisional diagnosis of gout is made by a combination of clinical and historical criteria . There are no validated clinical diagnostic criteria. Criteria that may be useful include:

1. Serum uric acid level >7.0mg/dL
2. Maximum inflammation with symptoms of pain, swelling, redness, and warmth within 24 hours
3. History of one or more episodes of monoarticular arthritis followed by period(s) of completely free symptoms
4. Unilateral first metatarsophalangeal joint attack
5. Presence of a visible or palpable lesion, which by location or appearance is likely to be a tophus
6. Consider risk factors: family history, age, weight, male gender (**See Table 1**)

2

Baseline Recommendations

- Patient education, with initiation of diet and lifestyle recommendations. **See Section IV**
- Consider secondary causes of hyperuricemia ("Co-morbidity checklist"). **See Table 1**
- Consider elimination of non-essential prescription medications that induce hyperuricemia. **See Table 1**
- Clinically evaluate gout disease burden (palpable tophi, frequency and severity of acute and chronic symptoms and signs)

3 **Clinical Features**

4 Asymptomatic

7 Therapy not warranted in asymptomatic patients

5
- Sudden onset of pain
- Erythema
- Swelling involving joints

8 See **Acute Gout** (Page 2)

6 Established diagnosis of gouty arthritis AND ≥ 1 of the following:

- **Tophus or tophi** by clinical exam or imaging study
- Evidence of radiographic damage attributable to gout
- **Frequent attacks** of acute gouty arthritis (≥2 attacks/year)

OR

First gout flare and ≥ 1 of the following:

- **CKD Stage 3 or worse** (Glomerular Filtration Rate (GFR) < 60 mL/min)
- **Recurrent urolithiasis**
- **Serum urate ≥ 9 mg/dl**

9 Meets indication for **Chronic Gout Prophylaxis** (Page 3)

Nurses: DMGs are to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.**

Acute Gout

10

- To provide optimal care, pharmacologic treatment should be **initiated within 24 hours of acute gout attack onset**, therefore treatment should preferably be prescribed as needed KOP in case of an acute gout attack.
- Ongoing pharmacologic prophylaxis treatment with urate lowering therapy agents (i.e., allopurinol) should not be interrupted during an acute gout attack.

11 Assess severity

12 Mild-Moderate pain , particularly for an attack affecting only 1 or a few small joints, or 1-2 large joints. **See Tables 2-4 and Figure 1**

13 Severe Pain, particularly for a polyarticular attack or an attack affecting multiple large joints. **See Tables 2-4 and Figure 1**

14 Initiate Monotherapy

15

NSAIDs (First line):
Naproxen 750 mg x 1 day, then reduce to 250 mg Q8H until attack resolved **or** Ibuprofen 800 mg three to four times daily until symptoms resolve
Avoid NSAIDs in patients with Chronic Kidney Disease (CKD) whenever possible

Systemic Corticosteroids (Second line):
For patients with a contraindication to NSAIDS
Prednisone 40-60 mg/day x 3 days, then decrease by 10-15 mg/day every 3 days until discontinued

Colchicine (Third line):
For patients who are intolerant or have an absolute contraindication to NSAIDs and systemic corticosteroids. Must have non-formulary approval. See **Table 6** for complete dosing.

Monitoring Recommendations: Patients should be assessed for improvement of pain symptoms after 24 hours of treatment with the selected agent. Typically the total duration for treatment of an acute attack is 5-7 days.

16 **Option:** Initial combination therapy. Acceptable combination therapy approaches include the initial simultaneous use of full doses (or, where appropriate, prophylaxis doses) of either: (1) Colchicine and Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), (2) Oral Corticosteroids and Colchicine, or (3) Intra-Articular Steroids with any of the above agents. **Refer to Table 6**

17 Treatment outcomes

18 **Successful outcomes** defined as > 50% improvement in pain score at ≥ 24 hours

19 **Inadequate Response** defined as < 50% improvement in pain score at ≥ 24 hours

20 **Patient Education**: Including diet and lifestyle changes and prompt self-treatment of subsequent acute gout attacks; Consider Indications for chronic therapy. (**Box 6)**

21 Switch to Alternate Monotherapy

22 Option: Add-on combination therapy in individuals who have failed monotherapy with all options. **Refer to Box 16**

Chronic Gout Prophylaxis

23

TREAT TO SERUM URATE TARGET

- The minimum serum urate target is **<6 mg/dl**
- Serum urate lowering below 5 mg/dL may be needed to improve gout signs and symptoms

24

Initiate urate-lowering therapy (ULT) and acute gout prophylaxis.

1. **ULT – Allopurinol**.
   - **First Line: Allopurinol**
     - **Initial Dose**: 100 mg/day*
       *In Stage 4 or worse CKD (GFR ≤ 29): Start at 50 mg/day
     - **Maintenance Dose:**
       Titrate dose upward by 100 mg every 2-5 weeks to appropriate dose in order to treat to chosen serum uric acid target or max tolerated dose; Max dose: 800 mg daily, even with renal impairment. Monitor for drug toxicity **(See Table 7)**.
     - **Monitoring:**
       - Monitor serum urate concentration within 2 to 4 weeks of dose adjustments. Confirm serum urate level 3 months later.
       - Once serum urate target is achieved, monitor levels every 6 months.
   - **Alternatives: (See Table 7 for Dosing)**
     - **Second Line: Febuxostat -** Consider in patients who have a contraindication or are intolerant to allopurinol **(Non-formulary)**
     - **Third Line: Probenecid** - Consider in patients who have a contraindication or are intolerant to both allopurinol and febuxostat **(Non-formulary)**
2. **Acute gout prophylaxis**
   - Initiate acute prophylaxis with or just prior to initiating ULT **(See Table 6)**
   - **Duration:**
     - At least 6 months
       OR
     - 3 months after achieving target serum urate if no tophi detected on physical exam
     - 6 months after achieving target serum urate appropriate for the patient if one or more tophi detected on physical exam
   - **First line: Low dose NSAIDs** (e.g., Naproxen 250 mg twice daily)
     - Avoid NSAIDs in patients with Chronic Kidney Disease (CKD) whenever possible
     - Initiate with a proton pump inhibitor (PPI) for patients at high risk for GI toxicity (high risk patients include those with a history of ulcer disease, dyspepsia or gastroesophageal reflux disease (GERD) symptoms, age ≥ 60 years, and concomitant antiplatelet ,anticoagulation, or corticosteroid therapy).
   - **Second line: Low dose Prednisone** (≤10mg/day)
   - **Third line: Low dose Colchicine:** 0.6 mg once or twice daily (non-formulary)

25 **TREAT TO TARGET** Serum urate target achieved?

No → 27

- Increase intensity of ULT and re-evaluate serum urate levels every 2-4 weeks during titration of dose until serum urate target achieved
- Consider specialty referral if:
  - Unclear etiology of hyperuricemia;
  - Refractory signs or symptoms of gout;
  - Difficulty in reaching target serum urate, particularly with renal impairment ; or
  - Multiple and/or serious adverse events from pharmacologic ULT
  - **Go to Box 25**

Yes → 26

Long-term management of gout

- Continue with ULT treatment indefinitely
- Regularly monitor serum urate every 6 months and monitor for ULT side effects
- After palpable tophi and all acute and chronic gout symptoms have resolved, continue with pharmacologic treatment and lifestyle /diet recommendations needed to maintain serum urate <6 mg/dL indefinitely

I. Risk Factors that promote hyperuricemia

Table 1

Risk Factors	
Comorbidities	• Hypertension • Obesity • Metabolic syndrome • Type 2 Diabetes Mellitus • Hyperlipidemia • Chronic Kidney Disease
Medications	• Diuretics (Loop and Thiazides) • Niacin • Aspirin (75 to 325 mg/day) • Pyrazinamide
Diet	• Excessive alcohol intake (particularly beer) (≥2 servings/day for a male and ≥ 1 serving/day for a female) • Organ meats high in purine content (e.g., sweetbreads, liver, kidney) • Beverages containing high fructose corn syrup • Overeating
Other	• Adult males (often between the ages of 30-45) • ≥65 years of age (regardless of gender)

II. Acute Gout

A. Define acute gouty arthritis attack features by classifying intensity of attack, duration of attack, and extent **(Tables 2 – 5)**.

Table 2: Severity of Acute Gouty Arthritis Attack

Intensity of attack based on self-reported pain (0-10 visual analog scale)	
Mild	≤4
Moderate	5-6
Severe	≥7

Figure 1: Visual Analog Scale (VAS)

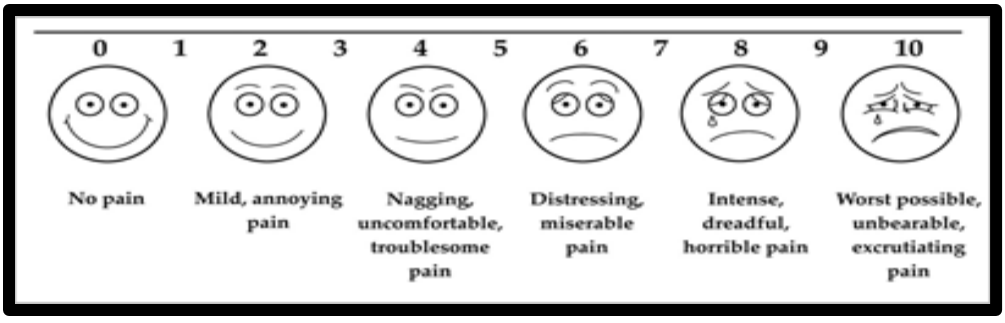

Table 3

Duration of the gouty arthritis attack since onset	
Early	<12 hours after attack onset
Well-Established	12 to 36 hours after attack onset
Late	>36 hours after attack onset

Table 4

Extent of acute gouty arthritis attack Based on number of active joints
One or a few small joints
1 or 2 large* joints ***defined as: ankle, knee, wrist, elbow, hip, shoulder***
Polyarticular • 4 or more joints, with arthritis involving more than 1 region◊ *◊Regions defined as: forefoot (metatarsophalangeal joints, toes), midfoot (tarsal joints), ankle/hindfoot, knee, hip, fingers, wrist, elbow, shoulder, other* • Acute gout attack involving 3 separate large joints is considered as a form of polyarticular gout

B. Recommendations for combination therapy for acute gout treatment

Table 5

Recommendations for Combination Therapy Approach to Acute Gouty Arthritis

• Initial combination therapy is an appropriate option for an acute, severe gout attack, particularly with involvement of multiple large organs or polyarticular arthritis.
• Acceptable combination therapy approaches include the initial simultaneous use of full doses (or, where appropriate, prophylaxis doses) of either:
  • (1) Colchicine and Nonsteroidal Anti-Inflammatory Drugs (NSAIDs);
  • (2) Oral Corticosteroids and Colchicine; or
  • (3) Intra-Articular Steroids with any of the above agents.
• For some patients not responding adequately to initial pharmacologic monotherapy, adding a second appropriate agent is an acceptable option.

Table 6. Acute Gout Treatment

Drug	Dosage Forms	Dosing	Side Effects/ Contraindications/Monitoring
Colchicine			
Colchicine (Colcrys®) **Status: Non-formulary**	0.6 mg tablet	**Initial:** 1.2 mg orally (two 0.6 mg tablets) followed by 0.6 mg in 1 hour (Max 1.8 mg over 1 hour) **Prophylaxis:** 0.6 mg orally once or twice daily beginning 12 hours after initial dose; Max 1.2 mg/day **If CrCl below 30 ml/min:** 0.3 mg/day (half-tablet) orally initially; may increase dose to a max of 1.2 mg/day with close monitoring for toxicity	**Common Side Effects:** • Nausea, vomiting, abdominal pain, diarrhea (Approximately 80% of patients at high doses > 1.8 mg) **Colchicine toxicity:** • Myelosuppression, rhabdomyolysis or myopathy, reversible peripheral neuropathy, liver failure, and death possible if overdosed **Contraindications:** • Do not repeat course more than once every 2 weeks in individuals with severe hepatic or renal impairment (CrCl below 30 mL/min) • Concomitant use of p-glycoprotein or strong CYP3A4 inhibitors in patients with hepatic or renal impairment (see Table 8)
NSAIDs			
Naproxen (Naprosyn®, others) **Status: Formulary**	250 mg, 500 mg tablet	750 mg x 1 day, then reduce to 250 mg orally every 8 hours until attack resolved	**Common Side Effects:** • Nausea, take with food **Contraindications:** • Allergic reaction following NSAIDs or aspirin use **Precautions:** • Avoid NSAIDs in patients with Chronic Kidney Disease (CKD) whenever possible • Consider bleeding risk in patients being treated with anticoagulants or those with active peptic ulcer disease • CVD risk (mostly with celecoxib) • Indomethacin was 1st NSAID approved and is the traditional drug of choice; however, it is more toxic than ibuprofen (Increased risk for GI toxicity) and has risk of psychiatric side effects including confusion, depression, psychosis
Ibuprofen (Motrin®) **Status: Formulary**	200 mg, 400 mg, 600 mg, 800 mg tablet	800 mg orally three to four times a day until symptoms resolve	
Meloxicam (Mobic®) **Status: Formulary**	7.5 mg, 15 mg	7.5 mg orally once daily; max 15 mg once daily	
Indomethacin (Indocin®) **Status: Non-Formulary**	25 mg, 50 mg tablet	50 mg orally three times a day until pain is tolerable, then taper down to avoid risk of rebound attack	
Steroids: Can be given PO, IM, IV, intra-articular			
Prednisone (orally) **Status: Formulary**	5 mg, 10 mg, 20 mg tablet	40-60 mg/day x 3 days, then decrease by 10-15 mg/day every 3 days until discontinued	**Acute Steroid Use Side Effects**: Increased blood glucose, elevated blood pressure, nervousness, insomnia, increased appetite, edema. **Injection:** Slight risk of infection, risk of joint damage with repeat injections
Methylprednisolone sodium succinate (Solu-Medrol®) **Status: Formulary**	125 mg injection – 2 ml vial	Initial 10 to 40 mg IM; may be repeated as clinically indicated (Option in patients with active acute gout affecting 1 or 2 large joints defines as: ankle, knee, wrist, elbow, hip, shoulder)	
Triamcinolone Acetonide **Status: Formulary**	10 mg/ml- 5 mL vial 40 mg/mL- 1 mL vial	60 mg IM, then oral prednisone as above	

III. Chronic Gout

Table 7. Chronic Gout Treatment

Drug	Dosage Forms	Dosing	Side Effects/Contraindications/Monitoring
Allopurinol (Zyloprim®) **Status: Formulary**	100 mg, 300 mg tablet	Mild: 100-300 mg/day orally as a single or divided doses (2-3 times daily) Moderate to severe: 400-600 mg/day orally in divided doses (2-3 times daily); Max dose 800 mg/day Stage 4 or worse CKD (CrCl <29 mL/min): Start at 50 mg/day; gradually titrate up every 2-5 weeks to appropriate maintenance dose (refer to mild and moderate/severe maintenance doses)	**Common Side Effects** • Precipitation of acute gout attacks • Nausea • Skin rash **Precautions** • Allopurinol hypersensitivity syndrome (AHS) - severe rash, fever, eosinophilla, hepatitis, and renal failure. Starting at lower doses can reduce the risk of AHS. Consider HLA-B*5801 screening in those populations at high risk for developing AHS: Koreans with Stage 3 or worse CKD (GFR < 59), those of Han Chinese or Thai descent, and African Americans.* **Monitoring** • Check LFTs at 2 and 4 months and periodically thereafter.
Febuxostat (Uloric®) **Status: Non-formulary**	40 mg tablet	Initial: 40 mg orally once daily Maintenance: May increase to 80 mg orally once daily in patients who do not achieve a serum uric acid level below 6 mg/dL after 2 weeks.	• May be safer in severe renal impairment and has decreased risk for hypersensitivity reactions but extremely costly. **Black Box Warning:** Cardiovascular death • Patients with established cardiovascular (CV) disease treated with febuxostat had a higher rate of CV death compared to those treated with allopurinol **Common Side Effects** • Precipitation of acute gout attacks • Rash • Nausea **Monitoring** • Liver enzyme elevations (requires LFT monitoring at 2 and 4 months, and then periodically thereafter)
Probenecid **Status: Non-Formulary**	500 mg tablet	250 mg orally BID for one week, followed by 500 mg BID thereafter; If symptoms persist, may incrementally increase by 500 mg every 4 weeks as tolerated; MAX 2000 mg/day.	• Uricosurics require adequate renal function. They are not commonly used, but may be used in younger patients with good renal function (CrCl greater than 50 mL/min). **Common Side Effects:** • Precipitation of acute gout attacks • Rash • GI intolerance • Uric acid stone formation **Contraindications:** • Renal impairment (CrCl below 50 mL/min) • Kidney stones

*To order an HLA-B*5801 genotype test, order a miscellaneous test and in the comments enter “X-Renal HLA-B* 5801 typing”.

Table 8

Drug Interactions	
Allopurinol	• Azathioprine, 6-mercaptopurine, cyclophosphamide, cyclosporine - Allopurinol may increase toxicity of these agents • Ampicillin and amoxicillin - Allopurinol may result in a higher probability of rash associated with these agents • Captopril and enalapril - May result in hypersensitivity reactions including Stevens-Johnson Syndrome in combination • Pegloticase - May result in an increased risk of anaphylaxis and infusion reactions in combination • Warfarin - Increased bleeding risk in combination

Colchicine	• Strong CYP3A4 inhibitors (increase colchicine concentrations): atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, and other
	• P-gp inhibitors (increase colchicine concentrations): vinca alkaloids, amiodarone, azole antifungals, clarithromycin, cyclosporine, diltiazem, erythromycin, quinidine, tacrolimus, verapamil, and others.
	• Dose adjustments:
	  • Strong CYP3A4 inhibitors; Gout flare: 1.2 mg oral for 1 dose, do not repeat dose earlier than 3 days.
	  • P-gp inhibitors; Gout flare: 0.6 mg oral for 1 dose, do not repeat dose earlier than 3 days.
	  • CYP3A4 or P-gp inhibitors; Gout Prophylaxis: Avoid use, but if unavoidable, consider reduction of daily dose of 0.3 mg orally every other day to 0.3 mg orally once a day.

Febuxostat	• Azathioprine and 6-meracaptopurine - contraindicated; febuxostat may increase plasma concentrations

IV. Patient Education

A. Causes of Gout

- Gout results from excessive uric acid in the body. Uric acid can build up and form crystals which may lead to kidney stones, joint pain, or deposits under the skin called tophi.

B. Risk Factors

- Certain risk factors increase the risk of developing gout including obesity, using medications that increase uric acid, consuming excessive amounts of alcohol (in particular beer), overeating, and disease states such as high blood pressure and chronic kidney disease (see Table 1).
- Certain characteristics increase the risk of gout flares in patients diagnosed with gout. These include meat, sugary drinks, excessive alcohol intake, and taking medications that increase uric acid .
    - Limit intake of meat, poultry, and fish to 4 to 6 ounces (113 to 170 grams daily).
    - Avoid or limit beverages and food containing high fructose corn syrup (soft drinks, juices, cereals, store-bought goods, ice cream, candy, processed foods at fast food restaurants).
    - For alcohol intake, limit to $\leq$ 2 servings/day for a male and $\leq$ 1 serving/day for a female.
    - Some examples of medications that affect blood levels of urate include aspirin (75 to 325 mg/day), diuretics, and niacin.

C. Gout Attacks

- Gout attacks are sudden with severe pain, burning, and swelling. If left untreated, the attacks may continue to develop. Gout attacks usually occur in the big toe but can occur in other joints.

D. Treatment goals

- The goal of treatment is to treat acute attacks, prevent future attacks, and reduce uric acid levels.

E. Acute gout treatment

- Pain and inflammation associated with acute gout attacks are treated using either an NSAID, colchicine, or steroids.
- The pain and inflammation of an acute gout attack usually reaches its peak of intensity within 12 to 24 hours and generally resolves completely within a few days to several weeks, even if untreated.
- Treat acute gout attacks within 24 hours of the onset of symptoms to receive the greatest benefit. Continue with treatment until symptoms resolve (usually within 5-7 days)
- NSAID counseling
    - Take with food to avoid upset stomach.
    - May cause bleeding in the stomach or intestine. Risk is higher in patients older than 60 years of age, history of stomach ulcer, using certain medications (steroids and blood thinners), individuals who smoke or drink regularly, or those with poor health.
    - May increase the risk of heart attack or stroke. Risk higher in patients with heart disease or long-term use of NSAIDs. Seek medical attention immediately if signs of a heart attack or stroke occur.
- Prednisone
    - May cause fluid retention, upset stomach (take with food), mood or behavior changes, increased appetite, weight gain, increase in blood glucose sugars, and high blood pressure.
    - Do not stop taking suddenly if using longer than 2 weeks. Must taper slowly to avoid withdrawal symptoms.
- Colchicine counseling
    - At the first sign of an attack take 2 tablets. Can take an additional tablet in one hour. Do not exceed more than 3 tablets in 24 hours.
    - Do not take 2nd dose if upset stomach, nausea, or diarrhea occurs.

F. **Chronic gout**

- Long term treatment with medications that lower urate acid levels, such as allopurinol, are used to prevent recurrent gout attacks.
- Therapy for chronic gout is lifelong. Patients should continue taking urate lowering medications even during an acute gout attack.
- Allopurinol counseling
  - Allopurinol decreases uric acid production. This reduces the chances of further gout attacks. It is important to take this medication daily (lifetime treatment).
  - Take once daily with a meal to reduce stomach upset.
  - It may take up to several weeks for this medication to have an effect . Acute gout attacks may occur for several months after starting this medicine while the body removes extra uric acid. If this occurs, treat with NSAIDs or another alternative agent such as colchicine and prednisone.
  - Notify provider if a rash develops. This rash can become serious.

G. **Discuss lifestyle and diet recommendations** (Tables 9 and 10)

Table 9

Lifestyle Recommendations for gout patients	
Exercise regularly	Engage in moderate-intensity physical activities for at least 30 minutes most days of the week
Maintain a healthy body weight	Obese patients are four times as likely to develop gout than someone with ideal body weight. Encourage weight loss for obese patients to achieve BMI that promotes general health
Stay well hydrated	Many dietitians recommend consuming at least 64 ounces of water daily, and more if the patient is exercising

Table 10

Diet Recommendations for Gout Patients		
Avoid	**Limit**	**Encourage**
• Organ meats high in purine content (e.g., sweetbreads, liver, kidney)	Serving size of: • Beef, Lamb, Pork • Seafood with high purine content (e.g., sardines, shellfish)	• Low-fat or non-fat dairy products
• High fructose corn syrup-sweetened sodas, other beverages, or foods	• Servings of naturally sweet fruit juices • Table sugar, sweetened beverages and desserts • Table salt, including in sauces and gravy	• Vegetables
• Alcohol overuse (Defined as more than 2 servings per day for a male and 1 serving per day for a female) • Any alcohol use in gout during periods of frequent gout attacks, or advanced gout under poor control	• Alcohol (Particularly beer, but also wine and spirits)	

Heart Failure

1

Heart failure (HF) suspected? (e.g., patient presents with ≥ 1 of the following symptoms: shortness of breath, cough, orthopnea, paroxysmal nocturnal dyspnea, dyspnea on exertion, edema, fatigue, weight gain)

Conduct appropriate clinical examinations, history and order relevant labs/tests.

- **Clinical Examination/Physical Signs:** Tachycardia, increasing weight, jugular, venous distention or hepatojugular reflux, presence of S3, S4, laterally displaced apical impulse, pulmonary crackles or wheezes, hepatomegaly, peripheral edema.
- **Clinical History:** Previous myocardial infarction (MI), hypertension, diabetes, angina, valve diseases, etc.
- **Relevant Labs/Tests:** Complete metabolic panel (including calcium and magnesium), complete blood count, electrocardiogram, B-type natriuretic peptide (BNP) chest X-ray, thyroid function tests.

Initiate appropriate non-pharmacological therapies (see page 4)

Consider referral to specialty clinic for evaluation and echocardiogram to determine HF classification and guide therapy.

2 HF with reduced ejection fraction (HFrEF) (EF ≤ 40%) or mildly reduced ejection fraction (HFmrEF) (EF 41-49%) confirmed?

No → 3 HF with preserved ejection fraction (HFpEF) confirmed?

3 → Yes → 4 See Table 4

3 → No → 5 Rule out other medical causes of symptoms

Yes → 6

Initiate Guideline Directed Medical Therapy (GDMT)

1) Angiotensin converting enzyme inhibitor (ACEI)

- Initiate lisinopril 2.5 mg to 40 mg daily depending on vitals. Consider increasing the dose every 2 weeks until target or maximally tolerated dose is achieved. Target dose = 20 - 40 mg daily
- Monitor K+, blood pressure, SCr
- If there is an ACEI intolerance or contraindication, consider nonformulary angiotensin receptor blocker (ARB) losartan, initial dose 25 mg to 100 mg daily

2) Beta blocker

- Initiate carvedilol 3.125 mg BID or metoprolol succinate 25 mg daily. Consider doubling the dose every 2 weeks (more slowly if needed) until target or maximally tolerated dose achieved. Target dose carvedilol = 25 mg BID, metoprolol = 200 mg daily
- Monitor blood pressure and heart rate

3) Mineralocorticoid receptor antagonist (MRA)

- Initiate spironolactone 25 mg daily IF eGFR is > 30 mL/min/1.73 m2 and serum potassium is < 5.0 mEq/L
- Monitor serum K+; if levels start to rise, reduce the dose to 25 mg every other day (e.g., MWF)

4) Sodium glucose transport protein 2 inhibitor (SGLT2i) *nonformulary*

- Request nonformulary empagliflozin 10 mg once daily if eGFR > 20 mL/min/1.73m2

7 Is patient tolerating recommended therapy?

No → 8 Continue last tolerated dose. Reassess in 2 weeks and return to circle 7.

Yes → 9 Is patient's LVEF ≤ 40%?

No → 10 HF with improved ejection fraction (HFimpEF): Continue GDMT and follow up in Chronic Care Clinic.

Yes → 11 Continue to Page 2

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

Nurses: DMGs are to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.**

Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee, Approved February 2000.
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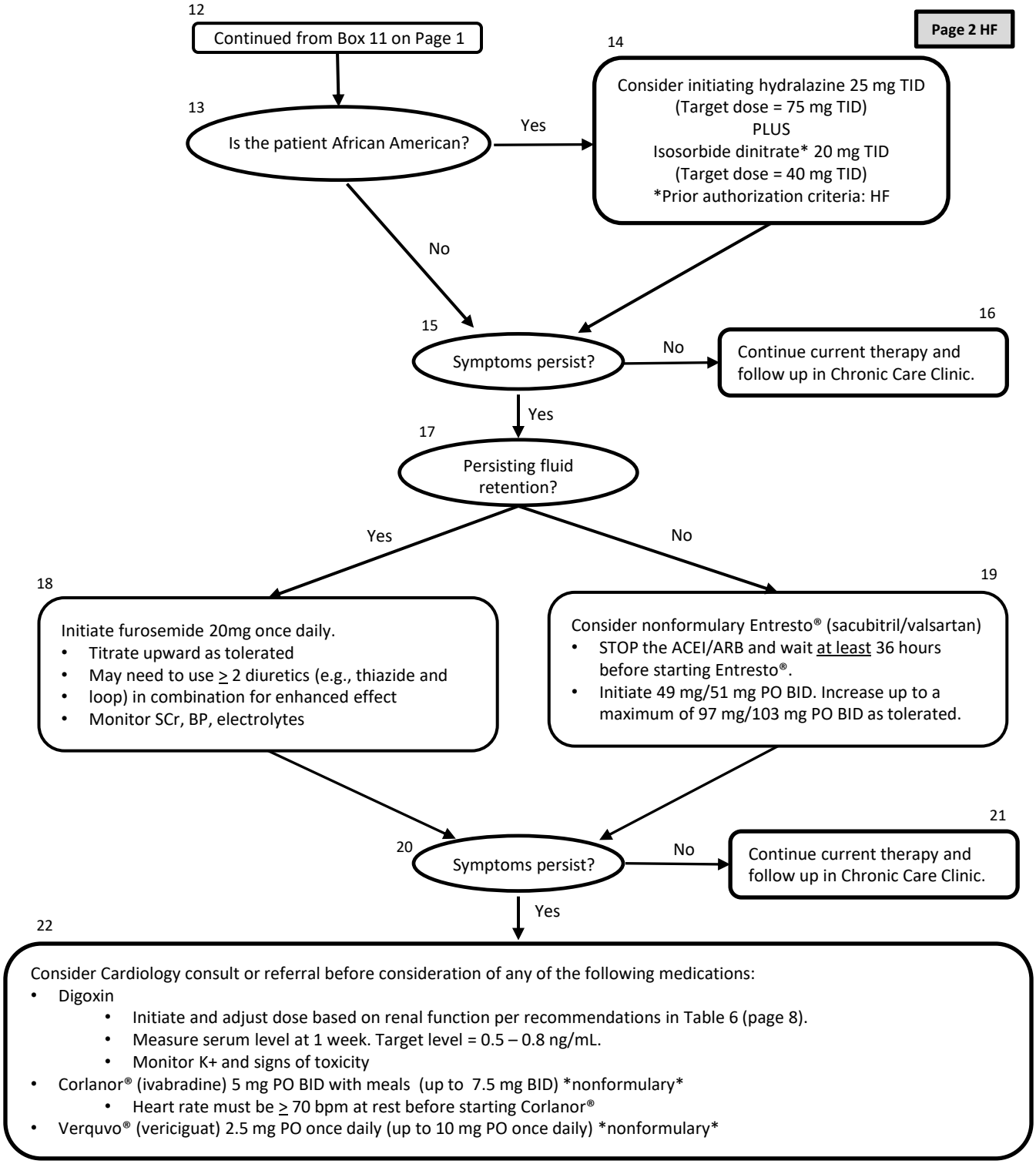

Abbreviations:

ACEI: angiotensin converting enzyme inhibitor
ACS: acute coronary syndrome
ARB: angiotensin receptor blocker
ARNI: angiotensin receptor/neprilysin inhibitor
GDMT: guideline directed medical therapy
HF: heart failure
HFimpEF: heart failure with improved ejection fraction
HFmrEF: heart failure with mildly reduced ejection fraction
HFpEF: heart failure with preserved ejection fraction
HFrEF: heart failure with reduced ejection fraction
LVEF: left ventricular ejection fraction
LVH: left ventricular hypertrophy
MI: myocardial infarction
MRA: mineralocorticoid receptor antagonist
NYHA: New York Heart Association
SGLT2i: sodium glucose transport protein 2 inhibitor

Health Care Provider Education

CLASSIFICATION AND DEFINITION OF MOST COMMONLY USED TERMS IN HEART FAILURE MANAGEMENT

Table 1: ACCF/AHA Stages of HF and NYHA Functional Classifications

ACCF/AHA Stages of HF		NYHA Functional Classification	
A	At high risk for HF but without structural heart disease or symptoms of HF	None	
B	Structural heart disease but without signs or symptoms of HF	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
C	Structural heart disease with prior or current symptoms of HF	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
		II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF.
		III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF.
		IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest.
D	Refractory HF requiring specialized interventions	IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest.

Table 2: Definitions of HF

Classification	EF (%)	Description
I. Heart failure with reduced ejection fraction (HFrEF)	≤ 40	• Most of the therapies that have been documented to have morbidity and mortality benefits in HF are mainly efficacious in patients with HFrEF • Effective therapies include Beta Blockers + ACEI/ARB/ARNI + SGLT2 inhibitors + MRA if EF is less than 35%
II. Heart failure with preserved ejection fraction (HFpEF)	≥ 50	• Diagnosis is based on excluding other probable causes of symptoms suggestive of CHF • Management typically involves controlling blood pressure and heart rate and treatment of symptoms with diuresis. • No therapy has a Class I recommendation, but MRA, SGLT2i, and/or ARB/ARNI, may be considered.
III. HF with mildly reduced EF (HFmrEF)	41 to 49	• The characteristics resemble those of patients with HFpEF. • Management typically involves controlling blood pressure and heart rate and treatment of symptoms with diuresis. • Similar treatment regimen utilized for HFrEF can be used, but no therapy has Class I recommendations in this group.
IV. HF with improved EF (HFimpEF)	> 40	• These are a subset of patients with HF who previously had LVEF < 40% and a follow-up measurement of LVEF > 40%. • The thought is that patients with improvement or recovery in EF may be clinically distinct from those with persistently preserved or reduced EF. • The patients typically continue medication regimen used when EF < 40%.

General non-pharmacological management measures:

- Control hypertension, diabetes, and hyperlipidemia to decrease risk of new cardiac injury
- Monitor weight closely (fast increase is a sign of exacerbation). Weight reduction in obese patients.
- Reduce fluid intake and restrict salt to a moderate degree (< 3 grams)
- Encourage exercise (as tolerated) to prevent or reverse physical unconditioning
- Influenza and pneumococcal vaccines to decrease risk of serious respiratory infections
- Medications to be AVOIDED include:
    - Non-steroidal anti-inflammatory drugs-can decrease the effectiveness of ACE inhibitors and diuretics and can worsen renal and cardiac function.
    - Anti-arrhythmics: heart failure patients can experience cardiodepressant and proarrhythmic effects.
    - Calcium Antagonists-lack of evidence supporting efficacy; safety concerns
- Provide patient with Heart Failure Inmate Education leaflet
- **Review referral guidelines to consider referral to cardiology specialist as clinically indicated**

Table 3. Treatment recommendations based on the various stages of HF

Stage		**Treatment Recommendations**
A: At Risk for HF	Patients with high risk for HF but no evidence of structural heart disease or symptoms of HF yet	• Risk factors include: hypertension, diabetes, obesity, atherosclerotic disease, metabolic syndrome, family hx, cardiotoxins etc. • Control hypertension, diabetes, and lipid-related disorders using current guidelines to reduce the risk of HF. • Avoid or control other conditions that may contribute to the development of HF including obesity, diabetes, cigarette smoking, etc.
B: Pre-HF	Patients with structural heart disease but no signs or symptoms of HF (Structural heart disease includes MI, LVH, Valve diseases, etc.). Patients could also be asymptomatic with LV dysfunction or could have systolic / diastolic HF	• Initiate ACEI in all patients with a history of MI or EF ≤40% to reduce risk of symptomatic HF and mortality. • Initiate evidence-based beta-blockers (such as carvedilol*, metoprolol succinate and bisoprolol) in all patients with a recent or remote history of MI or ACS and reduced EF. Beta-blockers have been shown to reduce mortality in patients with HFrEF. • Initiate statin in all patients with a recent or remote history of MI or ACS to prevent symptomatic HF and other cardiovascular events. • ACEIs and beta-blockers should be initiated in all patients with reduced EF (even in the absence of s history of MI) to prevent symptomatic HF. • Non-dihydropyridine calcium channel blockers such as diltiazem and verapamil may be harmful in asymptomatic patients with low LVEF and no symptoms of HF after MI because of their negative inotropic effects. • ARBs may be used to replace ACEI if patient is intolerant of ACEI.
C: Symptomatic HF	Structural heart disease with prior or current symptoms of HF. This include the presence of dyspnea, fatigue, reduced exercise tolerance, etc.	• Nonpharmacological interventions such as regular physical activity, sodium restriction, etc. should be part of the overall therapy for symptomatic HF patients. • Diuretics are recommended to manage fluid retention and to improve symptoms in HFrEF patients unless contraindicated. • ACEI* (or ARB if intolerant to ACEI, or ARNI) is recommended in all HFrEF patients to control symptoms and to reduce mortality. • Use of any of the three specific, evidenced based beta-blockers (e.g., carvedilol or metoprolol succinate) are recommended for all patients with HFrEF to control symptoms and to reduce mortality. • Use of a MRA such as spironolactone are recommended in patients with NYHA class II-IV and who have LVEF of 35% or less, unless contraindicated, to reduce morbidity and mortality. Creatinine should be 2.5 mg/dL or less in men or 2.0 mg/dL or less in women and potassium should be less than 5.0 mEq/L. Consistent and careful monitoring of potassium and renal function should be done to avoid hyperkalemia and renal insufficiency. • Use of a SGLT2 inhibitor (e.g., empagliflozin) is recommended in patients with symptomatic chronic HFrEF to reduce hospitalization for HF and cardiovascular mortality, irrespective of the presence of Type 2 diabetes. • The use of the combination of hydralazine and isosorbide dinitrate is recommended to reduce morbidity and mortality for patients self-described as African Americans with NYHA class III–IV HFrEF receiving optimal therapy with ACEI, beta blockers, and aldosterone antagonists, unless contraindicated. The combination can also be used to reduce mortality and morbidity in non-African American patients with symptomatic HFrEF who are either intolerant of ACEI/ARB or have other medical rationales to avoid ACEI/ARB. • Entresto® (sacubitril/valsartan) may be requested through the non-formulary process for patients who remain symptomatic despite GDMT. • Ivabradine may be considered upon the recommendation of a cardiologist for symptomatic, class II or III HF patients who have previously tolerated an ACEI or ARB.
D: Advanced HF	Marked HF symptoms that interfere with daily life and with recurrent hospitalizations despite attempts to optimize GDMT	• Referral to specialist is recommended to review HF management and assess suitability for advanced HF therapies (eg, LVAD, palliative care, and palliative inotropes)

Table 4. Treatment Options for HFpEF

Patients with HFpEF and hypertension should have blood pressure medications titrated to attain blood pressure targets in accordance with published clinical practice guidelines	
Medication	**Recommendations**
Initial Treatment	
Empagliflozin (Jardiance®) - nonformulary	SGLT2i, such as Jardiance®, can help decrease HF hospitalizations and cardiovascular (CV) mortality.
Additional Therapies to Consider if Clinically Indicated	
Spironolactone	MRA, such as spironolactone, may be considered to reduce hospitalizations
Furosemide	Loop diuretic agent should be considered for patients with fluid retention, NYHA class II-IV
ARB (Losartan®) – nonformulary	Use of ARB, such as Losartan®, can be considered to reduce hospitalizations
ARNI (Entresto®) – nonformulary	Use of ARNI, such as Entresto®, can be considered to reduce hospitalizations if patient is unable to tolerate ARB. Discontinue the ARB at least 36 hours before initiating Entrestro®.

Table 5. Initial and target doses for agents shown to provide mortality benefits in patients with HFrEF or HFpEF (GDMT)α

DRUG	INITIAL DOSE	TARGET DOSE
Angiotensin Converting Enzyme Inhibitor		
Lisinopril	2.5 mg PO QDAY	40 mg PO QDAY
Angiotensin Receptor Blocker (ARB)		
Losartan*	25 mg PO QDAY	150 mg PO QDAY
Mineralocorticoid Receptor Antagonist		
Spironolactone	12.5 mg PO QDAY	25 mg PO QDAY OR BID
Beta blockers		
Carvedilol	3.125 mg PO BID	25 mg PO BID if < 85 kg; 50 mg PO BID if ≥ 85 kg
Metoprolol succinate	25 mg PO QDAY	200 mg PO QDAY
Sodium Glucose Transport Protein 2 Inhibitor (SGLT2i)		
Empagliflozin* [Jardiance®]	10 mg PO QDAY	10 mg PO QDAY
Vasodilating Agent		
Hydralazine and isosorbide dinitrate	Hydralazine: 25 mg PO TID Isosorbide dinitrate: 20 mg PO TID	Hydralazine: 75 mg PO TID Isosorbide dinitrate: 40 mg PO TID
Angiotensin Receptor/Neprilysin Inhibitor (ARNI)		
Valsartan/sacubitril* [Entresto®]	49 mg/51 mg PO BID	97 mg/103 mg BID

*Nonformulary medication

α Guideline Directed Medical Therapy (GDMT) options differ for HFrEF and HFpEF

Formulary Medications (not in any specific order):

Lisinopril - ACE Inhibitor

- Benefit: All HFrEF patients should be on ACEI to promote favorable effects on cardiac remodeling and increase survival rate.
- When to use in HFrEF: In NYHA Class I-IV (at diagnosis or any point thereafter)
- Dosage titration: Begin initial dose monitoring potassium, SCr changes, and blood pressure. Increase dose to target based on toleration by the patient.
- Monitor: 1) BP for hypotension; 2) K+ for hyperkalemia; 3) SCr for unexpected elevation and renal insufficiency. If these occur, decrease dose and treat appropriately.
- NOTE: If contraindicated due to renal artery stenosis, consider isosorbide dinitrate and hydralazine

Carvedilol or metoprolol succinate – Beta-blockers

- Benefit: Beta-blocker use may prevent disease progression in HFrEF patients even if symptoms have not responded favorably to treatment
- When to use in HFrEF: Initiate therapy early – should be added to ACEI; can be used with vasodilators and digoxin (Class of Evidence is Strong: Class 1)
- Dosage and titration: Delay planned increments until the early side effects produced by the low doses of beta-blocker have disappeared
- Monitor: 1) BP for hypotension; 2) pulse for symptomatic bradycardia < 60 BPM; 3) fluid retention or worsening heart failure during up-titration
- NOTE: Use in **STABLE** patients **ONLY**
  Advise patients: 1) Side effects may occur early in therapy, but they do not generally prevent long-term use
  2) Improvements in symptoms may not be seen for 2-3 months
- Use with caution: asthma, Type 1 diabetes, bronchospasm, or acutely ill patients

Spironolactone – aldosterone antagonist

- Benefit: Cardioprotective and use can reduce symptoms, and risk of death and hospitalizations in HFrEF. In HFpEF patients, spironolactone can reduce risk of hospitalizations.
- When to use in HFrEF: In NYHA Class III or IV IF patients' eGFR is > 30 mL/min/1.73 m2 and serum potassium is < 5.0 mEq/L (Class of evidence is strong: Class 1-A)
- When to use in HFpEF: For women (all EFs), men with EF < 55 – 60%, those with fluid retention (Class of Evidence is Weak: Class 2–B)
- Dosage: Initiate at 25 mg daily.
- Monitor: 1) K+ for hyperkalemia 2) signs of gynecomastia-make patients aware of the side effect
- NOTE: Encourage patient developing gynecomastia to continue treatment because benefits of decreased mortality are so great

Hydralazine

- Benefit: Hydralazine in combination with isosorbide dinitrate has strong morbidity and mortality benefits in patients self-described as African-Americans and others with current HF symptoms who are unable to receive ACEI or ARB due to contraindications or drug intolerance in HFrEF.
- When to use in HFrEF: Initiate therapy in self-described African Americans patients with NYHA class III–IV HFrEF who have no contraindication to the medication and are receiving optimal therapy with ACEI and beta blockers, or non- African American patients who remain symptomatic on optimal therapy with ACEI or ARB and beta-blocker or who are unable to receive ACEI or ARB due to contraindications or drug intolerance. (Class of evidence is strong: Class 1)
- Dosage and titration: Start at 25 mg TID and up to a maximum of 75 mg TID (as tolerated by the patient).
- Monitor: 1) BP for hypotension; 2). Complete metabolic panel at baseline and periodically during prolonged treatment
- NOTE: Use in **combination with** isosorbide dinitrate to achieve HF benefits
- Contraindications: Coronary artery disease and mitral valvular rheumatic disease

Isosorbide Dinitrate (ISDN) – Prior Authorization Agent

- Benefit: When combined with hydralazine, isosorbide dinitrate has strong morbidity and mortality benefits in patient self-described as African-Americans and others with current HF symptoms who are unable to receive ACEI or ARB due to contraindications or drug intolerance in HFrEF.
- When to use in HFrEF: In self-described African Americans patients with NYHA class III–IV HFrEF who have no contraindication to ISDN and are receiving optimal therapy with ACEI and beta blockers, or non- African American patients who remain symptomatic on optimal therapy with ACEI or ARB and beta-blocker or are unable to receive ACEI or ARB due to contraindications or drug intolerance. (Class of evidence is strong: Class 1)
- Dosage and titration: Start at 20mg TID and up to a maximum of 40mg TID (as tolerated by the patient).
- Monitor: 1). BP and heart rate especially in patients with acute myocardial infarction or congestive heart failure
- NOTE: Use in combination with Hydralazine to achieve HF benefits
- Contraindications: Concomitant use of phosphodiesterase inhibitors, such as sildenafil, tadalafil, etc.

Formulary Medications (continued):

Furosemide – loop diuretic
- Benefit: Relieve congestion, improve symptoms, and prevent worsening of HF in patients with HF and fluid retention.
- When to use in HFrEF: In NYHA Class I-IV (Class of evidence is strong: Class 1-A)
- When to use in HFpEF: For individuals with fluid retention, NYHA class II – IV. (Class of evidence is strong: Class 1-A)
- Dosage and titration: Titrate dose to symptoms – stabilize patient and maintain patient on smallest dose.
- Monitor: 1) BP for symptomatic hypotension; 2) K+ for hypokalemia
- NOTE: Treat electrolyte imbalances and continue therapy - Slow the titration of furosemide and add a K+ supplement

Hydrochlorothiazide (HCTZ) – thiazide diuretic
- Benefit: Will assist in reducing blood pressure if a concomitant problem.
- When to use in HFrEF : In patients who do not respond to loop diuretics to minimize electrolyte abnormalities.
- Dosage titration: Start patient at 25 mg. There is no proven benefit to increasing this dose.
- Monitor: 1) BP for symptomatic hypotension; 2) K+ for hypokalemia
- NOTE: It does not reduce fluid as efficiently as furosemide.

Non-Formulary Medications (not in any specific order):

Entresto® (sacubitril/valsartan) - ARNI
- Benefit: Strong reduction in mortality and a strong reduction in hospitalization in HFrEF patients. In HFpEF patients, ARNI may be used to reduce the risk of hospitalization.
- When to use in HFrEF : In NYHA Class II or III patients (Class of evidence is strong: Class 1-A)
- When to use in HFpEF: In women (all EFs) or men with LVEF <55 – 60%) (Class of evidence is moderate: Class 2-B)
- Dosage: Initiate at 49mg/51mg PO BID
- Monitor: 1). SCr, general renal function especially in the setting of renal stenosis. 2). K+ for hyperkalemia, especially in patients with risk factors for hyperkalemia including those with diabetes, severe renal impairment, hypoaldosteronism, or high potassium diet. 3). BP for symptomatic hypotension
- NOTE: 1) Stop ACEI/ARB if starting ENTRESTO or any other ARNI. 2) DO NOT start ENTRESTO within 36 hours of stopping an ACEI/ARB. 3) DO NOT start ENTRESTO if any history of angioedema or history of intolerance to ACEI or ARB

Jardiance® (empagliflozin) – SGLT2 inhibitor
- Benefit: Strong reduction in mortality and hospitalizations in chronic symptomatic HFrEF and HFpEF patients
- When to use in HFrEF : In NYHA Class II or III (Class of evidence is strong: Class 1)
- When to use in HFpEF: In all patients with EF $\geq$ 50 with a diagnosis of HFpEF (Class of evidence is moderate: Class 2-A)
- Dosage: 10 mg PO once daily
- Monitor: 1) Glucose for hypoglycemia 2) BP for symptomatic hypotension 3) SCr for acute kidney injury (AKI) 4) urinalysis (UA) and urine culture, if urinary tract infection (UTI) is suspected
- NOTE: 1) Contraindicated in patients on dialysis. 2) Cases of ketoacidosis have been reported in patients with type 1 and type 2 diabetes mellitus receiving sodium-glucose cotransporter 2 (SGLT2) inhibitors

Losartan – ARB
- Benefit: Moderate reduction in hospitalizations in HFpEF.
- When to use in HFpEF: In NYHA Class I-IV (at diagnosis or any point thereafter) (Class of evidence is moderate: Class 2-B)
- Dosage titration: Begin initial dose monitoring potassium, SCr changes, and blood pressure. Increase dose to target based on toleration by the patient.
- Monitor: 1) BP for hypotension; 2) K+ for hyperkalemia; 3) SCr for unexpected elevation and renal insufficiency. If these occur, decrease dose and treat appropriately.

Corlanor® (ivabradine) - I_f Channel inhibitor
- Benefit: Use can reduce symptoms and hospitalizations in HFrEF patients
- When to use in HFrEF : In NYHA Class II or III with EF ≤ 35%, stable HF with HFrEF. Corlanor® should not be used without cardiology consultation. (Class of evidence is moderate: Class 2-A)
- Dosage: Initiate at 5mg BID with meals.
- Monitor: 1) Heart rate for bradycardia and cardiac arrhythmias
- NOTE: 1) Patient should be on maximally tolerated dose of beta blocker prior to initiation. 2) Patient must have a heart rate of 70bpm or higher at rest before starting Corlanor®.

Verquvo ® (vericiguat) – soluble guanylate cyclase stimulator
- Benefit: May be considered to decrease HF hospitalization and CV death in high-risk patients with HFrEF and recent worsening of HF (Class IIb recommendation)
- When to use in HFrEF: In NYHA II-IV; LVEF <45%, recent HF hospitalization or IV diuretics; elevated natriuretic peptide levels. Verquvo® should not be used without cardiology consultation. (Class of evidence is weak: Class 2-B)
- Dosage and titration: Initiate at 2.5 mg once daily and titrate up to 10 mg once daily
- Monitor: 1) BP; 2) weight
- NOTE: Negative pregnancy prior to starting treatment- BBW for embryo-fetal toxicity

CHRONIC HEPATITIS B EVALUATION AND TREATMENT PATHWAY

1

Chronic Hepatitis B (CHB)
(HBsAg + ≥ 6 months)

The pathway does not replace sound clinical judgment nor is it intended to strictly apply to all patients

2

1. Obtain baseline tests:
- CBC w/platelets
- Bili, Alb, ALT, AST, AFP
- Prothrombin time
- HCV (Hepatitis C)
- HIV
- HBsAb, HAV TAB

2. Vaccinate with Hepatitis A vaccine if not immune

Level 2 Labs† for Hepatitis B
- Quantitative HBV-DNA
- Abdominal ultrasound
- Alpha-fetoprotein
- Antinuclear antibody (ANA)
- HBeAG
- Chest Xray and EKG if over 40 or clinically indicated

If not done in the preceding 6 months:
- ALT, AST, bilirubin, albumin, BUN, creatinine
- CBC, platelets, PT
- T4, TSH
- Fe, TIBC

HBV-DNA units are in IU/mL. If results are given as log IU/mL, then
2,000 IU/mL = 3.3 log
20,000 IU/mL = 4.3 log

3

Refer to specialty clinic for treatment evaluation. Specialty clinic may order Level 2 labs† (to screen for other causes of liver disease).

4

HBeAg POSITIVE?

Yes → 5 Go to Page 2, Box 18

No →

6

ALT > 2x ULN?

No →

11

ALT > ULN but < 2x ULN?

Yes →

12

Is HBV DNA ≥ 2,000 IU/mL?

Yes →

13

If staging* indicates ≥ F2 or ≥ A3 or if persistent ALT > ULN, especially if age > 40, consider treatment (See Page 5, Table 2).

No →

14

Go to Circle 9

No →

15

Is HBV DNA ≥ 2,000 IU/mL?

No →

16

Do not treat. Follow in CCC. Monitor for disease progression (ALT and HBV DNA) every 3 months for 1 year to confirm inactive CHB then every 6 to 12 months and HBsAg annually.

Yes →

17

Go to Box 10

Yes →

7

Is HBV DNA ≥ 2,000 IU/mL?

Yes →

8

Consider treatment, determined by specialty clinic (Page 5, Table 2).

No →

9

Stage* ≥ F2 or ≥ A3?

Yes →

8

Consider treatment, determined by specialty clinic (Page 5, Table 2).

No →

10

Follow in CCC. Monitor for disease progression (ALT & HBV DNA) every 3 months for 1 year then every 6 months.

* Staging based on APRI, FIB-4, imaging, and/or biopsy with F2 fibrosis stage and A3 necroinflammatory stage (See Page 3, II.2).

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs).
As such, treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.

Prepared By the Correctional Managed Care Pharmacy & Therapeutics Committee.
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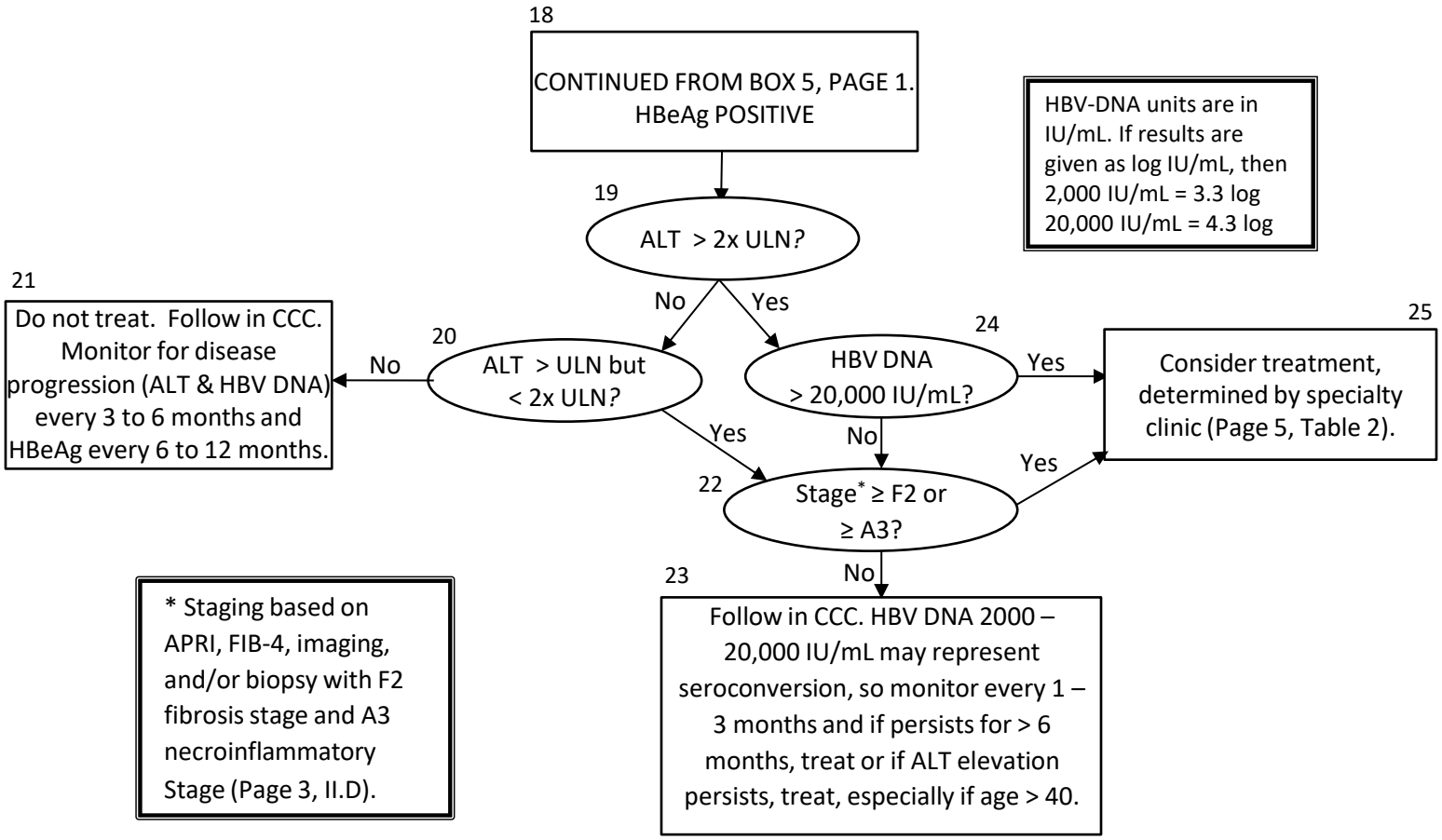
18
CONTINUED FROM BOX 5, PAGE 1.
HBeAg POSITIVE
HBV-DNA units are in IU/mL. If results are given as log IU/mL, then 2,000 IU/mL = 3.3 log 20,000 IU/mL = 4.3 log
19
ALT > 2x ULN?
No
Yes
21
Do not treat. Follow in CCC. Monitor for disease progression (ALT & HBV DNA) every 3 to 6 months and HBeAg every 6 to 12 months.
20
No
ALT > ULN but < 2x ULN?
24
HBV DNA > 20,000 IU/mL?
Yes
25
Consider treatment, determined by specialty clinic (Page 5, Table 2).
Yes
No
22
Stage* ≥ F2 or ≥ A3?
Yes
No
23
Follow in CCC. HBV DNA 2000 – 20,000 IU/mL may represent seroconversion, so monitor every 1 – 3 months and if persists for > 6 months, treat or if ALT elevation persists, treat, especially if age > 40.
* Staging based on APRI, FIB-4, imaging, and/or biopsy with F2 fibrosis stage and A3 necroinflammatory Stage (Page 3, II.D).

I. Definitions

A. **Chronic hepatitis B (CHB)** – chronic necroinflammatory disease of the liver caused by persistent infection with hepatitis B virus. CHB can be subdivided into HBeAg-positive and HBeAg-negative chronic hepatitis B. CHB is dynamic and individuals can transition through different clinical phases (Table 1) with variable levels of ALT, HBV-DNA, and HBV antigens. Levels of serum ALT, HBV-DNA and liver fibrosis are important predictors of long-term outcome that help inform decisions for treatment initiation as well as treatment response.

B. **Immune-tolerant phase** – may last for months, years, or decades and is characterized by high levels of HBV replication, as manifested by the presence of HBeAg and high levels of HBV-DNA in serum but no evidence of active liver disease, as manifested by normal or minimally elevated ALT concentrations.

C. **HBeAg-positive immune-active (clearance) phase** – during this phase, serum ALT is elevated and HBeAg seroconversion may occur.

D. **Inactive chronic HBV phase** – usually characterized by the absence of HBV-DNA (< 2000 IU/mL) and normalization of ALT. It is also known as latent, nonreplicative, or carrier phase.

E. **HBeAg seroconversion** – loss of HBeAg and detection of anti-Hbe in a person who was previously HBeAg positive and anti-Hbe negative. Among persons who undergo spontaneous HBeAg seroconversion, 67%-80% will continue to remain in the inactive CHB phase.

F. **HBeAg seroreversion** – reappearance of HBeAg in a person who was previously HBeAg negative

G. **Resolved CHB** – sustained loss of HBsAg in a person who was previously HBsAg positive, with undetectable HBV-DNA and absence of clinical or histological evidence of active viral infection

H. **Reactivation of hepatitis B** – reappearance of active necroinflammatory disease of the liver in a person known to have the inactive HBsAg carrier state or resolved hepatitis B. Reactivation may occur in patients who receive immunosuppressive therapy but can also occur spontaneously.

I. **Hepatitis flare** – ALT increase ≥ 3 times baseline and > 100 U/L

J. **Virological breakthrough** - > 1 $\log_{10}$ (10-fold) increase in serum HBV-DNA from nadir during treatment in a patient who had an initial virological response and who is adherent

Table 1. HBV Phases of Infection

HBV Phase	ALT/AST (U/L)	HBeAg	HBV DNA (IU/mL)	Liver Histology
Immune-tolerant	Normal or minimally elevated ALT and/or AST	Positive	Elevated, typically > 1 million (1 x 10^6)	Minimal inflammation and no fibrosis
Immune-active	Intermittent or persistently elevated ALT and/or AST	Positive	Elevated > 20,000	Moderate or severe necroinflammation with or without fibrosis
		Negative	Elevated > 2,000	
Inactive (carrier)	Persistently normal ALT and/or AST	Negative	Low or undetectable < 2,000	Minimal necroinflammation, variable fibrosis
Immune reactivation	Elevated	Negative	Elevated > 2,000	Moderate to severe inflammation or fibrosis

ULN = Upper limit of normal. ULN ALT for managing treatment in males is 35 U/L and 25 U/L in females.

II. Diagnosis

A. HBsAg present for greater than or equal to 6 months

B. HBV-DNA may vary from undetectable to > 2,000,000 IU/mL

C. ALT/AST may be normal or elevated

D. Liver biopsy shows chronic hepatitis with variable necroinflammation and/or fibrosis. Several scoring systems are used to assess chronic hepatitis. These systems help assess prognosis and clinical management. Metavir scoring is a semiquantitative classification system that consists of an activity score and a fibrosis score (represented by a two letter and two number coding system.

1. The activity score is graded according to the intensity of the necroinflammatory lesions (A0=no activity, A1=mild activity, A2=moderate activity, A3=severe activity).
2. The fibrosis score is assessed on a five-point scale (F0=no fibrosis, F1=portal fibrosis with septa, F2=few septa, F3=numerous septa with cirrhosis, F4=cirrhosis).

E. APRI (AST to Platelet Ratio Index) – A non-invasive method for the assessment of fibrosis in chronic liver disease. It is the ratio of the AST level, expressed as a percentage of the upper limit of normal, divided by the platelet count in thousands per cubic millimeter. It is a good predictor of liver fibrosis but cannot replace the liver biopsy in all cases. The APRI may be less predictive when there are co-morbid conditions other than liver disease that may affect the platelet count or AST level (APRI score ≥0.7 is associated with significant fibrosis (F2), APRI ≥1 indicates severe fibrosis (F3), APRI ≥2 associated with cirrhosis (F4)) .

F. FIB-4 – A non-invasive method for the assessment of fibrosis in chronic liver disease. Evaluates liver fibrosis based on age, platelet count, AST and ALT (FIB-4 <1.45 = excludes severe fibrosis, FIB-4 between 1.45-3.25 is inconclusive, FIB-4 >3.25 indicates significant fibrosis (F3-F4).

E. Evaluate for other causes of liver disease (e.g., drug-induced liver injury, alcohol-associated liver disease, HCV or HDV, fatty liver or autoimmune liver disease).

III. Management
- A. Treatment Principles
  1. Patient-specific factors to consider in choosing between peginterferon alfa-2a (Peg-IFN), entecavir, tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) include the following:
     - a. Desire for finite therapy (See Treatment Duration)
     - b. Anticipated tolerability of treatment side effects
     - c. Comorbidities:
       - i. peg-IFN is contraindicated in persons with autoimmune disease, uncontrolled psychiatric disease, cytopenia, severe cardiac disease, uncontrolled seizures, and decompensated cirrhosis.
       - ii. Renal dysfunction: Entecavir or TAF may be considered in patients with or at risk for renal dysfunction. TAF is not recommended in patients with creatinine clearance <15 mL/min or those on dialysis.
       - iii. HIV co-infection is discussed separately in III.D.
       - iv. HCV co-infection is discussed separately in III.D.
     - d. Previous history of lamivudine resistance (entecavir is not preferred in this setting)
     - e. Pregnancy: TDF is considered safe in pregnancy
     - f. HBV genotype: A and B genotypes are more likely to achieve HBeAg and HBsAg loss with peg-IFN than non-A or non-B genotypes
  2. Combination therapy with peg-IFN and nucleos(t)ide analogs (NAs) (e.g., entecavir, tenofovir, lamivudine) has not yielded higher rates of off-treatment response and is not recommended.
  3. Treatment with antivirals does not eliminate the risk of hepatocellular carcinoma (HCC), and surveillance for HCC should continue in persons at risk. This includes persons with resolved CHB or functional cure, particularly if HBsAg loss occurred in patients older than 50 years or in those with cirrhosis or coinfection with HCV or hepatitis D virus.
- B. Treatment Recommendations
  1. Antiviral therapy is recommended for immune-active CHB (HBeAg negative or positive) to reduce the risk of liver related complications (Table 2). Treatment guidelines recommend peg-IFN, tenofovir (TDF or TAF) and entecavir as preferred treatments. Patient specific factors (III.A.1) and preference should be considered.
     - a. Factors to consider for treatment in patients with ALT above ULN but <2 times ULN include severity of liver disease (defined by biopsy or noninvasive testing), older age (> 40 years), family history of cirrhosis or HCC, or presence of extrahepatic manifestations.
  2. Antiviral therapy is not recommended in immune-tolerant CHB. Immune-tolerant status should be defined by ALT levels, utilizing 35 U/L for men and 25 U/L for women as ULN rather than local laboratory ULN.
- C. Treatment Duration
  1. peg-INF: 48 weeks is most studied and preferred. This duration yields HBeAg seroconversion rates of 20-31% and sustained off-treatment HBV-DNA suppression of <2000 IU/mL in 65% of persons who achieve HBeAg to anti-Hbe seroconversion.
  2. Duration of therapy is variable for NA-based therapy and influenced by HBeAg status, duration of HBV-DNA suppression, and presence of cirrhosis and/or decompensation.
- D. HIV Co-Infection
  1. All patients with HBV and HIV coinfection should initiate antiretroviral therapy (ART). ART should include 2 drugs with activity against HBV, TDF or TAF plus lamivudine. The rate of resistance to lamivudine monotherapy in HBV- and HIV-coinfected patients reaches 90% at 4 years.
  2. Patients who are already receiving effective ART that does not include antiviral activity against HBV should have treatment changed to include TDF or TAF with lamivudine. Alternatively, entecavir is reasonable if patients are receiving fully suppressive ART.
  3. When ART regimens are altered, drugs that are effective against HBV should not be discontinued without substituting another drug with HBV activity.
  4. Hepatitis flares may occur during the first few weeks of treatment from immune reconstitution or when drugs with HBV activity are discontinued, particularly in the absence of HBeAg seroconversion.
  5. Elevation of ALT can also be attributed to hepatotoxicity of ART or HIV-related opportunistic infections.
  6. HBV treatment should be continued indefinitely with monitoring of virologic response and adverse effects.
- E. HCV Co-Infection
  1. Preferred HBV treatment is with entecavir (nonformulary), TDF (formulary) or TAF (nonformulary).
  2. HBsAg-positive patients are at risk of HBV-DNA and ALT flares with HCV direct-acting antiviral (DAA) therapy and monitoring of HBV-DNA levels every 4-8 weeks during treatment and for 3 months post-treatment is indicated for those who do not meet HBV treatment criteria.
  2. HBsAg-negative, anti-HBc-positive patients with HCV are at very low risk of reactivation with HCV DAA therapy. ALT levels should be monitored at baseline, at the end of treatment, and during follow up, with HBV-DNA and HBsAg testing reserved for those whose ALT levels increase or fail to normalize during treatment or posttreatment.

Table 2. Hepatitis B virus treatments

Medication	Dosage	Dosage Adjustment	Adverse Effects*	Monitoring[1]
Preferred				
Entecavir (ETV Baraclude®) NON-FORMULARY	Nucleoside-treatment naive, compensated liver disease: 0.5 mg once daily Decompensated liver disease or if lamivudine- or telbivudine-experienced: 1 mg once daily	Dosing: CrCl ≥50 mL/minute: No dosage adjustment necessary. CrCl 30 to 49 mL/minute: Administer 50% of usual dose daily or administer the normal dose every 48 hours CrCl 10 to 29 mL/minute: Administer 30% of usual dose daily or administer the normal dose every 72 hours CrCl <10 mL/minute (including HD and CAPD): Administer 10% of usual dose daily or administer the normal dose every 7 days; administer after hemodialysis	**Common**: Nausea, dizziness, headache, fatigue **Serious**: lactic acidosis (decompensated cirrhosis only), hepatomegaly with steatosis	Lactic acid levels if there is clinical concern. Test for HIV before treatment initiation.
peginterferon alfa-2a (Pegasys®, Peg-IFN) NON-FORMULARY	180 mcg subQ once a week for 48 weeks	CrCl < 30 mL/min or HD: Reduce to 135 mcg/wk or lower based on tolerance.	**Common**: alopecia, dermatitis, injection site reactions, pruritis, elevated triglycerides, weight loss, abdominal pain, diarrhea, anorexia, nausea and vomiting, elevated serum transaminases, arthralgia, myalgia, dizziness, headache, insomnia, reduced concentration, cough, dyspnea, fatigue, fever, flu-like symptoms **Serious**: pancreatitis, mood disturbances, cytopenia, autoimmune disorders, hypersensitivity reaction	CBC (monthly to every 3 months) TSH (every 3 months) Clinical monitoring for autoimmune, ischemic, neuropsychiatric, and infectious complications. Peg-IFN is contraindicated in persons with autoimmune disease, uncontrolled psychiatric disease, cytopenias, severe cardiac disease, uncontrolled seizures, and decompensated cirrhosis.
Tenofovir (TAF, Vemlidy®) NON-FORMULARY	25 mg daily with food.	CrCl < 15: Use not recommended. HD: No adjustment; on days of hemodialysis, give TAF post dialysis.	**Common**: abdominal pain, backache, headache, cough, fatigue **Serious**: lactic acidosis, pancreatitis, hepatomegaly with steatosis, acute renal failure, acute renal failure, Fanconi syndrome, renal impairment	Lactic acid levels if clinical concern. Assess serum creatinine, serum phosphorus, creatinine clearance, urine glucose, and urine protein before initiating and during therapy as clinically appropriate. Test for HIV before treatment initiation.
Tenofovir (TDF, Viread®) FORMULARY	300 mg daily and best if taken with food.	CrCl: Dose: 30-49 300 mg q 48 hours 10-29 300 mg twice a week HD 300 mg q 7 days	**Common**: pruritis, rash, abdominal pain, diarrhea, nausea, vomiting, headache, asthenia, dizziness, insomnia, fever **Serious:** lactic acidosis, hepatomegaly with steatosis, angioedema, immune reconstitution syndrome, acute renal failure, Fanconi syndrome, nephrogenic diabetes insipidus, renal impairment	Lactic acid levels if there is clinical concern. Creatinine clearance at baseline. If at risk for renal impairment, creatinine clearance, serum phosphate, urine glucose, and protein at least annually. Test for HIV before treatment initiation.
Nonpreferred				
Lamivudine (3TC, Epivir HBV®) FORMULARY	100 mg daily (Using 150 mg daily available on the CMC Formulary)	CrCl: Dose: 30-49 50 mg once daily 15-29 25 mg once daily 5-14 15 mg once daily <5 or HD 10 mg once daily	**Common**: diarrhea, nausea, headache, cough, nasal symptoms, fever, malaise and fatigue **Serious:** pancreatitis, lactic acidosis	Amylase if symptoms are present. Lactic acid levels if there is clinical concern. Test for HIV before treatment initiation.

*not a complete list of adverse effects. Adapted from 2018 AASLD Update on Prevention, Diagnosis, and Treatment of Chronic Hepatitis B.
HD=hemodialysis, CAPD = Continuous Ambulatory Peritoneal Dialysis, CrCl=Creatinine clearance in mL/min

F. Decompensated cirrhosis
   1. Antiviral therapy has been shown to improve outcomes in both liver function and increased survival. Transplant-free survival has been shown to exceed 80% in treated patients.
   2. Indefinite therapy is recommended
   3. High risk for HCC and long-term HCC surveillance is recommended (Table 3)
   4. Peg-IFN is contraindicated because of safety concerns
   5. Entecavir or TDF are preferred first-line agents
   6. Patients should be monitored for development of adverse effects of antiviral therapy, such as renal insufficiency or lactic acidosis.

Table 3. Host, Viral/Disease and Environmental Factors Associated with Cirrhosis and HCC

	Cirrhosis	**HCC**
Host	• 40 years of age • Male sex • Immune compromised	• 40 years of age • Male sex • Immune compromised • Positive family history • Born in Sub-Saharan Africa
Viral/disease	• High serum HBV DNA (>2,000 IU/mL) • Elevated ALT levels • Prolonged time to HBeAg seroconversion • Development of HBeAg-negative CHB • Genotype C	• Presence of cirrhosis • High serum HBV DNA (>2,000 IU/mL) • Elevated ALT • Prolonged time to HBeAg seroconverion • Development of HBeAg-negative CHB • Genotype C
Environmental	• Concurrent viral infections (HCV, HIV, and HDV) • Heavy alcohol use • Metabolic syndrome (obesity, diabetes)	• Concurrent viral infections (HCV, HIV, and HDV) • Heavy alcohol use • Metabolic syndrome (obesity, diabetes) • Smoking

Adapted from AASLD 2016 Guidelines for Treatment of Chronic Hepatitis B.

G. Resistance
   1. Adherence with antivirals should be encouraged to reduce the risk of drug resistance with NAs
   2. Testing for viral resistance in treatment naïve patients is not recommended but can be useful in the following situations:
      a. Considering peg-IFN therapy
      b. Past treatment experience
      c. Persistent viremia on NA therapy
      d. Virological breakthrough during treatment
   3. Virological breakthrough is usually followed by ALT elevation
   4. Antiviral resistance can lead to hepatitis flares and hepatic decompensation
   5. Antiviral resistance may also result in cross-resistance with other NAs, thus reducing future treatment options.
   6. Entecavir should not be used in patients with lamivudine or telbivudine resistance, because the risk of subsequent entecavir resistance is high.
   7. TDF monotherapy has been shown to be effective in patients with lamivudine-, adefovir-, or entecavir-resistant HBV and is the preferred salvage therapy particularly if NA history is unclear.
   8. Switching to an alternative antiviral with a high genetic barrier to resistance is preferred in patients that develop drug resistance versus combination therapy except if HBV is multidrug resistant.

H. Patients not receiving treatment should be assessed regularly to determine whether an indication for treatment has developed.

IV. Patient Education
   A. Disease transmission
      1. Have household and sexual contacts vaccinated
      2. Use barrier protection during sexual intercourse if partner is not vaccinated or naturally immune
      3. Do not share toothbrushes, tweezers or razors
      4. Do not share injection equipment (e.g., tattooing equipment)
      5. Cover open cuts and scratches
      6. Do not donate blood, organs, or sperm
   B. Natural history of HBV
   C. Abstinence or minimal alcohol ingestion
   D. Optimization of body weight
   E. Treatment of metabolic complications, including diabetes and dyslipidemia to prevent concurrent development of metabolic syndrome and fatty liver.
   F. Early signs and symptoms of infection
   G. Adherence with medications, lab and medical appointments

Chronic Hepatitis C Evaluation and Treatment Pathway

1

Initial Management of Chronic Hepatitis C Patients (Page 4)
- Complete baseline evaluation and confirmation of chronic HCV diagnosis
- Offer preventive health measures
- Enroll in chronic care clinic and follow up at least every 12 months or as clinically indicated (Page 5)
- If patient has cirrhosis, refer to the End Stage Liver Disease guideline for management of ESLD in addition to following this pathway.

2

Determine if patient should be referred to the designated provider and/or clinic for treatment evaluation. Document in EMR. Refer if all of the following is true.
- Willing and interested in undergoing treatment
- Cirrhosis (even if APRI score ≤ 0.5)
- No contraindications to therapy (page 7)
- Sufficient time left in system to complete work-up, treatment, and follow up evaluation of SVR
- APRI score > 0.5

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.**

3 Candidate for drug treatment evaluation?

No → 4

Continue to Monitor:
- Rule out other causes of liver disease (Table 7) & obtain Alpha-1 antitrypsin, ceruloplasmin, ANA, ferritin, serium iron, and TIBC. Consider specialty referral if indicated.
- Screen for hepatocellular carcinoma and obtain AFP. If AFP is elevated, consider screening for liver mass (refer to Liver Mass Referral Guideline).
- Follow in chronic care clinic at least every 12 months (Page 5)

Yes → 5

- Refer to designated HCV provider and/or clinic for continued treatment evaluation.
- Alpha-fetoprotein (AFP) should be ordered at the time of referral. If AFP is elevated, consider screening for liver mass (refer to Liver Mass Referral Guideline).

6

Treatment Evaluation
(Completed by Virology HCV Treatment Team in UTMB Sector or per Utilization Management review process for Texas Tech Sector)
- Factors to consider when determining if the patient is an eligible candidate for drug therapy
  - No contraindications to therapy (page 7)
  - Sufficient time left in the system to complete work-up , treatment, and follow up evaluation of SVR
  - Life expectancy is not ≤12 months
  - No evidence of ongoing participation in high risk behavior associated with the transmission of hepatitis C
  - Not pregnant
  - Demonstrated willingness to complete therapy, compliant with pretreatment work-up, or has not refused treatment
- Complete pre-treatment workup (Table 8)
- If the patient is <u>not</u> a candidate or chooses <u>not</u> to receive drug therapy, document the reason(s) in the EMR

7 Candidate for drug treatment?

No → 8

Patient will be referred back to the Unit Provider to:
- Follow in chronic care clinic at least every 12 months (Page 5)
- Periodically re-evaluate for treatment.
- If patient has cirrhosis, consider for MRIS or hospice as indicated.

Yes → 9

HCV Provider and/or HCV Clinic will:
- Distribute patient education information and obtain informed consent for treatment.
- Ensure patient is housed or transferred to a Center of Excellence and place on medical hold prior to therapy is initiation.
- Select drug (Table 13), document treatment plan, and response to therapy in EMR
- Follow monitoring schedule while on drug therapy.

10 Did patient successfully complete HCV treatment (SVR achieved)?

Yes → 11

Patient will be referred back to Unit Provider:
- For patients who <u>do not</u> have advanced fibrosis or abnormal LFTs, follow-up is the same as if never infected with HCV
- For patients with cirrhosis or abnormal LFTs, follow-up per ESLD disease management guideline

No → 12

Patient will continue to follow up by the HCV Provider and /or HCV Clinic

The pathway does not replace sound clinical judgment nor is it intended to strictly apply to all patients

By The Correctional Managed Care Pharmacy & Therapeutics Committee, Approved July 2008; Reviewed 5/11; Revised 9/13, 1/15, 11/16, 11/17, 3/18, 7/18, 5/20, *9/23*.

Definitions

1. APRI (AST to Platelet Ratio Index) – A non-invasive method for the assessment of fibrosis in chronic liver disease. It is the ratio of the AST level, expressed as a percentage of the upper limit of normal, divided by the platelet count in thousands per cubic millimeter. It is a good predictor of liver fibrosis but cannot replace the liver biopsy in all cases. . The APRI may be less predictive when there are co-morbid conditions other than liver disease that may affect the platelet count or AST level.

Table 1: APRI Calculation
[(AST ÷ ULN) ÷ Platelet Count] x 100 • Use most recent lab results. ULN = upper limit of normal for the AST level and platelet count is in 1,000/mm^3 • Available on CMCWEB under Tools and in the EMR under Guidelines • APRI ≥ 0.7 associated with significant fibrosis (F2) • APRI ≥ 1 associated with severe fibrosis (F3) • APRI ≥ 2 associated with cirrhosis (F4)

2. Cirrhosis - Cirrhosis or advanced liver disease is a chronic disease of the liver in which liver tissue is replaced by connective tissue or scar tissue, resulting in the loss of liver function.
   - Compensated cirrhosis - Compensated cirrhosis (CTP Class A) is characterized by laboratory evidence of liver dysfunction such as
     - Low albumin but ≥3.0,
     - Low platelet count but ≥ 70,000,
     - Elevated bilirubin but <2.0, and/or
     - Prolonged prothrombin time but less than 2 seconds greater than control in the absence of clinical complications associated with cirrhosis.
   - Decompensated cirrhosis - Decompensated cirrhosis (CTP Class B or C) is characterized by the presence of one or more of the clinical complications of chronic liver disease including ascites, encephalopathy, spontaneous bacterial peritonitis, variceal bleeding, jaundice, and/or impaired hepatic synthetic function (e.g., hyperbilirubinemia and hypoalbuminemia). Laboratory results consistent with decompensated cirrhosis are
     - Albumin < 3.0,
     - Platelet count < 70,000,
     - Bilirubin > 2,
     - Prothrombin time > 2 seconds longer than control

Table 2: Child Turcotte-Pugh (CTP) Calculator

	Points		
	1	**2**	**3**
Encephalopathy	None	Grade 1-2 (or precipitant-induced)	Grade 3-4 (or chronic)
Ascites	None	Mild / Moderate (diuretic-responsive)	Severe (diuretic-refractory)
Bilirubin (mg/dL)	< 2	2 – 3	> 3
Albumin (g/dL)	> 3.5	2.8 – 3.5	< 2.8
PT (second prolonged) or INR	< 4 < 1.7	4 – 6 1.7 – 2.3	> 6 > 2.3

CTP score is obtained by adding the score for each parameter
CTP class: A = 5 – 6 points
B = 7 – 9 points
C = 10-15 points

3. FRT (Fibrous Routine Test) - A non-invasive method for the assessment of fibrosis in chronic liver disease utilizing routine laboratory markers (age, albumin, APRI and AFP).

Table 3: FRT Calculation
3.31 + (age x 0.09) + (APRI x 1.5) + (AFP x 0.4) – (Alb x 0.14) • Use most recent lab results • Found in the EMR under Guidelines • FRT > 4 predictive Metavir score F2 – F4 (portal fibrosis with rare bridges – cirrhosis)

Definitions Cont.

4. Liver biopsy scoring schemas

Table 4: Comparison of Liver Biopsy Scoring Schemas			
Stage	Batts-Ludwig	Metavir	Ishak
No fibrosis	Stage 0	F0	0 = no fibrosis
Mild portal fibrous	Stage 1	F1	1 = Fibrous expansion some portal areas +/-septa 2 = fibrous expansion most portal areas +/-
Moderate periportal fibrosis or portal-portal septa	Stage 2	F2	3 = Fibrous expansion most portal areas with occasional portal-portal bridging
Severe bridging fibrosis	Stage 3	F3	4 = Fibrous expansion portal areas + marked bridging 5 = Marked bridging + occasional nodules
Cirrhosis	Stage 4	F4	6 = cirrhosis, probable or definite

5. Response to therapy
   - End of treatment response (ETR) - Undetectable HCV RNA level at the conclusion of a course of drug therapy
   - Sustained virologic response (SVR) - Undetectable HCV RNA level 12 weeks after the conclusion of a course of drug therapy
   - Relapse - Reappearance of serum HCV RNA after achieving an undetectable level at the conclusion of a course of drug therapy
   - Null response - Failure to reduce HCV RNA by at least 2 logs after treatment. Considered a non-responder.
   - Partial response - At least a 2 log drop in HCV RNA, but inability to fully remove the virus from the blood after treatment. Considered a non-responder.

Classification of Direct-Acting Antiviral (DAA) Agents

Table 5: Trade and Generic Names for First Line HCV DAA Medications		
DAA Trade Name	DAA Generic Name	Abbreviation
Harvoni®	ledipasvir/sofosbuvir	LDV/SOF
Zepatier®	elbasvir/grazoprevir	EBR/GZR
Epclusa®	Sofosbuvir/velpatasvir	SOF/VEL
Vosevi®	Sofosbuvir/velpatasvir/voxilaprevir	SOF/VEL/VOX
Mavyret®	glecaprevi/pibrentasvir	GLE/PIB

Classification of Direct-Acting Antiviral (DAA) Agents cont.

Table 6: HCV DAA Treatment Regimens by Class			
DAA Treatment Regimen	NS3/4A Protease Inhibitor	NS5B Nucleotide Polymerase Inhibitor	NS5A Polymerase Inhibitor
LDV/SOF ± RBV		✓	✓
EBR/GZR ± RBV	✓		✓
SOF/VEL ± RBV		✓	✓
SOF/VEL/VOX	✓	✓	✓
GLE/PIB	✓		✓
*RBV = ribavirin			

Initial Management

1. Baseline evaluation
   - Confirmation of diagnosis - A positive HCV antibody test should be followed by HCV RNA testing.
     - If HCV RNA is detected, the diagnosis of HCV infection is confirmed.
     - If HCV RNA is not detected, this likely represents either past infection that subsequently cleared or a false-positive antibody test. The estimated rate of spontaneous clearance after infection is 20 to 45 percent. These patients do not have chronic HCV and can be diagnosed with HCV Resolved.
   - History including probable date of HCV infection, alcohol use, co-infection with HIV or hepatitis B, drug use, symptoms of liver disease, and previous treatment for HCV.
   - Physical including signs of advanced liver disease, evidence of other causes of liver disease, and extra-hepatic manifestations of HCV (e.g., leukocytoclastic vasculitis, cryoglobulinemia, porphyria cutanea tardia, membranoproliferative glomerulonephritis, and type 2 diabetes)
   - Laboratories
     - CBC with differential & platelets
     - Prothrombin time, INR
     - ALT, AST, alkaline phosphatase, bilirubin, albumin, BUN, creatinine
     - HIV
     - HBsAB, HBcAB , HBsAg, HAVAb-Total
2. Offer preventive health measures
   - Vaccinations if indicated
     - Hepatitis B vaccine if hepatitis serum markers are negative
     - Hepatitis A vaccine if the HAVAb-Total test is negative
   - Patient education
     - Natural history of disease
     - Behaviors to avoid (e.g., alcohol)
     - Avoiding transmission (e.g., sharing needles, tattooing, or grooming items such as razors & toothbrushes; unprotected sex)
     - Potential treatments
   - Additional care if cirrhosis present
     - Pneumococcal vaccine
     - Annual influenza vaccination
     - Refer to the End Stage Liver Disease (ESLD) guideline for complete recommendations on management
3. Enroll in chronic care clinic and follow up at least every 12 months or as clinically indicated
4. Job assignments
   - Patients with chronic HCV should be restricted from plumber's helper or bar trap cleaner job assignments unless they have been vaccinated against hepatitis A or have been documented as positive HAVAb-Total.
   - Other restrictions should be made on a case-by-case basis if clinically indicated.

Chronic Care Clinic Follow Up

1. Unit provider needs to continue to follow the patient in CCC even after referral has been made to HCV Provider and/or Clinic.
2. Evaluate for clinical signs and symptoms of liver disease.
3. Laboratories
    - ALT, AST, bilirubin, albumin, CBC with differential & platelets, PT, INR
    - APRI score – if not available in the labs, calculate and record in results entry of EMR.
    - Other laboratories as clinically indicated
4. If cirrhotic
    - Calculate the MELD score. Available on CMCWEB under Tools and in the EMR under Guidelines
    - Refer to the ESLD guideline for recommendations on management and consider referral to ESLD clinic
    - Patients with decompensated cirrhosis and MELD score ≥ 22 or recurrent ascites, bleed or encephalopathy requires MRIS referral
    - Patients with MELD ≥ 30 should be referred to hospice
    - Patients unable to care for themselves in general population should be considered for sheltered housing or assisted living
5. Evaluate patient to determine if he/she is a candidate for drug treatment and document in the medical record.
    - If not a candidate initially
        - Re-evaluate the patient at least annually and refer the patient for evaluation of drug treatment if clinically indicated.
        - Rule out other causes of liver disease & obtain Alpha-1 antitrypsin, ceruloplasmin, ANA, ferritin, serium iron, and TIBC (See Table7). Consider specialty referral if indicated.
        - Screen for hepatocellular carcinoma (HCC) and obtain AFP. If AFP is elevated, consider screening for liver mass (refer to Liver Mass Referral Guideline).
    - Refer the patient to the designated HCV provider and/or clinic for treatment evaluation if all of the following are true:
        - Patient is willing and interested in undergoing treatment
        - No contraindications therapy
        - Sufficient time left in system to complete work-up and treatment
        - APRI score > 0.5*
            - May consider referring patients with an APRI score ≤ 0.5 if there is clinical or laboratory evidence of a failing liver, or the patient has co-morbid conditions that might cause elevation of the platelet count or unusually low AST levels resulting in an unreliable APRI Score.
            - Refer patients with cirrhosis even if APRI score ≤ 0.5.
        - Alpha-fetoprotein (AFP) should be ordered at the time of referral. If AFP is elevated, consider screening for liver mass (refer to Liver Mass Referral Guideline).
6. If there has been a change in the patient's health status and referral to HCV Provider and/or clinic has been made, contact the HCV team to notify them of the change.

Table 7: Causes of Liver Disease

Signs & Symptoms	Lab Test	Disease
Shortness of breath, cough, wheezing, early COPD ≤ 45, frequent lung infections, necrotizing panniculitis (looks like raised red spots on the skin)	↓ Alpha-1 antitrypsin	Alpha-1 antitrypsin deficiency
Swelling arms & legs; jaundice; joint pain; bruising; difficulty speaking, walking, & swallowing; drooling; shaking; rash	↓ Ceruloplasmin	Wilson Disease
Joint pain, irregular heart rhythm, skin color changes (bronze, ashen-gray green), hair loss, enlarged liver or spleen, fatigue	↑ Ferritin, serum iron, TIBC	Iron overload
Associated with other autoimmune diseases, jaundice, abdominal discomfort, enlarged liver, pruritus, spider angiomas, joint pain	↑ Antinuclear antibody (ANA)	Autoimmune hepatitis

Drug Treatment Evaluation

1. Patients should be evaluated for drug therapy by a provider experienced in the treatment of chronic hepatitis C. This is completed by the Virology HCV Treatment Team in the UTMB Sector or per the Utilization Management review process for the Texas Tech Sector
2. If the patient is not a candidate for drug therapy, document the reason(s) in the medical record.
3. If the patient chooses to not receive drug therapy, document the reason(s) in the medical record.
4. If no contraindications to drug therapy are present and the patient is a potential candidate for drug therapy, complete pre-treatment evaluation.

Table 8: Pre-treatment Workup

- Physical examination if not done in last 12 months
- If not done in preceding 12 weeks: ALT, AST, alkaline phosphatase, bilirubin, albumin, BUN, creatinine, CBC with differential, platelets, TSH, PT, INR, calculated GFR
- A1C if diabetic and not done in preceding 6 months
- HCV RNA and genotype
- Screen for HCC: Alpha-fetoprotein (AFP) and liver imaging
- Obtain liver ultrasound if FRT > 5, clinical evidence of cirrhosis, or as clinically indicated
- Pregnancy test if female
- Chest x-ray and EKG if clinically indicated
- Review previous HCV treatment history and clinical outcome

Candidate for Drug Therapy

1. There are factors to consider when determining if the patient is an eligible candidate for drug therapy.
   - No contraindications to therapy
   - Sufficient time left in the system to complete work-up, treatment, and follow up evaluation of SVR
   - Life expectancy is not ≤ 12 months
   - No evidence of ongoing participation in high risk behavior associated with the transmission of hepatitis C
   - Not pregnant
   - Demonstrated willingness to complete therapy and compliance with pretreatment work-up or refusal of treatment
2. If the patient is an eligible candidate for drug therapy and meets the criteria, he/she will be prioritized for treatment by the HCV provider and/or clinic.

Initiation of Therapy

1. Distribute patient education materials to patient
2. Obtain informed consent and document in the medical record
3. Patients should be housed at a Center of Excellence while on therapy.
4. Patients must be placed on medical hold while on therapy.(refer to Standard Operating Procedure: Placing Patients on Medical Hold During Hepatitis C Treatment)
5. Monitor the patient per monitoring schedule while on drug therapy

Contraindications to Drugs Used for the Treatment of Chronic Hepatitis C

Note: Modifiable or treatable contraindications should be controlled or resolved and the patient reconsidered for treatment whenever possible.

Table 9: Velpatisvir/Sofosbuvir (Epclusa®)

Contraindications	Relative Contraindications

Previously demonstrated hypersensitivity to the drug
Concomitant usage with
• Anticonvulsant: Carbamazepine, Oxcarbazepine, Phenobarbital, Phenytoin, *Primidone*
• Antimycobacterials: Rifampin, Rifabutin, Rifapentine
• Omeprazole[1]
• St. John's wort
• Amiodarone[2]
• HIV medications:
  • Efavirenz, etravirine, nevirapine
  • Tipranavir
	Concomitant usage with
	• Acid reducing agents:
	  • Antacids (e.g., aluminum and magnesium hydroxide)[3]
	  • H2-antagonists (e.g., Famotidine)[4]
	• Digoxin[5]
	• HIV medications: regimens containing tenofovir *DF*[5,6]
	• Rosuvastatin and atorvastatin[6,7]
	• Warfarin[8]

1. Co-administration of omeprazole is not recommended. If it is considered medically necessary to coadminister, velpatasvir/sofosbuvir should be administered with food and taken 4 hours before omeprazole 20mg qd.
2. *Severe bradycardia may occur with co-administration of amiodarone. If coadministration is required, cardiac monitoring is recommended.*
3. Separate antacid and velpatasvir/sofosbuvir by 4 hours.
4. H_2–receptor antagonists may be administered simultaneously with or 12 hours apart from velpatasvir/sofosbuvir at a dose that does not exceed *doses comparable to famotidine 40 mg twice daily*.
5. Therapeutic monitoring of digoxin is recommended when co-administered with velpatasvir/sofosbuvir.
6. Monitor for tenofovir-associated adverse reactions in patients receiving velpatasvir/sofosbuvir concomitantly with a regimen containing tenofovir.
7. Co-administration of HMG-CoA reductase inhibitors with velpatasvir/sofosbuvir will increase the concentration of the HMG-CoA reductase inhibitor. Rosuvastatin should be limited to 10mg daily when co-administered with velpatasvir/sofosbuvir. Side effects of atorvastatin such as myopathy and rhabdomyolysis should be monitored when co-administered.
8. DAAs may diminish the anticoagulant effect of warfarin (reduced INR, thrombosis). Frequent monitoring of PT/INR is recommended upon initiation and discontinuation of DAA therapy.

Table 10: Glecaprevir/Pibrentasvir (Mavyret®)

Contraindications	Relative Contraindications

Previously demonstrated hypersensitivity to the drug
Concomitant usage with
• Antimycobacterials: Rifampin
• HIV medications: Atazanavir, ritonavir, darunavir, lopinavir, efavirenz[1], etravirine, nevirapine.
	Concomitant usage with
	• Anticonvulsant: Carbamazepine[1]
	• Cyclosporine[2]
	• Digoxin[3]
	• Dabigatran[4]
	• Ethinyl estradiol[5]
	• St. John's wort[1]
	• Antihyperlipidemics
	  • Atorvastatin, lovastatin, simvastatin[6]
	  • Rosuvastatin, pravastatin, fluvastatin, pitavastatin[7]
	• Warfarin[8]

1. Carbamazepine, efavirenz, and St. John's wort may significantly decrease plasma concentrations of glecaprevir/pibrentasvir, leading to reduced therapeutic effect.
2. Co-administration with cyclosporine is not recommended in patients receiving cyclosporine > 100 mg per day.
3. Measure serum digoxin concentrations before initiating glecaprevir/pibrentasvir. Digoxin dose reduction of 50% may be required.
4. Follow dabigatran prescribing information for dose modifications in combination with P-gp inhibitors in the setting of renal impairment.
5. Co-administration with ethinyl estradiol may increase the risk of ALT elevations.
6. Increased statin concentration may increase the risk of myopathy including rhabdomyolysis. Co-administration with these statins is not recommended.
7. Rosuvastatin may be co-administered at a dose not to exceed 10mg, reduce pravastatin dose by 50%, use the lowest approved dose of fluvastatin and pitavastatin.
8. DAAs may diminish the anticoagulant effect of warfarin (reduced INR, thrombosis). Frequent monitoring of PT/INR is recommended upon initiation and discontinuation of DAA therapy.

Contraindications to Drugs Used for the Treatment of Chronic Hepatitis C - Continued

Table 11: Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi®)	
Contraindications	**Relative Contraindications**

Previously demonstrated hypersensitivity to the drug
Concomitant usage with
• Antimycobacterials: Rifampin, rifabutin, rifapentine
• *Amiodarone*[1]
• *Anticonvulsant: Carbamazepine, oxcarbazepine, phenobarbital, phenytoin, primidone*
• *St. John's wort*
• *HIV medications:*
  • *Efavirenz, etravirine, nevirapine*
  • *Atazanavir, atazanavir/r, lopinavir, tipranavir*
	Concomitant usage with
	• Acid reducing agents[3]:
	  • Antacids (e.g., aluminum and magnesium hydroxide)
	  • H2-antagonists (e.g., Famotidine)
	  • *Omeprazole*[2]
	• Cyclosporine
	• Digoxin[4]
	• Dabigatran[5]
	• HIV medications: regimens containing *tenofovir DF*[6]
	• Antihyperlipidemics
	  • Pravastatin, rosuvastatin, pitavastatin[7]
	  • Atorvastatin, fluvastatin, lovastatin, simvastatin[8]
	• Warfarin[9]

1. Severe bradycardia may occur with co-administration of amiodarone. *If coadministration is required, cardiac monitoring is recommended.*
2. *Co-administration of omeprazole is not recommended. If it is considered medically necessary to coadminister, velpatasvir/sofosbuvir/voxilaprevir should be administered with food and taken 4 hours before omeprazole 20mg qd.*
3. Drugs that increase gastric pH are expected to decrease concentrations of sofosbuvir/velpatasvir/voxilaprevir. Separate antacid administration by 4 hours. H2-receptor antagonists may be administered simultaneously. Omeprazole 20mg can be administered with sofosbuvir/velpatasvir/voxilaprevir. Other PPIs have not been studied.
4. Therapeutic monitoring of digoxin is recommended when co-administered.
5. Clinical monitoring of dabigatran is recommended. Follow dabigatran prescribing information for dose modifications in the setting of renal impairment.
6. *Monitor for tenofovir-associated adverse reactions in patients receiving velpatasvir/sofosbuvir concomitantly with a regimen containing tenofovir.*
7. Increased statin concentration may increase the risk of myopathy including rhabdomyolysis. Co-administration with these statins is not recommended.
8. Increased risk of myopathy including *rhabdomyolysis*. Use the lowest approved statin dose based on risk/benefit assessment.
9. DAAs may diminish the anticoagulant effect of warfarin (reduced INR, thrombosis). Frequent monitoring of PT/INR is recommended upon initiation and discontinuation of DAA therapy.

Table 12: Ribavirin	
Absolute Contraindications	**Relative Contraindications**
• Pregnancy (during treatment and for 6 months afterward; also applies to partners of males who are treated) • Hemoglobinopathies (e.g., sickle cell, thalassemia major) • Hemolytic or other severe anemias • Unstable or significant cardiac disease. • Renal insufficiency with serum creatinine > 2.0 • Co-administration with didanosine • Previously demonstrated hypersensitivity to the drug	• *Azathioprine*[1]

1. *The use of ribavirin for the treatment of chronic hepatitis C in patients receiving azathioprine has been reported to induce severe pancytopenia and may increase the risk of azathioprine-related myelotoxicity.*

Drug Selection

1. Selection of drug regimen is based on patient specific characteristics including genotype, prior HCV treatment history, degree of cirrhosis, and co-morbidities.

2. The treatment regimens listed below are no longer recommended unless completing a course of treatment that has been previously initiated.
   - Monotherapy with peginterferon
   - Dual therapy with peginterferon plus ribavirin
   - Triple therapy with peginterferon, ribavirin, plus boceprevir or telaprevir
   - Triple therapy with peginterferon, ribavirin, plus sofosbuvir

3. Antiretroviral regimen changes may be necessary prior to initiating HCV drug treatment due to drug-drug interactions.
   - Glecaprevir/pibrentasvir co-administration is contraindicated with atazanavir and atazanavir/r.
   - Glecaprevir/pibrentasvir co-administration is listed as do not coadminister with darunavir, lopinavir, efavirenz, and etravirine.
   - Sofosbuvir/velpatasvir/voxilaprevir do not coadminister with atazanavir, atazanavir/r, lopinavir, tipranavir, efavirenz, etravirine or nevirapine
   - Sofosbuvir/velpatasvir/voxilaprevir should be used cautiously with tenofovir DF and patients should be monitored for adverse effects associated with tenofovir DF
   - Velpatasvir/sofosbuvir should be used cautiously with HIV regimens containing tenofovir.
   - Velpatasvir/sofosbuvir do not coadminister with tipranavir, efavirenz, etravirine, or nevirapine

4. Discontinuation of therapy
   - If viral load is detectable at week 4 of treatment, repeat the viral load after 2 additional weeks of treatment (treatment week 6). If it has increased by greater than 10-fold (>1 log10 IU/mL) on repeat testing at week 6, then discontinue treatment.

Dose Modification Guide

Notes:
- Information is adapted from manufacturer package inserts and is not expected to cover every clinical scenario.
- Information does not preclude the exercise of clinical judgment

Table 13: Hematological Dose Modification Guide	
Lab Value	**Action**
Hemoglobin 8.5 - 10 g/dL patient no cardiac disease	• Dose reduction: Ribavirin 600 mg/day • Continue dose direct-acting antiviral
Hemoglobin < 8.5 g/dL patient no cardiac disease	• Discontinue ribavirin until resolved[1] • May need to discontinue direct-acting antiviral[2]
Hgb ≥ 2g/dL reduction in 4 weeks patient with stable cardiac disease	• Dose reduction: Ribavirin 600 mg/day • Continue dose direct-acting antiviral
Hemoglobin < 12 g/dL after 4 weeks at reduced dosage patient with stable cardiac disease	• Discontinue ribavirin until resolved[1] • May need to discontinue direct-acting antiviral[2]

1. Once ribavirin is discontinued due to a laboratory abnormality or clinical adverse reaction, an attempt may be made to restart at 600 mg daily and further increase the dose to 800 mg daily. However, it is not recommended that ribavirin be increased to the original dose (1000 mg or 1200 mg).
2. Direct-acting antiviral for hepatitis C (e.g., velpatisvir/sofosbuvir) may need to be discontinued. Consult experienced physician.

Table 14: ALT Dose Modification Guide	
Lab Value	**Action**
10-fold increase in ALT at week 4	Promptly discontinue therapy
Any increase in ALT of less than 10-fold at week 4 if accompanied by any weakness, nausea, vomiting, or jaundice, or accompanied by increased bilirubin, alkaline phosphatase, or INR	Promptly discontinue therapy
Asymptomatic increases in ALT of less than 10-fold at week 4	Monitor ALT at week 6 and week 8. If levels remain persistently elevated, consideration should be given to discontinuation of therapy.

Table 15: Renal Impairment Dose Modification				
Creatinine clearance	**Ribavirin**	Velpatisvir/sofosbuvir (Epclusa®)	Sofosbuvir/velpatasvir/ voxilaprevir (Vosevi®)	Glecaprevir/Pibrentasvir (Mavyret®)
30 to 50 mL/min	Alternating doses, 200 mg and 400 mg every other day	1 tablet once daily	1 tablet once daily	3 tablets once daily
< 30 mL/min	200 mg once daily	No dosage adjustment required†	No dosage adjustment required	No dosage adjustment required
Hemodialysis	200 mg once daily	No dosage adjustment required†	No dosage adjustment required	No dosage adjustment required
†Preferred agent in CKD 4 and 5.				

Table 16: Velpatasvir/sofosbuvir	
Brand Name	Epclusa®
Special Notes	• Store only in original container • Treatment is not guided by on treatment HCV RNA response • Preferred in patients with CKD Stage 4 or 5
Formulation	Fixed-dose combination tablet Velpatasvir 100mg/sofosbuvir 400mg
Dose	1 tablet orally once daily with or without food
Mechanism of Action	• Direct-acting antiviral • Velpatasvir is an inhibitor of the HCV NS5A protein, which is required for viral replication • Sofosbuvir is an inhibitor of the HCV NS5B RNA-dependent RNA polymerase, which is required for viral replication
Duration of Therapy	
G1, G2, G3, G4, G5, G6: Treatment naïve without cirrhosis or *with* compensated cirrhosis	12 Weeks (For G3, with compensated cirrhosis: add weight-based ribavirin)
G1, G2, G3, G4, G5, G6: Treatment naïve with decompensated cirrhosis	12 Weeks with weight-based ribavirin (low initial dose of ribavirin is recommended for patients with CTP class C cirrhosis; increase as tolerated) *or 24 weeks* if ineligible for ribavirin
G1, G2, G3, G4, G5, G6: SOF- or NS5A inhibitor-Treatment failure with decompensated cirrhosis	24 weeks with Weight-based ribavirin, if CTP is Class C, then a low initial dose of ribavirin is recommended
Adverse effects*	• Fatigue (most common) • Headache (most common) • Nausea • Asthenia • Insomnia • Transient, asymptomatic lipase elevations of greater than 3 times upper limit of normal

Drug interactions*	• Acid reducing agents:
	  • Antacids (e.g., aluminum and magnesium hydroxide)[1]
	  • H2-antagonists (e.g., ranitidine)[2]
	  • Proton pump inhibitors (e.g., omeprazole)[3]
	• Antiarrhythmics:
	  • Amiodarone[4]
	  • Digoxin[5]
	• HIV medications:
	  • Do not coadminister with tipranavir, efavirenz[6], etravirine, or nevirapine
	  • Regimens containing Tenofovir[7]
	• Anticonvulsant: Carbamazepine, Oxcarbazepine, Phenobarbital, Phenytoin[8]
	• Antimycobacterials: Rifampin, Rifabutin, Rifapentine[8]
	• St. John's wort[8]
	• HMG-CoA Reductase Inhibitors: Atorvastatin and Rosuvastatin[9]
	• Warfarin [10]

*Note: refer to the manufacturer's product information for additional information and a complete list

1. Separate antacid and velpatasvir/sofosbuvir administration by 4 hours
2. Administer H2-receptor antagonist simultaneously with velpatasvir/sofosbuvir or 12 hours apart at a dose that does not exceed ranitidine 150mg bid
3. Co-administration of any proton pump inhibitor is not recommended. If it is considered medically necessary to coadminister, velpatasvir/sofosbuvir should be administered with food and taken 4 hours before omeprazole 20mg.
4. Coadministration of amiodarone wwith velpatasvir/sofosbuvir may result in serious bradycardia. Coadministration is not recommended;
5. Co-administration of velpatasvir/sofosbuvir with digoxin may increase the concentration of digoxin. Therapeutic concentration monitoring of digoxin is recommended
6. Co-administration of velpatasvir/sofosbuvir with efavirenz is not recommended as efavirenz may decrease the concentration of velpatasvir.
7. Monitor for tenofovir-associated adverse reactions in patients receiving velpatasvir/sofosbuvir.
8. Co-administration is not recommended.
9. Co-administration of velpatasvir/sofosbuvir with rosuvastatin or atorvastatin increases the concentration of the statin, which is associated with increased risk of myopathy. Monitor close for statin-associated adverse reactions, such as myopathy and rhabdomyolysis.
10. DAAs may diminish the anticoagulant effect of warfarin (reduced INR, thrombosis). Frequent monitoring of PT/INR is recommended upon initiation and discontinuation of DAA therapy.

Glecaprevir/pibrentasvir Drug Information

Table 17: Glecaprevir/pibrentasvir	
Brand Name	Mavyret®
Special Notes	• Store only in original container. Supplied in a 4-week (monthly) carton. • Treatment is not guided by on treatment HCV RNA response • Contraindicated in patients with decompensated cirrhosis
Formulation	Fixed-dose combination tablet glecaprevir 100mg/pibrentasvir 40mg
Dose	3 tablets orally once daily with food
Mechanism of Action	• Direct-acting antiviral • Glecaprevir is an inhibitor of the HCV NS3/4A protease, which is required for viral replication • Pibrentasvir is an inhibitor of the HCV NS5A protein, which is required for viral replication and viral assembly
Duration of Therapy G1, G2, G3, G4, G5, G6: Treatment naïve, without cirrhosis or with compensated cirrhosis G1, G2, G4, G5, G6: Sofosbuvir- based treatment failure, without cirrhosis or with compensated cirrhosis**	 8 weeks 16 weeks, not recommended for patients with prior exposure to an NS5A inhibitor plus NS3/4A protease inhibitor regimen (e.g., elbasvir/grazoprevir)
Adverse effects*	• Fatigue (most common) • Headache (most common) • Nausea (most common) • Elevated of total bilirubin

Drug interactions*	• Anticonvulsant: Carbamazepine[1]
	• Antimycobacterials: Rifampin[2]
	• HIV medications
	  • Atazanavir and Atazanavir/r [2]
	  • Do not coadminister with darunavir, lopinavir, efavirenz, or etravirine
	  • Consider alternative with nevirapine
	• Cyclosporine[3]
	• Digoxin[4]
	• Dabigatran[5]
	• Ethinyl estradiol[6]
	• St. John's wort[1]
	• Antihyperlipidemics
	  • Atorvastatin, lovastatin, simvastatin[7]
	  • Rosuvastatin, pravastatin, fluvastatin, pitavastatin[8]
	• Warfarin[9]

** *as an alternative therapy to Sofosbuvir/Velpatasvir/Voxilaprevir treatment*

*Note: refer to the manufacturer's product information for additional information and a complete list

1. Carbamazepine and St. John's wort may significantly decrease plasma concentrations of glecaprevir/pibrentasvir, leading to reduced therapeutic effect.
2. Co-administration with atazanavir or rifampin is contraindicated.
3. Co-administration with cyclosporine is not recommended in patients receiving cyclosporine > 100 mg per day.
4. Measure serum digoxin concentrations before initiating glecaprevir/pibrentasvir. Digoxin dose reduction of 50% may be required.
5. Follow dabigatran prescribing information for dose modifications in combination with P-gp inhibitors in the setting of renal impairment.
6. Co-administration with ethinyl estradiol may increase the risk of ALT elevations.
7. Increased statin concentration may increase the risk of myopathy including rhabdomyolysis. Co-administration with these statins is not recommended.
8. Rosuvastatin may be co-administered at a dose not to exceed 10mg, reduce pravastatin dose by 50%, use the lowest approved dose of fluvastatin and pitavastatin.
9. DAAs may diminish the anticoagulant effect of warfarin (reduced INR, thrombosis). Frequent monitoring of PT/INR is recommended upon initiation and discontinuation of DAA therapy.

Sofosbuvir/velpatasvir/voxilaprevir Drug Information

Table 18: Sofosbuvir/velpatasvir/voxilaprevir	
Brand Name	Vosevi®
Special Notes	• Store only in original container • Treatment is not guided by on treatment HCV RNA response • Not recommended in patients with moderate or severe hepatic impairment (Child-Pugh B or C) • Indicated for patients who are DAA treatment experienced
Formulation	Fixed-dose combination tablet sofosbuvir 400mg/velpatasvir 100mg/voxilaprevir 100mg
Dose	1 tablet orally once daily with food
Mechanism of Action	• Direct-acting antiviral • Sofosbuvir is an inhibitor of the HCV NS5B RNA-dependent RNA polymerase, which is required for viral replication • Velpatasvir is an inhibitor of the HCV NS5A protein, which is required for viral replication • Voxilaprevir is an inhibitor of the HCV NS3/4A protease, which is required for viral replication
Duration of Therapy G1, G2, G3, G4, G5, G6: glecaprevir/pibrentasvir- based treatment failure, without cirrhosis OR *sofosbuvir-based treatment failure,* without cirrhosis G1, G2, G4, G5, G6: *sofosbuvir-based treatment failure,* with compensated cirrhosis	12 weeks
G1, G2, G3, G4, G5, G6: glecaprevir/pibrentasvir based treatment failure, with compensated cirrhosis G3 Sofosbuvir based treatment failure, with compensated cirrhosis	12 weeks *+ weight-based ribavirin*
Adverse effects*	• Fatigue (most common) • Headache (most common) • Nausea (most common) • Diarrhea (most common) • Elevated total bilirubin, lipase, and creatine kinase

Table 18: Sofosbuvir/velpatasvir/voxilaprevir cont. Footnotes

Drug interactions*	• Antimycobacterials: Rifampin, rifabutin, rifapentine
	• Amiodarone[1]
	• Acid reducing agents[2]:
	  • Antacids (e.g., aluminum and magnesium hydroxide)[2]
	  • H2-antagonists (e.g., ranitidine)[3]
	• Anticonvulsant: Carbamazepine, Oxcarbazepine, Phenobarbital, Phenytoin
	• Cyclosporine
	• Digoxin[3]
	• Dabigatran[4]
	• St. John's wort
	• HIV medications:
	  • Do not coadminister with atazanavir, atazanavir/r, lopinavir, tipranavir, efavirenz, etravirine, or nevirapine
	  • tenofovir use with caution
	• Antihyperlipidemics
	  • Pravastatin, rosuvastatin, pitavastatin[5]
	  • Atorvastatin, fluvastatin, lovastatin, simvastatin[6]
	• Warfarin[7]

1. Severe bradycardia may occur with co-administration.
2. Drugs that increase gastric pH are expected to decrease concentrations of sofosbuvir/velpatasvir/voxilaprevir. Separate antacid administration by 4 hours. H2-receptor antagonists may be administered simultaneously. Omeprazole 20mg can be administered with sofosbuvir/velpatasvir/voxilaprevir. Other PPIs have not been studied.
3. Therapeutic monitoring of digoxin is recommended when co-administered.
4. Clinical monitoring of dabigatran is recommended. Follow dabigatran prescribing information for dose modifications in the setting of renal impairment.
5. Increased statin concentration may increase the risk of myopathy including rhabdomyolysis. Co-administration with these statins is not recommended.
6. Increased risk of myopathy including rhabdomyolosis. Use the lowest approved statin dose based on risk/benefit assessment.
7. DAAs may diminish the anticoagulant effect of warfarin (reduced INR, thrombosis). Frequent monitoring of PT/INR is recommended upon initiation and discontinuation of DAA therapy.

Ribavirin Drug Information

Table 19: Ribavirin

Brand Name	Rebetol®, Ribasphere®
Special Notes	• Not effective as monotherapy • Pregnancy category X • Do not use in pregnancy and for 6 months after treatment • Must have a negative pregnancy test prior to therapy and monthly pregnancy tests
Formulation	200 mg capsule
Weight Based Dose	**Weight < 75 kg** • 400mg orally in the morning • 600mg orally in the evening **Weight ≥ 75 kg** • 600mg orally twice daily
Mechanism of Action	Not fully understood. Inhibits autonomous HCV RNA replication.

Adverse effects*	• Serious adverse effects:
	  • Birth defects and fetal death
	  • Hemolytic anemia resulting in worsening of cardiac disease and myocardial infarction
	  • Severe hypersensitivity reactions including urticaria, angioedema, bronchoconstriction, and anaphylaxis, and serious skin reactions such as Stevens-Johnson Syndrome

Drug interactions*	• Azathioprine due to reports of severe pancytopenia and myelotoxicity • Didanosine due to reports of fatal hepatic failure, as well as peripheral neuropathy, pancreatitis, and symptomatic hyperlactatemia/lactic acidosis • Zidovudine due to reports of severe neutropenia and anemia

*Note: refer to the manufacturer's product information for additional information and a complete list

Monitoring Schedule for **Velpatasvir/sofosbuvir** (Epclusa®) –
12 WEEK SCHEDULE

Week of Treatment	**Base-line**	**2**	**4**	**8**	**12**	**Post Treatment**
Date						
Clinical Evaluation[1]	√	√	√	√	√	12 weeks post treatment
HCV genotype	√					
HCV RNA PCR[2]	√		**√[5]**		√	12 weeks post treatment
CBC with diff[3]	√					
CMP[4]	√		√	√	√	
Calculated Glomerular filtration rate (GFR)	√		√	√	√	
PT/INR	√					
Medication Adherence		√	√	√	√	
HIV	√					
HBsAB, HBcAB, HBsAg, HAVAb-Total	√					
Alpha-fetoprotein (AFP)	√					
Liver imaging studies	√					

1. Clinical evaluations should be scheduled a few days after laboratory results are expected to be available.
2. HCV RNA PCR quantitative
3. CBC = Complete blood count with differential
4. CMP = complete metabolic panel includes albumin, alkaline phosphatase, ALT, AST, bilirubin, calcium, carbon dioxide, chloride, potassium, sodium, glucose, creatinine, protein, BUN
5. If viral load is detectable at week 4 of treatment, repeat the viral load after 2 additional weeks of treatment (treatment week 6). If it has increased by greater than 10-fold (>1 log10 IU/mL) on repeat testing at week 6, then discontinue treatment

Monitoring Schedule for **Ribavirin plus Velpatasvir/sofosbuvir** (Epclusa®) –
12 WEEK SCHEDULE

Week of Treatment	**Base-line**	**2**	**4**	**8**	**12**	**Post Treatment**
Date						
Clinical Evaluation[1]	√	√	√	√	√	12 weeks post treatment
HCV genotype	√					
HCV RNA PCR[2]	√		**√[7]**		√	12 weeks post treatment
Urine Pregnancy Test[3]	√		√	√	√	Monthly x 6 months
CBC with diff[4]	√	√	√	√	√	
CMP[5]	√	√	√	√	√	
Calculated Glomerular filtration rate (GFR)	√		√	√	√	
PT/INR	√	√	√	√	√	
Medication Adherence		√	√	√	√	
Weight	√	√	√	√	√	
HIV	√					
HBsAB, HBcAB, HBsAg, HAVAb-Total	√					
EKG[6]	√					
Chest x-ray[6]	√					
Alpha-fetoprotein (AFP)	√					
Liver imaging studies	√					

1. Clinical evaluations should be scheduled a few days after laboratory results are expected to be available.
2. HCV RNA PCR quantitative
3. Urine pregnancy test = Females should be tested monthly during treatment and during the 6 months after treatment is stopped if childbearing potential
4. CBC = Complete blood count with differential
5. CMP = complete metabolic panel includes albumin, alkaline phosphatase, ALT, AST, bilirubin, calcium, carbon dioxide, chloride, potassium, sodium, glucose, creatinine, protein, BUN
6. If clinically indicated.
7. If viral load is detectable at week 4 of treatment, repeat the viral load after 2 additional weeks of treatment (treatment week 6). If it has increased by greater than 10-fold (>1 log10 IU/mL) on repeat testing at week 6, then discontinue treatment

Monitoring Schedule for **Velpatasvir/sofosbuvir** (Epclusa®) –
24 WEEK SCHEDULE

Week of Treatment	**Base-line**	**2**	**4**	**8**	**12**	**16**	**20**	**24**	**Post Treatment**
Date									
Clinical Evaluation[1]	√	√	√	√	√	√	√	√	12 weeks post treatment
HCV genotype	√								
HCV RNA PCR[2]	√		**√[5]**					√	12 weeks post treatment
CBC with diff[3]	√								
CMP[4]	√		√	√	√	√	√	√	
Calculated Glomerular filtration rate (GFR)	√		√	√	√	√	√	√	
PT/INR	√								
Medication Adherence		√	√	√	√	√	√	√	
HIV	√								
HBsAB, HBcAB, HBsAg, HAVAb-Total	√								
Antinuclear antibody (ANA)	√								
Alpha-fetoprotein (AFP)	√								
Alpha-1 antitrypsin	√								
Liver imaging studies	√								

1. Clinical evaluations should be scheduled a few days after laboratory results are expected to be available.
2. HCV RNA PCR quantitative
3. CBC = Complete blood count with differential
4. CMP = complete metabolic panel includes albumin, alkaline phosphatase, ALT, AST, bilirubin, calcium, carbon dioxide, chloride, potassium, sodium, glucose, creatinine, protein, BUN
5. If viral load is detectable at week 4 of treatment, repeat the viral load after 2 additional weeks of treatment (treatment week 6). If it has increased by greater than 10-fold (>1 log10 IU/mL) on repeat testing at week 6, then discontinue treatment

1

HIV DISEASE MANAGEMENT

Initial evaluation of HIV+ patients to be done at the intake facility by facility provider:

1) Obtain medical history including sexual history, social history, medication history, & history of opportunistic infections.
2) Complete physical examination: vitals, weight, general exam, neurologic examination, and pelvic exam with PAP and GC/chlamydia tests.
3) Obtain baseline laboratories: CBC with differential, Chemistry profile to include LFTs, serum creatinine, fasting blood sugar and lipid profile, Hepatitis serology (HbsAg, Anti-HBs, anti-HBc total antibody, anti-HCV and anti-HAV total antibody), Syphilis screen (RPR), Urinalysis, calculated estimate of glomerular filtration rate (GFR) (available in Tools on the CMC Web), CD4+ lymphocyte analysis, HIV RNA viral load, Varicella-Zoster Immune Status, Chest X-ray, PPD skin test. Test for serum Cryptococcal Antigen (CrAg) in people with newly diagnosed HIV for patients whose CD4 counts are ≤100 cells/mm3. A positive test generally should prompt CSF evaluation for CNS infection, particularly when the serum LFA titer is ≥1:160.
4) Screen patients for risk of chronic kidney disease by obtaining urinalysis, calculating GFR, and assessing risk. Risk factors include family history of renal disease, African American, CD4 < 200 cells/mm^3, VL > 4000 copies/ml, certain diseases (diabetes, HTN, hepatitis C co-infection), & concomitant use of nephrotoxic agents. If 1+ proteinuria or calculated GFR < 60 ml/min/1.73m^2, consider further evaluation. If normal & high risk based on risk factors, reassess and recheck annually. If normal & patient does not have risk factors, reassess annually in chronic care clinic (CCC).
5) Update vaccines: influenza vaccine annually; pneumococcal vaccine with single revaccination 5 years after the first dose; hepatitis A & B vaccine if not already immune; varicella vaccine if CD4 > 200 and patient born after 1979 with no history of disease, vaccination, or evidence of immunity.
6) Initiate prophylactic medication(s) for opportunistic infection(s) as indicated in box A page 3 & box B page 4.
7) Refer to dental for oral/periodontal evaluation within 30 days from initial chronic care visit.
8) Refer all HIV + patients regardless of CD4 count to the CMC Virology Clinic offered via DMS (UTMB sector) or designated physician (Texas Tech sector) for evaluation for antiretroviral treatment (ART). If patient refuses, contact the CMC Virology Clinic (UTMB sector) or designated physician (Texas Tech sector) for drug therapy and ITP recommendations.
    a. Expedited referrals should be obtained for patients that are symptomatic or have a CD4 count < 200 cells/mm^3. For patients on nonformulary treatment at intake, expedited referrals should be obtained within 2 weeks.

2

Follow-up for HIV+ Patients:

1) Evaluate in chronic care clinic at least every 6 months.
2) Refer patients with CD4 count < 100 cells/mm^3 to Ophthalmology for a retinal examination to rule out HIV retinopathy & CMV retinitis.
3) Laboratories:

- CD4 count every 3 to 6 months if not on treatment. For patients beginning ART, CD4 count should be repeated as follows:
    - Every 3 months for the first 2 years of suppressive ART if CD4 counts <300 cells/mm3
    - Every 6 months if CD4 count is ≥300 cells/mm3

After 2 years of suppressive ART, CD4 count monitoring can be reduced as follows:

- Every 6 months for patients whose CD4 counts remain at <300 cells/mm3
- Every year for patients with CD4 counts between 300 cells/mm3 and 500 cells/mm3
- Optional for those with CD4 counts >500 cells/mm3

- Viral load measurement should be repeated every 3 to 4 months or as clinically indicated to confirm continuous viral suppression.

Clinicians may extend the interval to 6 months for adherent patients whose viral load has been suppressed for more than a year.

- Obtain CBC with differential when checking CD4 count or every 12 months when no longer checking CD4 count.
- Chemistries including LFTs, serum creatinine, blood sugar every 6 months.
- Lipids annually.

4) Consider discontinuing prophylactic medication(s) for opportunistic infection(s) as indicated in box A & B, pages 3-4.

3

1. Antiretroviral therapy (ART) is recommended for all individuals with HIV, regardless of CD4 T lymphocyte cell count, to reduce the morbidity and mortality associated with HIV infection.
2. Discuss pros & cons of drug therapy, adherence, resistance, administration, possible adverse effects & management.
3. If patient is committed, begin HAART. Consider follow up in 2 to 4 weeks to assess medication tolerance.
4. If patient is poor candidate for drug therapy and/or does not want to start therapy, return to clinic every 3 to 6 months for follow-up.

4

Go to box #5 on page 2

Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee.
Approved 9/96, reviewed 2/03, revised 4/97, 9/97, 9/98, 3/99, 7/02, 4/03, 1/04,1/05, 5/06, 3/07, 5/07, 9/09, 7/10, 9/14, 5/15, 11/18, 03/23, 11/25.

WHEN POSSIBLE, IT IS PREFERRED THAT ALL HIV MEDICATIONS AND LABORATORIES BE ORDERED BY THE CMC VIROLOGY CLINIC (UTMB SECTOR) OR DESIGNATED PHYSICIAN (TT SECTOR).

5 Continued from box #4 on page 1

6 Is adherence perceived to be ≥ 80% and is the patient tolerant?

Yes → 7 Reinforce education. Return to clinic 1 month.

No → 8

Verify that administration is correctly documented on the computer :
1) Counsel patient regarding the importance of adherence and warn patient noncompliance may lead to medication discontinuation.
2) Identify & treat adverse effects if present
3) Return to clinic in 1 month

10 Is adherence perceived to be ≥ 80%?

Yes → 12 Go To Box #15.

No → 11

When adherence < 80% for 2 consecutive months:
1) Provide adherence counseling and education. After 3 consecutive counseling attempts 1 month apart, can consider discontinuation.
2) Obtain expedited referral for evaluation by CMC Virology Clinic (UTMB sector) or designated physician (Texas Tech sector) to determine subsequent management.
3) Consideration may be given to discontinuing therapy in patients that do not want to continue therapy, or are non-adherent to medications and clinic appointments, due to the possibility of developing resistance and to pause therapy to reflect on treatment options.
4) Follow up in CCC at least every 3-6 months.

9 Is adherence perceived to be ≥ 80%?

Yes → 17

No → 13

Verify administration is correctly documented on the computer or Notify unit administration:
1) Counsel patient regarding the importance of adherence and warn patient noncompliance may lead to med discontinuation.
2) Identify & treat adverse effects.
3) Return to clinic in 1 month.

14 Is adherence perceived to be ≥ 80%?

No → 11

Yes → 15 Obtain viral load.

16 Has viral load decreased > 10-fold (1 log)?

Yes → 17

No → 18 Repeat viral load in 1 month

19 Has viral load decreased > 10-fold (1 log)?

Yes → 17

No → 20

Continue current drug therapy so that reliable resistance testing may be obtained:
1) Refer patient to CMC Virology Clinic (UTMB sector) or designated physician (Texas Tech sector) to evaluate patient for poor adherence, intolerance, versus resistance & to consider changing drug therapy.
2) Reinforce education at each visit.

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Continue current drug therapy:
1) Return to CCC at least every 6 months and CMC Virology Clinic (UTMB sector) or designated physician (Texas Tech sector) as indicated.
2) Laboratories: CD4 count every 3 to 6 months if not on treatment.
For patients beginning ART, CD4 count should be repeated as follows:
- Every 3 months for the first 2 years of ART if CD4 counts <300 cells/mm3
- Every 6 months if CD4 count is ≥300 cells/mm3

After 2 years of ART, CD4 count monitoring can be reduced as follows:
- Every 6 months for patients whose CD4 counts remain at <300 cells/mm3
- Every year with CD4 counts between 300 cells/mm3 and 500 cells/mm3
- Optional for those with CD4 counts >500 cells/mm3

Viral load measurement should be repeated every 3 to 4 months or as clinically indicated to confirm continuous viral suppression.
Clinicians may extend the interval to 6 months for adherent patients whose viral load has been suppressed for more than a year.
3) Reinforce education at each visit.
4) Goal of therapy is 10-fold (1 log) decrease in viral load at 8 weeks, non-detectable viral load at 4-6 months after starting drug therapy & increased CD4 count.
5) Obtain expedited referral to CMC Virology Clinic (UTMB sector) or designated physician (Texas Tech sector) to consider change in drug therapy if: Goal viral load (non-detectable) not achieved within 4-6 months after starting drug therapy; Re-appearance of viremia after viral load is non-detectable (confirmed by at least 2 tests 4 weeks apart); Increase in viral load ≥ 3-fold from nadir (confirmed by at least 2 tests 4 weeks apart); Declining CD4 count (at least 2 tests); Severe, unusual, or life-threatening adverse effect suspected; or Patient wants to discontinue therapy

The pathways do not replace sound clinical judgment, nor are they intended to strictly apply to all patients

Box A: Primary Prophylaxis of Opportunistic Infections				
Initiate based on CD4 count	Organism	Recommended Regimen	Alternative Regimen Or Directions	Discontinuation Criteria†
All (regardless of CD4 count)	**M. tuberculosis PPD ≥ 5 mm**	INH 300 mg po daily plus pyridoxine 50 mg po daily x 9 months	Rifampin 600 mg po daily x 4 months	
	S. pneumoniae	Pneumococcal vaccine (repeat one time only in 5 years)		
	Influenza virus	Influenza vaccine (one dose annually)		
	Hepatitis A virus	Hepatitis A vaccine to all susceptible HIV patients (2 dose series)	Assess antibody response 1 - 2 months after series. If negative, revaccinate when CD4 > 200.	
	Hepatitis B virus	Double dose, three-dose series of recombinant hepatitis B vaccine to all susceptible HIV patients.	Assess antibody response in 1 or 2 months after series. If negative, revaccinate when CD4 > 200.	
CD4 count 100 – 200 cells/mm^3 if plasma HIV RNA level is detectable OR if CD4 count is < 100 cells/mm^3 regardless of plasma HIV RNA level	**Pneumocystis jirovecii**	TMP-SMX DS Once daily or three times weekly	Dapsone* 50 mg daily + pyrimethamine 50 mg q week + leucovorin 25 mg q week or Dapsone* 200 mg q week+ pyrimethamine 75 mg q week + leucovorin 25 mg q week or Atovaquone 1500 mg daily (nonformulary approval required)	CD4 count ≥ 200 for ≥ 3 months; when CD4 count 100-200 if HIV RNA remains below limit of detection for at least 3-6 months **(restart if CD4 count < 100 or 100-200 and HIV RNA above detection limit)**
CD4 count < 100 cells/mm^3 and antibody positive	**Toxoplasma gondii**	TMP-SMX DS Once daily or three times weekly	Dapsone ~~100~~50 mg daily + pyrimethamine 50 mg q week + leucovorin 25 mg q week or Dapsone 200 mg weekly + pyrimethamine 75 mg q week + leucovorin 25 mg q week or Atovaquone 1500 mg daily (nonformulary approval required)	CD4 count > 200 for > 3 months; when CD4 count 100-200 if HIV RNA remains below limit of detection for at least 3-6 months **(restart if CD4 count < 100 or 100-200 and HIV RNA above detection limit)**
CD4 count < 50 cells/mm^3 and not receiving antiretroviral treatment or remains viremic on treatment, or has no options for a fully suppressive regimen	M. avium complex₮	Azithromycin 1200 mg q week	Clarithromycin 500mg bid or rifabutin 300mg daily	Once HIV Viral Load is undetectable (regardless of CD4 count)

*Prior to administration with dapsone, complete G6pD deficiency testing; use alternative agent if G6pd deficient
†in response to ART and virally suppressed
₮only if not beginning antiretroviral treatment

Box B: Secondary Prophylaxis of Opportunistic Infections				
Indication	Organism	Recommended Regimen	Alternative Regimen	Discontinuation Criteria§
Prior PCP	Pneumocystis jirovecii	TMP-SMX DS daily	TMP-SMX DS three times weekly or Dapsone¶ 50 mg daily + pyrimethamine 50 mg q week + leucovorin 25 mg q week or Dapsone¶ 200 mg q week-+ pyrimethamine 75 mg q week + leucovorin 25 mg q week or Atovaquone 1500 mg daily (Nonformulary approval required)	CD4 count ≥ 200 for ≥ 3 months; when CD4 count 100-200 if HIV RNA remains below limit of detection for at least 3-6 months **(restart if CD4 count < 100 or 100-200 and HIV RNA above detection limit or PCP recurrence)**
Prior toxoplasmic encephalitis	Toxoplasma gondii	Sulfadiazine 1000 mg to 2000 mg po bid + Pyrimethamine 25-50 mg po daily + Leucovorin 10-25 mg po daily	Clindamycin 600 mg po q 6 hr + Pyrimethamine 25-50 mg po daily + Leucovorin 10-25 mg po daily	CD4 count > 200 for > 6 months* **(restart if CD4 count < 200)**
Prior disseminated disease	M. avium complex	Clarithromycin 500mg po bid + Ethambutol 15 mg/kg po daily +/- Rifabutin 300 mg po daily	Azithromycin 500 mg po daily + Ethambutol 15 mg/kg po daily +/- Rifabutin 300 mg po daily	CD4 count > 100 for > 6 months* **(restart if CD4 count < 100)**
Prior end-organ disease	Cytomegalovirus (CMV)	Ganciclovir 5-6 mg/kg/day IV 5-7 days a week or for retinitis ganciclovir 1 gm po TID + SR implant q 6-9 months	Foscarnet IV 90 mg/kg/day , Cidofovir 5 mg/kg IV q 2 weeks, or Valganciclovir 900 mg po daily	CD4 count > 100 for > 3-6 months† **(restart if CD4 count < 100)**
Prior disease	Cryptococcus neoformans	Fluconazole 200 mg po daily	Itraconazole 200 mg po daily, or Amphotericin 0.6-1 mg/kg IV weekly – 3 times weekly	CD4 count ≥ 100 for > 3 months* **(restart if CD4 count < 100)**
Prior disease	Histoplasma capsulatum	Itraconazole 200 mg po bid	Amphotericin 1 mg/kg IV weekly or Fluconazole 800 mg daily	Histoplasma antigen and fungal culture undetectable , CD4 count > 150 for ≥ 6 months* **(restart CD4 count ≤ 150)**
Prior disease	Coccidioides immitis	Fluconazole 400 mg po daily	Itraconazole 200 mg po bid or Amphotericin 1 mg/kg IV weekly	
Bacteremia	Salmonella species	Ciprofloxacin 500 mg po bid x several months		CD4 count > 200
Frequent/ severe recurrences	Herpes simplex virus‡	Valacyclovir 400 mg po bid	Acyclovir 400 mg po bid or famciclovir 250 mg bid	
Frequent/ severe recurrences	Candida‡ (oropharyngeal, vulvovaginal, esophageal)	Fluconazole 100-200 mg po daily	Itraconazole 200 mg po daily	

*if completed ≥ 12 months of treatment and asymptomatic
†if initial treatment completed, asymptomatic, & regular ophthalmology exams
‡recommended only if subsequent episodes are frequent or severe
§ in response to ART and virally suppressed
¶prior to administration with dapsone, complete G6pD deficiency testing; use alternative agent if G6pd deficient.

Patient and Provider Education

I. Who is educated?
   A. Health Services Personnel – updated on HIV so accurate and easy to understand information is provided to patients
   B. All inmates with HIV

II. Who educates?
   A. Unit team will delegate educational responsibility - physicians and mid-level providers have the final responsibility to ensure education occurs
   B. Educator must document education in patient's chart

III. When does education take place?
   A. Upon identification of having HIV
   B. Individual education at clinic visit
   C. Group education if available

IV. What is included in education?
   A. Health Services Personnel
      1. Pathophysiology & diagnostic criteria
      2. Monitoring parameters
      3. Pharmacologic treatments
      4. Adverse event monitoring & management
      5. Drug resistance & importance of adherence
      6. Opportunistic infections & prophylactic therapy
      7. Goals of therapy
   B. Patients
      1. Pathophysiology
      2. Routes of transmission
      3. Complications/risks of disease
      4. Pharmacologic treatments
      5. Monitoring parameters – frequency & importance
      6. Drug resistance & importance of adherence
      7. Individual treatment plan
      8. Dental hygiene to include daily brushing in the morning and evening and flossing once daily

Medication	Dosage	Drug Interactions*	Adverse Effect*
Atripla®† (emtricitabine 200 mg, tenofovir 300 mg, & efavirenz 600 mg)	1 tablet daily Do not use if CrCl < 50	Same as single entity drugs	Same as single entity drugs
Biktarvy® (bictegravir 50 mg, emtricitabine 200 mg, & tenofovir alafenamide 25 mg)	1 tablet daily Do not use if CrCl < 30	Same as single entity drugs	Headache, skin rash, diarrhea, nausea, increased LDL cholesterol
Cabenuva® (cabotegravir 400 mg & rilpivirine 600 mg)	After initiation, monthly injection doses of 400-mg (2-mL) intramuscular injection of cabotegravir and 600-mg (2-mL) intramuscular injection of rilpivirine	Anticonvulsants: Carbamazepine, Oxcarbazepine, Phenobarbital, Phenytoin Antimycobacterials: Rifampin, Rifapentine, Rifabutin. Glucocorticoid (systemic): Dexamethasone	Injection site reactions (83%), Pyrexia, Fatigue, Headache, Musculoskeletal pain, Nausea.
Cimduo®† (lamivudine 300 mg, & tenofovir 300 mg)	1 tablet daily Do not use if CrCl < 50	Same as single entity drugs	Same as single entity drugs
Combivir®† (zidovudine 300 mg & lamivudine 150 mg)	1 tablet BID Do not use if CrCl < 50	Same as single entity drugs	Same as single entity drugs
Complera®† (emtricitabine 200 mg, tenofovir 300 mg, & rilpivirine 25 mg)	1 tablet daily with food Do not use if CrCl < 50	Rifampin, carbamazepine, primidone, phenobarbital, phenytoin, H2-antagonists (ranitidine), proton pump inhibitors (omeprazole), dexamethasone	Diarrhea, rash, headache, insomnia, hepatitis B exacerbation, renal insufficiency, lactic acidosis with hepatic steatosis.
Delstrigo®† (doravirine 100 mg, lamivudine 300 mg, & tenofovir 300 mg)	1 tablet daily Do not use if CrCl < 50	Carbamazepine, oxcarbazepine, phenobarbital, phenytoin, and rifampin	Sleep disturbance, dizziness, abnormal dreams, depression, skin rash, nausea, diarrhea, increased serum creatinine
Dovata®† (dolutegravir 50 mg & lamivudine 300 mg)	1 tablet daily Not recommended with creatinine clearance less than 30 mL per minute.	Same as single entity drugs.	Same as single entity drugs.
Epzicom®† (lamivudine 300 mg & abacavir 600 mg)	1 tablet daily Do not use if CrCl < 50	Same as single entity drugs	Same as single entity drugs
Genvoya® (emtricitabine 200 mg, tenofovir 300 mg, elvitegravir 150 mg, & cobicistat 150 mg) Prior Authorization	1 tablet daily with food Do not use if CrCl < 30	Ergotamine, rifampin, carbamazepine, primidone, midazolam, lovastatin, Maraviroc, triazolam	Nausea, diarrhea, headache, renal insufficiency, increased LDL cholesterol, decreased bone mineral density, lactic acidosis with hepatic steatosis.
Juluca®† (dolutegravir 50 mg, & rilpivirine 25 mg)	1 tablet daily	Same as single entity drugs	Same as single entity drugs
Stribild®† (emtricitabine 200 mg, tenofovir 300 mg, elvitegravir 150 mg, & cobicistat 150 mg)	1 tablet daily with food Do not use if CrCl < 70	Ergotamine, rifampin, cisapride, primidone, midazolam, lovastatin, Maraviroc, triazolam	Nausea, diarrhea, abnormal dreams, headache, insomnia, upper respiratory infection, renal insufficiency, lactic acidosis with hepatic steatosis.

Table 1: Combination Products Continued

Medication	Dosage	Drug Interactions*	Adverse Effect*
Symfi®† (efavirenz 600 mg, lamivudine 300 mg, & tenofovir 300 mg) Symfi Lo®† (efavirenz 400 mg, lamivudine 300 mg, & tenofovir 300 mg)	1 tablet daily with food Do not use if CrCl < 50	Same as single entity drugs	Same as single entity drugs
Symtuza®† (darunavir 800 mg, cobicistat 150 mg, emtricitabine 200 mg, & tenofovir 10 mg)	1 tablet daily Do not use if CrCl < 30	Same as single entity drugs	Same as single entity drugs
Triumeq®† (dolutegravir 50 mg, abacavir 600 mg, & lamivudine 300 mg)	1 tablet daily Triumeq is not for people with known HIV resistance to abacavir, lamivudine or any of the approved integrase inhibitors.	Same as single entity drugs	Same as single entity drugs
Trizivir®† (zidovudine 300 mg, lamivudine 150 mg, & abacavir 300 mg)	1 tablet BID Do not use if CrCl <50	Same as single entity drugs	Same as single entity drugs
Truvada®† (emtricitabine 200 mg & tenofovir 300 mg)	1 tablet daily CrCl Dose 30-49 1 tab q 48hr < 30 do not use	Same as single entity drugs	Same as single entity drugs

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; BID = twice daily; cobi = cobicistat; EC = enteric coated; EFV = efavirenz; EVG = elvitegravir; FTC = emtricitabine; HSR = hypersensitivity reaction; MI = myocardial infarction; RPV = rilpivirine; TDF = tenofovir ; TID = three times a day; WHO = World Health Organization; ZDV = zidovudine

*not a complete list of drug interactions or adverse effects

† Non-formulary medication. See "Nonformulary Conversion DMG" for formulary substitutions

Table 2: Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

Medication	Dosage	Drug Interactions*	Adverse Effects*
Abacavir (ABC, Ziagen®)	300 mg BID or 600 mg daily		Hypersensitivity reaction characterized by fever, nausea, vomiting, malaise, anorexia, respiratory symptoms, +/- rash. **Should not be restarted if occurs. Record in medical record as allergy**. Lactic acidosis with hepatic steatosis.
Emtricitabine (FTC, Emtriva®) Non-formulary	200 mg daily CrCl Dose 30-49 200 mg q 48 15-29 200 mg q 72 <15 or HD 200 mg q 96		Nausea, vomiting, diarrhea, headache, hyperpigmentation of palms & soles. Lactic acidosis with hepatic steatosis.
Lamivudine (3TC, Epivir®)	150 mg BID or 300 mg daily CrCl Dose 30-49 150 mg daily 15-29 100 mg daily 5-14 50 mg daily <5 or HD 25 mg daily		Minimal effects, lactic acidosis with hepatic steatosis.
Tenofovir† (TDF, Viread®)	300 mg daily best if taken with food CrCl Dose 30-49 300 mg q 48 10-29 300 mg twice a week HD 300 mg q 7 days	Didanosine, atazanavir	GI upset, flatulence, headache, asthenia, renal insufficiency, lactic acidosis with hepatic steatosis.
Zidovudine (AZT, ZDV, Retrovir®)	300 mg BID CrCl < 15 or hemodialysis 100 mg TID or 300 mg daily	Stavudine, ribavirin	Initial GI upset, headache, nail discoloration, fatigue, anemia, neutropenia, myopathy, lactic acidosis with hepatic steatosis.

*not a complete list of drug interactions or adverse effects
†nucleotide reverse transcriptase inhibitor (NtRTI)

Table 3: Protease Inhibitors (PIs)

Medication	Dosage*	Drug Interactions†	Adverse Effects†
Atazanavir (ATV, Reyataz®)	400 mg daily best if taken with food Boosted or With Tenofovir or EFV ATV 300 + RTV 100 daily	Clarithromycin, diltiazem, lovastatin, rifabutin, rifapentine, ergotamine, H2-antagonists (ranitidine), proton pump inhibitors (omeprazole), efavirenz, tenofovir	Diarrhea, nausea, prolongation of the PR interval, hyperbilirubinemia, jaundice hyperglycemia, fat redistribution, increase bleeding in hemophilia
Darunavir (DRV, Prezista®)	Treatment Naïve patient DRV 800 + RTV 100 daily Treatment Experienced patient DRV 600 + RTV 100 BID (must be given with RTV)		Skin rash, SJS, hepatotoxicity, diarrhea, nausea, headache, elevated transaminase hyperglycemia, fat redistribution, increase bleeding in hemophilia
Fosamprenavir (FPV, Lexiva®)	1400 mg BID Boosted f-APV 1400 + RTV 100-200 daily f-APV 700 + RTV 100 BID With EFV f-APV 700 + RTV 100 BID f-APV 1400 + RTV 300 daily	Lovastatin, rifampin, rifabutin, rifapentine, ergotamine	Diarrhea, nausea, vomiting, rash hyperglycemia, fat redistribution, lipid abnormalities, increased bleeding in hemophilia
Lopinavir 200mg + Ritonavir 50mg (LPV/r, Kaletra®)	2 tabs BID or 4 tabs daily With EFV or NVP 3 tabs BID	Lovastatin, rifampin, rifabutin, rifapentine, ergotamine	Nausea, vomiting, diarrhea, asthenia, elevated LFTs hyperglycemia, fat redistribution, lipid abnormalities, increased bleeding in hemophilia
Nelfinavir (NFV, Viracept®)	1250 mg BID best if taken with meal or snack	Atorvastatin, lovastatin, rifampin, rifabutin, rifapentine, ergotamine	Diarrhea hyperglycemia, fat redistribution, lipid abnormalities, increased bleeding in hemophilia
Ritonavir (RTV, Norvir®)	600mg q 12 hr food may decrease GI upset Usually given as 100 to 400 mg once or twice daily to boost effected drug levels	Lovastatin, amiodarone, quinidine, clozapine, rifabutin, rifapentine, ergotamine, desipramine, theophylline, cobicistat	Nausea, vomiting, diarrhea, paresthesias, pancreatitis, taste perversion, elevated LFTs hyperglycemia, fat redistribution, lipid abnormalities, increased bleeding in hemophilia
Saquinavir (SQV, Invirase®)	SQV 1000 + RTV 100 BID (must be given with RTV) Take with meals or within 2 hours after a meal	Lovastatin, rifampin, rifabutin, rifapentine, ergotamine	Nausea, vomiting, diarrhea, rash, elevated LFTs hyperglycemia, fat redistribution, lipid abnormalities, increased bleeding in hemophilia
Tipranavir (TPV, Aptivus®) Non-formulary	500mg + RTV 200mg BID (must be given with RTV) Best if taken with food.	Lovastatin, rifampin, amiodarone, quinidine, ergotamine, fluticasone	Hepatotoxicity, rash, hyperlipidemia hyperglycemia, fat redistribution, lipid abnormalities, increased bleeding in hemophilia

*dosage if used as the only PI in the drug regimen, dosages are often adjusted if used in combination with other agents
† not a complete list of drug interactions or adverse effects

Table 4: Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Medication	Dosage	Drug Interactions*	Adverse Effects*
Doravirine (DOR, Pifeltro®) Non-formulary	100 mg daily	Carbamazepine, oxcarbazepine, phenobarbital, phenytoin, and rifampin	Nausea, headache, fatigue, diarrhea, abdominal pain, dizziness, abnormal dreams
Efavirenz (EFV, Sustiva®)	600 mg q HS best if taken on empty stomach	Rifampin, rifabutin, rifapentine, ergotamine, clarithromycin	Rash, CNS symptoms (e.g., dizziness, insomnia, vivid dreams), elevated LFTs, false positive cannabinoid test
Etravirine (ETR, Intelence®) Non-formulary	200 mg BID best if taken with food	Phenytoin, carbamazepine, other NNRTIs, PI's (except DRV/RTV, SQV/RTV, and LPV/RTV with caution), clarithromycin, rifampin, warfarin	Rash, nausea
Nevirapine (NVP, Viramune®)	200 mg daily x 14 days then 200 mg BID or 400 mg daily	Ketoconazole, rifampin, phenytoin, carbamazepine	Rash, elevated LFTs, hepatitis
Ripilvirine (RPV, Edurant®) Prior Authorization	25 mg daily with a meal	Acid suppression therapy, rifampin, rifabutin, carbamazepine, primidone, phenobarbital, phenytoin	Rash, depression, insomnia, headache, hepatotoxicity

*Not a complete list of drug interactions or adverse effects

Table 5: Integrase Inhibitors

Medication	Dosage	Drug Interactions*	Adverse Effect*
Bictegravir (BIC, Only as Biktarvy®) Non-formulary	bictegravir 50 mg, emtricitabine 200 mg, & tenofovir alafenamide 25 mg 1 tablet daily Do not use if CrCl < 30	Rifampin, phenytoin, carbamazepine	Headache, skin rash, diarrhea, nausea, increased LDL cholesterol
Dolutegravir (DTG, Tivicay®)	50 mg daily With certain resistance or drug interactions 50 mg BID	Inducers (efavirenz, boosted fosamprenavir, boosted tipranavir, rifampin)	Nausea, headache, diarrhea Preliminary data suggests use before pregnancy and through conception may be associated with an increased risk of neural tube defects in the infant.
Elvitegravir (EVG) Only as Genvoya® (Prior Authorization) Or Stribild® (Non-formulary)	Genvoya® (emtricitabine 200mg, tenofovir 300 mg, elvitegravir 150 mg, & cobicistat 150 mg) Stribild® (emtricitabine 200 mg, tenofovir 300 mg, elvitegravir 150 mg, & cobicistat 150 mg) Tablet once daily with food	Ergotamine, rifampin, cisapride, primidone, midazolam, lovastatin, maraviroc, triazolam	Nausea, diarrhea, abnormal dreams, headache, insomnia, upper respiratory infection, renal insufficiency Lactic acidosis with hepatic steatosis.
Raltegravir (RAL, Isentress®)	400 mg BID With rifampin 800 mg BID	rifampin	Nausea, headache, diarrhea, pyrexia, fatigue, elevated CPK

*Not a complete list of drug interactions or adverse effects

Table 6: Entry Inhibitors

Medication	Dosage	Drug Interactions*	Adverse Effects*
CCR5 Antagonist			
Maraviroc (MVC, Selzentry®) Non-formulary	Tropism testing is required before use. With Protease Inhibitors except tipranivir, delavirdine, itraconazole, ketoconazole, clarithromycin 150 mg BID With all NRTI, Enfuvirtide, TPV, NVP 300 mg BID With EFV, rifampin, carbamazepine, phenytoin 600 mg BID	Potent CYP3A inhibitors such as protease inhibitors, delavirdine, itraconazole, ketoconazole, clarithromycin Potent CYP3A inducers such as efavirenz, rifampin, carbamazepine, phenytoin	Abdominal pain, cough, dizziness, musculoskeletal symptoms, pyrexia, rash, upper respiratory track infections, hepatotoxicity, orthostasis
Fusion Inhibitor			
Enfuvirtide (T20, Fuzeon®) Non-formulary	90 mg SQ BID		Local injection site reaction (e.g., pain erythema, induration, nodules, cysts), increased rate of pneumonia, hypersensitivity reaction (rechallenge is not recommended)
Anti-CD4 Monoclonal Antibody			
Ibalizumab (IBA, Trogarzo®) Non-Formulary	2000 mg IV loading dose followed by 800 mg IV every 2 weeks		Dizziness, skin rash, diarrhea, nausea, decreased neutrophils, leukopenia, increased serum creatinine
HIV-1 GP120 Directed Attachment Inhibitor			
Fostemsavir (FTR, Rukobia®) Non-formulary	600 mg orally twice daily with or without food	Based on drug interaction study results, the following drugs can be given with fostemsavir without a dose adjustment: atazanavir/ritonavir, buprenorphine/naloxone, cobicistat, darunavir/cobicistat, darunavir/ritonavir with and without etravirine, etravirine, famotidine, maraviroc, methadone, norethindrone, raltegravir, ritonavir, rifabutin with and without ritonavir, tenofovir disoproxil fumarate.	Nausea, diarrhea, headache, abdominal pain, indigestion/heartburn, fatigue, rash, sleep disturbance, immune reconstitution inflammatory syndrome, drowsiness, vomiting

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; BID = twice daily; cobi = cobicistat;; EC = enteric coated; EFV = efavirenz; EVG = elvitegravir; FTC = emtricitabine; HSR = hypersensitivity reaction; MI = myocardial infarction; RPV = rilpivirine; TDF = tenofovir ; TID = three times a day; WHO = World Health Organization; ZDV = zidovudine

*not a complete list of drug interactions or adverse effects

Table 7: Capsid inhibitors

Medication	Dosage	Drug Interactions*	Adverse Effect*
Blocking HIV-1 Virus Protein Shell (Capsid)			
Lenacapavir (GS-CA1, GS-6207, Sunlenca®) Non-formulary	927 mg (two 1.5-mL injections) subcutaneously every 6 months from the date of the last injections +/- 2 weeks.	Carbamazepine Dexamethasone Fosphenytoin Phenobarbital Phenytoin Primidone Rifampin Rifabutin St. John's wort	Reactions at the injection site and nausea

*Not a complete list of drug interactions or adverse effects

Table 8: Pharmacokinetic Enhancer

Medication	Dosage	Drug Interactions*	Adverse Effect*
CYP3A Inhibitor			
Cobicistat (COBI, Tybost®) Non-formulary	150 mg Once Daily	Complex or unknown mechanisms of drug interactions preclude extrapolation of ritonavir drug interactions to certain cobicistat interactions. Protease inhibitors, itraconazole, ketoconazole, clarithromycin, rifampin and rifabutin, carbamazepine, phenytoin, fluticasone.	Jaundice (13%), Ocular icterus (15%), and Nausea (12%).

*Not a complete list of drug interactions or adverse effects

I. Background
   A. More than 50% of people do not know they are HIV-infected until they become symptomatic (an indicator of advanced disease).
   B. Since the correctional setting is often an inmate's first interaction with the health care system, a thorough history of risk factors is important and HIV testing should be recommended to all new intakes.

II. Etiology
   A. HIV (human immunodeficiency virus)
      1. Member of the Lentivirus family of retroviruses.
      2. There are two serotypes: HIV-1 and HIV-2. HIV-1 is the primary serotype in the U.S. HIV-2 is the primary serotype in Africa and is molecularly and serologically distinct. The two serotypes share only about 40% amino acid homology in their env surface glycoproteins.
      3. HIV is characterized by the presence of three main genes. The **gag** gene encodes for structural proteins of the viral core, the **env** gene encodes for the surface proteins of the virus, and the **pol** gene encodes for functional proteins including reverse transcriptase, ribonuclease, integrase, and protease.
   B. AIDS (acquired immunodeficiency syndrome)
      1. Clinical syndrome characterized by profound immunologic deficits (CD4 count < 200 cells/mm^3), opportunistic infections, and malignant neoplasms seen with prolonged HIV infection.

III. Transmission
   A. All routes of transmission involve contact with contaminated blood or bodily fluids
   B. Parenteral
      1. Occupational exposure - needle sticks
      2. Intravenous drug use - sharing contaminated needles
      3. Blood transfusion
      4. Organ transplant
   C. Sexual
      1. Vaginal intercourse
      2. Anal intercourse
      3. Oral intercourse
   D. Perinatal

IV. Presentation
   A. Early
      1. Symptoms: fever, lymphadenopathy, pharyngitis, rash, myalgia, arthralgia, diarrhea, headache, nausea, vomiting, hepatosplenomegaly, weight loss
      2. Positive HIV antibody usually develops by 4-6 weeks following transmission, but rarely could be up to 12-24 weeks.
      3. Extremely high levels of HIV in the blood during acute infection is a hallmark of this disease stage
      4. Within days, HIV disseminates into sanctuary sites (lymph nodes, central nervous system) where it "hides out" and remains dormant.
      5. HIV viral levels decrease over the first 4 months post-transmission until plateauing to a set point (varies person to person)
      6. Lower HIV viral set point = longer time it will take for an individual's disease to progress over time
   B. Intermediate
      1. T cell destruction by HIV begins to weaken the immune system over time (in contrast to the acute stage, where the immune system "keeps pace" by producing an equivalent amount of CD4 cells).
      2. In general if untreated, there is an 8–10-year period during which an HIV+ individual undergoes a gradual decline in immune function (monitored by laboratory testing of CD4 count) and increase in HIV viral load (monitored by laboratory testing of viral load).
      3. Often no symptoms exhibited during this stage
      4. Factors which influence how long individuals will remain in this stage before progressing to advanced disease:
         a. How high the viral load is at set point
         b. If and when antiretroviral treatment is initiated
   C. Late
      1. Untreated, the rapid replication of HIV will eventually deplete the immune system in most people to such an extent that the patient will lose critical body defenses and can succumb to infections, AIDS and ultimately death.
      2. Symptoms: opportunistic infections or malignancies, rashes, neuropathy, diarrhea, recurrent vaginal candidiasis, thrush, herpes zoster, recurrent infections, anemia, weight loss
      3. Actual diagnosis of AIDS is made when the CD4 count falls below 200 cells/cm^3 or when an AIDS-defining condition is diagnosed.
      4. Once a diagnosis of AIDS has been made, it remains with the patient even if his/her CD4 count returns to above 200 with antiretroviral therapy.

V. Diagnosis

A. Laboratories should conduct initial testing for HIV with an FDA-approved antigen/antibody combination immunoassay that detects HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen to screen for established infection with HIV-1 or HIV-2 and for acute HIV-1 infection. No further testing is required for specimens that are nonreactive on the initial immunoassay.

B. Specimens with a reactive antigen/antibody combination immunoassay result (or repeatedly reactive, if repeat testing is recommended by the manufacturer or required by regulatory authorities) should be tested with an FDA-approved antibody immunoassay that differentiates HIV-1 antibodies from HIV-2 antibodies. Reactive results on the initial antigen/antibody combination immunoassay and the HIV-1/HIV-2 antibody differentiation immunoassay should be interpreted as positive for HIV-1 antibodies, HIV-2 antibodies, or HIV antibodies, undifferentiated.

C. Specimens that are reactive on the initial antigen/antibody combination immunoassay and nonreactive or indeterminate on the HIV-1/HIV-2 antibody differentiation immunoassay should be tested with an FDA-approved HIV-1 nucleic acid test (NAT).

VI. Treatment

A. Recommendations for ART therapy

1. ART is recommended for all individuals with HIV, regardless of CD4 T lymphocyte cell count, to reduce the morbidity and mortality associated with HIV infection
2. ART is also recommended for individuals with HIV to prevent HIV transmission
3. Primary Care providers should refer patients to CMC Virology Clinic (UTMB Sector) or designated physician (Texas Tech Sector) for recommendations and initiation of therapy.

VII. Monitoring Therapy

A. CD4 Count

1. Indicator of immune system damage and risk for developing opportunistic infection, i.e., measure of immunological response
2. Specifically, it is a measure of the peripheral pool of CD4 cells which only accounts for approximately 2% of total lymphocyte population in the body
3. Together with viral load it is used to predict a patient's risk for disease progression
4. Used to determine when to start or stop opportunistic infection prophylaxis
5. Measurements can vary due to technical & biological variations and have diurnal variation. As a result, it is important to follow the trend in CD4 count versus single value.
6. CD4 count should be monitored at baseline and every 3 to 12 months based on patient status.
7. +/- 30% change is considered a significant change

B. Viral Load

1. Indicator of the magnitude of viral replication & response to drug therapy, i.e., virological response
2. Specifically, it is a measure of viral replication and is reported as number of viral copies/mL of blood
3. Used to monitor a patient's response to drug therapy
4. Decisions should be based on 2 measurements obtained 1-2 weeks apart due to technical & biological variations
5. Do not obtain within 4 weeks of intercurrent illness or immunization
6. Monitor at baseline, 2-8 weeks after initiating or changing therapy, and every 3 to 6 months thereafter based on status
7. > 0.5 log or 3-fold change in viral load is considered significant
8. Should see 1 log (10-fold) decrease in viral load within 8 weeks (may take as long as 16 weeks if very high) of initiating drug therapy and should be undetectable within 4-6 months

C. Resistance Testing

1. Should be performed by experienced provider (e.g., Infectious Diseases Specialist) since requires expert interpretation
2. Absence of resistance should be interpreted cautiously in conjunction with previous drug use history
3. Should be performed at baseline, while on antiretroviral therapy or immediately (within 4 weeks) after discontinuation of therapy
4. Drug-resistance testing is recommended in patients on combination ART with HIV-RNA levels confirmed >200 copies/mL. In patients with confirmed HIV-RNA levels between 201–500 copies/mL, testing may not be successful but may still be considered.

D. HLA-B*5701 screening – Should be considered prior to prescribing abacavir. Abacavir should not be prescribed if positive and an abacavir allergy should be recorded in the patient's medical record.
E. Co-receptor tropism assay – Must be obtained prior to prescribing a CCR5 inhibitor.
F. Response to Therapy
   1. Generally see virologic, immunologic, and then clinical progression when a patient is failing therapy. These stages may be separated by months to years and discordant responses are possible.
   2. Virologic Failure
      a. Incomplete virologic response: VL ≥ 200 copies/mL after 24 weeks of therapy
      b. Virologic rebound is the confirmed detectable HIV RNA (to ≥ 200 copies/mL) after virologic suppression. This excludes isolated episodes of viremia (i.e., single level 50-1000)
      c. Low-level viremia: Confirmed detectable HIV RNA <200 copies/mL.
   3. Immunologic Failure
      a. Failure to increase CD4 count by 25-50 cells/mm^3 above baseline over 1 year
      b. CD4 count decreases below baseline
      c. Immunologic failure may not warrant drug therapy change if viral load is undetectable
      d. In the setting of virologic suppression, there is no consensus on how to define or treat immunologic failure
   4. Clinical Progression
      a. Occurrence or recurrence of HIV-related illness after 3 months excluding immune reconstitution which is generally seen within first 3 months of starting therapy
      b. Clinical progression may not warrant drug therapy change if viral load is undetectable

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients

***Clinical ASCVD defined as:** ACS, or a history of MI, angina, coronary or other arterial revascularization, stroke, TIA, or PAD presumed to be of atherosclerotic origin

****10 yr ASCVD risk defined as:** risk of developing 1st ASCVD event, including MI or stroke, fatal or nonfatal

1

Does the patient meet criteria for dyslipidemia evaluation? Screen:
- All adults age ≥ 20 years. Use clinical judgment based on life expectancy when screening patients >75 years
- Patients at risk for familial dyslipidemia
- Patients that have diabetes (DM)
- History of clinical atherosclerotic cardiovascular disease (ASCVD)*

No → 2 Re-screen as clinically indicated

Yes

3

1. H&P: Rule out secondary causes due to diabetes mellitus, hypothyroidism, chronic renal disease, obstructive liver disease, drugs (e.g., progestins, anabolic steroids, corticosteroids, anti-hypertensives)
2. Baseline laboratories: urinalysis, thyroid function tests, lipid profile (fasting), comprehensive metabolic panel

4

Does the patient fall into one of the following groups?
- Clinical ASCVD* or
- Low-density lipoprotein (LDL) ≥ 190 and ≥ 20yo

Yes → 5

1. Encourage heart-healthy lifestyle habits
2. Initiate high-intensity statin therapy†
   - Age >75 years: consider benefits vs. risk before initiating statin. Consider moderate vs. high intensity statin based on tolerability, drug-drug interactions, and patient frailty. It is reasonable to continue high-intensity statin if patient is tolerating and has a low risk of competing comorbidities.
3. Go to box 14

No

6

Does the patient have diabetes?

Yes → 7

1. Encourage heart-healthy lifestyle habits
2. **Age 20-39 years with diabetes risk enhancers (Table 1):**
   - May consider moderate-intensity statin‡. Discuss benefits vs. risk of statin.
3. **Age 40-75 years and LDL 70-189 mg/dl:**
   - Recommend moderate-intensity statin‡ if ≤ 1 risk enhancer
   - Recommend high-intensity statin† if multiple risk enhancers
4. **Age > 75 years:** consider benefits vs. risk before initiating statin. Consider moderate vs. high intensity statin based on tolerability, drug-drug interactions, duration of diabetes (Table 1), and patient frailty.
5. Go to box 14

No

8 Go to Page 2, box 9

§Low intensity statin: pravastatin 10-20 mg
‡Moderate intensity statin: atorvastatin 10-20 mg, pravastatin 40-80 mg
†High intensity statin: atorvastatin 40-80 mg

Moderate-intensity therapy should be used instead of high-intensity therapy if any of the following factors are present that are associated with increased risk of statin adverse effects:
1. Multiple or serious co-morbidities, including impaired renal or hepatic function.
2. History statin intolerance or muscle disorders
3. Unexplained ALT elevations >3 times the upper limit of normal
4. Patient characteristics or concomitant use of drugs affecting statin metabolism

Table 1: Diabetes-specific risk enhancers:

- Long history of diabetes (≥ 10 years for Type 2 DM or ≥ 20 years for Type 1 DM)
- Albuminuria: Albumin-to-creatinine ratio ≥ 30 mcg/mg creatinine
- Estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2
- Retinopathy
- Neuropathy
- Ankle-brachial index (ABI) < 0.9

Table adapted from ACC/AHA

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider

Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee,
Approved February 1998. Revised April 4/00, 7/02, 4/03, 3/05, 7/09, 3/12, 1/13, 11/14, 9/19, 11/22, 2/23, 05/2024. Reviewed 2/03, 1/12.

9 Continued from box 8

10 Is patient age 40 – 75 years and LDL 70-189 mg/dL?

Yes → 11

11 Calculate estimated 10 year ASCVD risk** (ASCVD risk calculator found on EHR Note builder Guidelines tab and additional information provided on page 6)

No → 12

12
Age 20-39 years:
- Estimate lifetime risk and encourage lifestyle changes (ASCVD lifetime risk calculator found on EHR Note Builder Guidelines tab and additional information provided on page 6)
- Consider statin if family history of premature ASCVD (onset < 55 years in a first degree male relative or < 65 years in a first degree female relative) and LDL ≥ 160 mg/dL

If a statin is not initiated:
- A fasting lipid profile should be obtained as clinically indicated or every 5 years
- Recalculate estimated 10-year ASCVD risk every 5 years in individuals aged 40-75

For hypertriglyceridemia see Page 4, Hypertriglyceridemia.

13
Approach to treatment is based on estimated 10-yr ASCVD risk and presence of ASCVD risk enhancers (Table 2)
- **ASCVD risk <5% (Low Risk):**
  - Emphasize lifestyle changes
- **ASCVD risk 5% - < 7.5% (Borderline Risk) with ASCVD risk enhancers:**
  - Moderate-intensity statin ‡
- **ASCVD risk 7.5% - < 20% (Intermediate Risk) with ASCVD risk enhancers:**
  - Moderate- to high-intensity statin ‡ †
- **ASCVD risk ≥ 20% (High Risk):**
  - High-intensity statin †

Table 2: ASCVD Risk Enhancers for clinician-patient risk discussion:

- Family history of premature ASCVD (male < 55 y, female < 65 y)
- Persistently elevated LDL ≥ 160 mg/dL
- Chronic kidney disease (eGFR 15-59 mL/min/1.73 m^2 not treated with dialysis or kidney transplantation)
- Metabolic syndrome (increased waist circumference, TG > 175 mg/dL, elevated blood pressure, elevated glucose, and HDL <40 mg/dL in men or <50 mg/dL in women; tally of 3 makes the diagnosis)
- Premature menopause (before 40 years old), and history of pregnancy-associated conditions that increase later ASCVD risk such as preeclampsia
- Inflammatory diseases (especially rheumatoid arthritis, psoriasis, HIV)
- Ethnicity (e.g., South Asian ancestry)
- Persistently elevated triglycerides (≥ 175 mg/dL)

Table adapted from ACC/AHA

14
If a statin is not initiated:
- A fasting lipid profile should be obtained as clinically indicated or every 5 years
- Recalculate estimated 10-year ASCVD risk every 5 years in individuals aged 40-75

Once statin is initiated:
1. Enroll in Chronic Care Clinic.
2. Follow up in 4-12 weeks and repeat lipid profile to assess response and compliance with lifestyle modifications.
3. Monitor LFTs if symptoms suggest hepatotoxicity (e.g., unusual fatigue or weakness, loss of appetite, abdominal pain, dark colored urine, or yellowing of skin or sclera).
4. Monitor creatinine phosphokinase (CK) if patient has symptoms associated with myopathy (e.g., pain, tenderness, stiffness, cramping, weakness, or generalized fatigue).

15 Goal therapeutic response met?
- Low intensity statin§ : LDL lowering of < 30%
- Moderate intensity statin‡: LDL lowering of 30% to 49%
- High intensity statin†: LDL lowering of ≥ 50%

If the patient belongs to high-risk groups, additional therapy may be needed **(Refer to Box 20).**

No → 16 Assess for intolerance to statin therapy. Reinforce medication adherence and lifestyle changes.

16 → 18 Go to Page 3, box 19

Yes → 17
Follow-up in 1 year
1. Reinforce continued adherence
2. Monitor lipid profile (TC, LDL, HDL, TG**) at least** every 12 months
3. Monitor LFT and CK as clinically indicated (see box 14)
4. Continue Lifestyle Modifications and reinforce at follow up

§**Low intensity statin**: pravastatin 10-20mg
‡**Moderate intensity statin**: atorvastatin 10-20mg, pravastatin 40-80mg
†**High intensity statin**: atorvastatin 40-80mg

19

Continued from box 18

20

1. If the patient cannot tolerate statin, consider reducing statin dose or switch to a more hydrophilic statin (e.g., pravastatin) before considering a non-statin therapy. Statin intolerance is usually bilateral myalgias of proximal muscles with onset within weeks or months after initiation of statins and resolves after discontinuation of statin. Myopathy or rhabdomyolysis with increased CK is rare.
2. May consider increasing statin dose if not already on maximally tolerated statin.
3. If high risk patient on maximally tolerated statin has inadequate LDL lowering response, may consider addition of non-statin cholesterol lowering drug(s) if the ASCVD risk-reduction benefit outweighs potential risk for adverse effects.

   High risk groups:
   - Individuals with clinical ASCVD who are at very high risk for future ASCVD event (Table 3) and LDL remains ≥ 70 mg/dL
   - Individuals 20-75 years old with baseline LDL ≥190 mg/dL and follow up LDL remains ≥ 100 mg/dL

Non-statin therapies to consider (non-formulary approval required), see page 9:

- Ezetimibe (Zetia®)
  - Add-on for patients who do not achieve goal LDL lowering while on maximally tolerated statin or monotherapy in patients who cannot tolerate statin
- Bile acid sequestrant (e.g., cholestyramine (Questran®)) if TG < 300 mg/dL
- Consider PCSK9 inhibitors (e.g., evolocumab (Repatha®) or alirocumab (Praluent®)) if recommended by Cardiology for:
  - Very high risk for ASCVD (Table 3) and LDL ≥70 mg/dL despite maximally tolerated statin and ezetimibe

Follow up as clinically indicated or at least annually.

§**Low intensity statin**: pravastatin 10-20mg
‡**Moderate intensity statin**: atorvastatin 10-20mg, pravastatin 40-80mg
†**High intensity statin**: atorvastatin 40-80mg

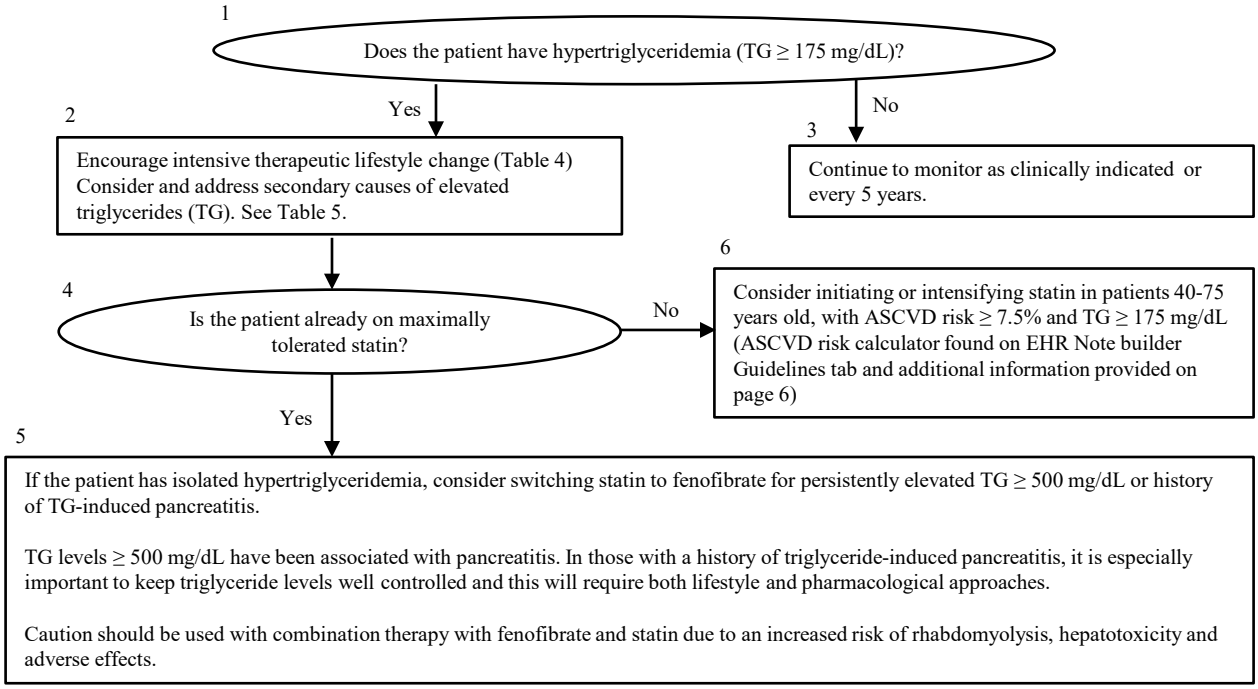
Table 3: Very high-risk of future ASCVD events (history of multiple major ASCVD events or 1 major ASCVD event and multiple high risk conditions):

Major ASCVD Event:
- Recent ACS (within the past 12 months)
- History of MI (other than recent ACS event listed above)
- History of ischemic stroke
- Symptomatic peripheral arterial disease (history of claudication with ABI <0.85, or previous revascularization or amputation)

High-risk conditions:
- Age ≥ 65 y
- Heterozygous familial hypercholesterolemia
- History of coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)
- Diabetes mellitus
- Chronic kidney disease (eGFR 15-59 mL/min/1.73m2)
- Current smoking
- LDL remains > 100 mg/dL despite maximally tolerated statin and ezetimibe
- History of congestive heart failure

Table adapted from ACC/AHA

HYPERTRIGLYCERIDEMIA



Once therapy is initiated:

1. Enroll in Chronic Care Clinic.
2. Follow up in 4-12 weeks and repeat lipid profile to assess response and compliance with lifestyle modifications.
3. Monitor LFTs if symptoms suggest hepatotoxicity (e.g., unusual fatigue or weakness, loss of appetite, abdominal pain, dark colored urine ,or yellowing of skin or sclera).
4. Monitor creatinine phosphokinase if patient has symptoms associated with myopathy (e.g., pain, tenderness, stiffness, cramping, weakness, or generalized fatigue).
5. Follow up as clinically indicated or at least annually.

Table 4: Dietary and Lifestyle Management of Hypertriglyceridemia

1. Balance calorie intake and physical activity to achieve or maintain a healthy body weight (10-20% loss of body weight results in 20% reduction in TG level)
2. Consume a diet rich in vegetables and fruits
3. Choose whole-grain, high-fiber foods
4. Consume fish (salmon, sardines, mackerel)
5. Limit intake of saturated fat
   - Choose lean meats and vegetables
   - Select fat free or low-fat products
   - Minimize margarine, vegetable shortening, packaged snacks, sweets, fried foods, coffee creamers

Table 5: Causes of Very High Triglycerides that May be Associated with Pancreatitis

Genetic:
- Lipoprotein lipase deficiency
- Apolipoprotein CII or AV deficiency
- GPIHBP1 deficiency
- Marinesco-Sjogren syndrome
- Chylomicron retention disease
- Familial hypertriglyceridemia (in combination with acquired causes)

Acquired disorders of metabolism:
- Hypothyroidism
- Pregnancy
- Poorly controlled insulinopenic diabetes

Drugs:
- Alpha-interferon
- Atypical antipsychotics
- Beta-blockers
- Bile acid resins (cholestyramine)
- Estrogens, oral
- Protease inhibitors
- Raloxifen
- Sirolimus
- Steroids
- Tamoxifen
- Thiazides
- Isotretinoin

Diet: High saturated fat diet

Diseases:
- Renal disease
- Chronic idiopathic urticaria

Table adapted from the American Heart Association

Table 6: Formulary Statin Therapy as recommended by ACC/AHA

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL on average by approximately ≥50%	Daily dose lowers LDL on average by 30% to <50%	Daily dose lowers LDL on average by <30%
Atorvastatin 40-80 mg	Atorvastatin 10-20 mg Pravastatin 40-80 mg	Pravastatin 10-20 mg

- Atorvastatin is associated with drug interactions due to its effects on the cytochrome P450 enzymatic pathway; however, pravastatin is not metabolized extensively via this pathway and is associated with fewer drug interactions.
- Pravastatin is more hydrophilic than atorvastatin therefore it has less muscle penetration and less statin-associated muscle symptoms (SAMs). SAMs are usually bilateral myalgia of proximal muscles with onset within weeks or months after initiation of statins and resolve after discontinuation of statin. Muscle weakness (myopathy) associated with a significant increase in creatinine phosphokinase (CK) levels is rare. Rhabdomyolysis (CK>10 times upper normal limit with renal injury) is exceedingly rare and usually encountered in the setting of several predisposing comorbidities and concomitant high-risk medications.

Table 7: Formulary Lipid-Lowering Agents

Drug Class	Starting Dose	Effect on Lipids	ADR	Contraindications
1. **Statins**		LDL ↓ 18-55%	myopathy	**absolute**: liver disease
Pravastatin	See page 1 ‡	HDL ↑ 5-15%	↑ LFT	**relative**: certain drugs†
Atorvastatin	See page 1 ‡	TG ↓ 7-30%		
2. **Fibric Acid**		LDL ↓ 5-20%	dyspepsia	**absolute**: severe renal or
Fenofibrate	48 - 145 mg	HDL ↑ 10-20%	↑ LFT	liver disease
		TG ↓ 20-50%	myopathy	

‡ The starting dose is dependent upon statin indication
† cyclosporine, macrolide antibiotics, azole antifungals, protease inhibitors, cytochrome P450 inhibitors (use fibrates with caution)

Table 8: Key abbreviations

TG: Triglyceride
TC: Total Cholesterol
HDL: High-density lipoprotein cholesterol
LDL: Low-density lipoprotein cholesterol

ASCVD: Atherosclerotic cardiovascular disease
CHD: Coronary heart disease
ACS: Acute coronary syndrome
MI: Myocardial infarction
TIA: Transient ischemic attack
PAD: Peripheral artery disease

Table 9: Notable Drug Interactions With Lipid-Lowering Agents

STATINS		DOSING MODIFICATIONS: ATORVASTATIN	DOSING MODIFICATIONS: PRAVASTATIN
HIV Medications:			
Protease Inhibitors	• **Darunavir (F)**	• MAX dose Atorvastatin 20mg	• LOWEST effective dose Pravastatin
	• **Lopinavir/Ritonavir (F)**	• MAX dose Atorvastatin 20mg	• NO dose adjustment
	• **Fosamprenavir (F)**	• MAX dose Atorvastatin 20mg	• NO dose adjustment
	• **Atazanavir (F)**	• LOWEST effective dose Atorvastatin	• LOWEST effective dose Pravastatin
Cobicistat	• **Cobicistat/Elvitegravir/ Emtricitabine/tenofovir. (GENVOYA®) (PA)**	• MAX dose Atorvastatin 20mg	• NO dose adjustment
Hepatitis Medications	• **Sofosbuvir/Velpatasavir (EPCLUSA®) (PA)**	• Consider Atorvastatin 10mg in most patients and do not exceed Atorvastatin 40mg	• NO dose adjustment
	• **Sofosbuvir/Velpatasavir/ Voxilaprevir (VOSEVI®) (NF)**	• MAX dose Atorvastatin 20mg	• MAX dose Pravastatin 40mg
	• **Glecaprevir/ Pibrentasvir (MAVYRET®) (NF)**	• **AVOID** Atorvastatin – do not coadminister	• MAX dose Pravastatin 20mg
Macrolide Antibiotics	• **Erythromycin (F)**	• Use cautiously and monitor	• MAX dose Pravastatin 40mg
	• **Clarithromycin (NF)**	• MAX dose Atorvastatin 20mg	• MAX dose Pravastatin 40mg
Immunosuppressants	• **Cyclosporine (F)**	• **AVOID** Atorvastatin	• MAX dose Pravastatin 20mg
Antiviral	• **Nirmatrelvir/Ritonavir (PAXLOVID®) (NF)**	• Use cautiously and monitor or consider temporary discontinuation	• NO dose adjustment

F = Formulary, NF = Nonformulary, PA = Prior Authorization

PATIENT EVALUATION

A. Initial Clinical Evaluation
   1. Age
   2. Sex
   3. Family History of lipid disorders, premature CHD, diabetes mellitus (DM)
   4. Patient History of
      a. CHD
      b. Hypertension (HTN)
      c. DM
      d. Cerebrovascular disease (CVD)
      e. Peripheral vascular disease (PVD)
      f. Pancreatitis
      g. Peptic ulcer disease (PUD)
      h. Gout or hyperuricemia
      i. Thyroid disease
      j. Chronic renal insufficiency (CRI)
      k. Liver disease
      l. Tobacco and alcohol use
   5. Diet History
   6. Activity Level
   7. Medication profile
   8. Previous lipid levels
   9. Physical Exam
      a. Height
      b. Weight
      c. Xanthomas
      d. Evidence of atherosclerosis

B. Risk Assessment :
   1. Clinical ASCVD, defined as a ACS, or a history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or PAD presumed to be of atherosclerotic origin
   2. LDL ≥ 190 mg/dL and ≥ 20 years of age
   3. Diabetes
      - Patient-clinician risk and benefit discussion may help identify specific risk factors and support decision to initiate or intensify statin therapy
   4. Individuals with no diabetes 40–75 years of age and LDL-C 70–189 mg/dL with estimated 10-year ASCVD risk ≥ 5%
      - ASCVD risk score should not determine whether statin should be intensified but rather it should begin a discussion with the patient about the potential benefits vs. risks with a high-intensity statin
   5. Additional factors influencing ASCVD risk are listed in Tables 1, 2, and 3
   6. ASCVD Risk Calculator (Text adapted from The American Heart Association and the American College of Cardiology)
      a. Calculator enables health care providers and patients to estimate 10-year and lifetime risks for ASCVD, defined as coronary death or nonfatal myocardial infarction, or fatal or nonfatal stroke based on the Pooled Cohort Equations and the work of Lloyd-Jones, et al., respectively. The information required to estimate ASCVD risk includes age, sex, race, total cholesterol, HDL cholesterol, systolic blood pressure, blood pressure lowering medication use, diabetes status, and smoking status.
      b. Estimates of 10-year risk for ASCVD are based on data from multiple community-based populations and are applicable to African-American and non-Hispanic white men and women 40 through 79 years of age. For other ethnic groups, the American Heart Association recommends use of the equations for non-Hispanic whites, though these estimates may underestimate the risk for persons from some race/ethnic groups, especially American Indians, some Asian Americans (e.g., of south Asian ancestry), and some Hispanics (e.g., Puerto Ricans), and may overestimate the risk for others, including some Asian Americans (e.g., of east Asian ancestry) and some Hispanics (e.g., Mexican Americans). The calculator may not be used to calculate a risk score if age <40 or >79 years, total cholesterol is <130 or >320 mg/dL, HDL < 20 or > 100 mg/dL, or systolic blood pressure < 90 or > 200 mmHg.
      c. Estimates of lifetime risk for ASCVD are provided for adults 20 through 59 years of age and are shown as the lifetime risk for ASCVD for a 50-year-old without ASCVD who has the risk factor values entered into the spreadsheet. The estimates of lifetime risk are most directly applicable to non-Hispanic whites. We recommend the use of these values for other race/ethnic groups, though as mentioned above, these estimates may represent under- and overestimates for persons of various ethnic groups. Because the primary use of these lifetime risk estimates is to facilitate the very important discussion regarding risk reduction through lifestyle change, the imprecision introduced is small enough to justify proceeding with lifestyle change counseling informed by these results.
      d. The ASCVD risk calculator evaluates smoking status prior to estimating risk. This question is a “yes” or “no” answer which should be selected based upon current smoking status.

a. The ASCVD risk calculator evaluates smoking status prior to estimating risk. This question is a "yes" or "no" answer which should be selected based upon current smoking status.

C. Who To Test

1. Initial Screening:

PATIENTS	INITIAL SCREENING
Males and females ≥ 20 years	TC, HDL, LDL, TG
> 75 years	Use clinical judgment based on life expectancy, TC, HDL, LDL, TG

Patients should be screened with a fasting lipid profile (TC, HDL, LDL, TG).

D. Secondary Causes of Lipid Abnormalities

1. Drugs:
   a. Alpha-agonists & antagonists- decrease TC & TG, increase HDL cholesterol
   b. Alpha-interferon – increase TG
   c. Amiodarone – increase LDL
   d. Anabolic steroids – increase TG
   e. Atypical antipsychotics – increase TG
   f. Beta-blockers- increase TG; decrease HDL-cholesterol
   g. Bile acid resins – increase TG
   h. Cyclosporine- increase LDL-cholesterol
   i. Ethanol- increase TG
   j. Glucocorticoids- increase TC & TG
   k. Isotretinoin- increase TC & TG; decrease HDL-cholesterol
   l. Oral contraceptives- increase TC, TG & HDL-cholesterol
   m. Protease inhibitors – increase TG
   n. Raloxifen – increase TG
   o. Sirolimus – increase TG
   p. Tamoxifen – increase TG
   q. Thiazide diuretics- increase TC, TG & HDL-cholesterol

2. Effects of Various Conditions

Secondary Cause	Elevated LDL–C	Elevated Triglycerides
Diet	Saturated or trans fats, weight gain, anorexia	Weight gain, very low-fat diets, high intake of refined carbohydrates, excessive alcohol intake
Diseases	Biliary obstruction, nephrotic syndrome	Nephrotic syndrome, chronic renal failure, lipodystrophies
Disorders and altered states of metabolism	Hypothyroidism, obesity, pregnancy*	Diabetes (poorly controlled), hypothyroidism, obesity; pregnancy*

*Treatment with statins, niacin, and ezetimibe are contraindicated during pregnancy and lactation.
Table adapted from ACC/AHA

E. Factors That Alter Lipid Levels

1. Fasting: TC levels and HDL-cholesterol can be measured in the non-fasting patient. TG concentrations, however, are affected by recent food intake, and will affect the calculation of LDL-cholesterol by the Friedewald equation: LDL = [TC] – [HDL] – [TG/5]. Therefore, patients should be fasting for at least 12 hours prior to having blood drawn for lipid profile testing.
2. Elevated TG: If the TG concentration is > 400 mg/dl, a calculated LDL may be inaccurate. In this instance, a direct LDL measurement may be appropriate.
3. Illness: Recent myocardial infarction, stroke, surgery, trauma, or infection may transiently lower cholesterol.

MANAGEMENT

A. General Approach: Clinical decisions should be based on 2 lipid profiles, performed 1 to 8 weeks apart.
B. Non-Pharmacologic Therapy
   1. Diet
   2. Exercise
   3. Weight reduction in obese patients
   4. Stop smoking
   5. Decrease alcohol consumption
C. Pharmacotherapy
   1. Dietary changes and exercise should be attempted prior to initiation of drug therapy in select patients where ASCVD prevention benefit of statin therapy may be less clear. In patients who are at particularly high risk, diet therapy and drug therapy may be initiated concurrently.
   2. The first-line agents to treat hyperlipidemia are the HMG-COA Reductase Inhibitors ("Statins"). The statins on formulary including pravastatin and atorvastatin, are usually well tolerated and convenient to take. Consult dosing of 'statins' in notable drug interactions table 9 on page 6.
   3. Other agents to treat hyperlipidemia require nonformulary approval:
      a. Ezetimibe may be used as add-on or monotherapy in patients who cannot tolerate statin or who do not achieve goal LDL lowering while on maximally tolerated statin.
      b. Bile acid sequestrant (cholestyramine) can be added on for patients who do not achieve goal LDL lowering while on statin and/or ezetimibe. Cholestyramine should be not be considered in patients with TG > 300 mg/dL.
      c. PCSK9 inhibitors such as evolucumab (Repatha®) or alirocumab (Praluent®) may be considered if recommended by Cardiology for very high-risk patients whose LDL remains > 70 mg/dl despite maximally tolerated statin and ezetimibe. They can be administered every 2 weeks or once monthly subcutaneously.
   4. Isolated hypertriglyceridemia may be treated with fenofibrate (see table 7 for a comparison of lipid lowering agents and refer to Page 4, Hypertriglyceridemia). Triglyceride (TG) levels ≥ 500 mg/dL have been associated with pancreatitis.
D. Follow-up
   1. History
      a. Diet Compliance
      b. Compliance with exercise program
      c. Medication compliance and presence of symptoms suggesting adverse drug reactions (if indicated)
      d. Current medications or pertinent changes in other drug therapy
      e. Re-evaluation of the modifiable risk factors
      f. Presence of muscle aches in large muscle groups
   2. Physical Examination
      a. Weight
      b. Blood Pressure
   3. Laboratory tests
      a. Fasting lipid profile
      b. LFTs as clinically indicated for patients on statins
      c. Creatinine kinase (CK) if symptoms of myositis
   4. Adverse event monitoring (including but not limited to)
      a. Significant elevations of liver enzymes (>3 times the upper limit of normal) while on statins
      b. Symptoms of myositis while on statin therapy alone or in combination with other drugs

PATIENT EDUCATION
HYPERLIPIDEMIA CLINIC

Hyperlipidemia (hyper = high levels, lipidemia = fats in the blood) may be caused by high levels of cholesterol, high levels of triglycerides, or a combination of the two. In the hyperlipidemia clinic, we will discuss your lipid disorder as well as a plan of treatment for you. The treatment plan will depend on several factors such as your current risk for heart disease, your current disease states, how high your lipids are, what medications you are taking, as well as other factors. You should read the information contained in this handout carefully. If any of the information that you are told is unclear, please do not hesitate to ask for clarification.

HIGH CHOLESTEROL

Many studies have shown that high cholesterol levels in the blood are a major risk factor for developing coronary heart disease (CHD). Some cholesterol in the blood is necessary. However, excess cholesterol in the blood may lead to fatty deposits in the walls of the arteries. These deposits can build up in the blood making blood flow to the heart more difficult. This process is known as atherosclerosis or "hardening of the arteries." This can lead to a heart attack and/or other heart diseases. If the deposits build up in the carotid arteries in the neck, this could lead to a stroke. Lowering of elevated cholesterol levels has been proven to decrease your risk of death from CHD, decrease the incidence of atherosclerosis and stroke. Cholesterol is a waxy compound that the body needs and uses for many important functions. The liver makes some of the cholesterol from fat in the diet. The fat in the diet comes from meat, eggs and dairy products. There are two types of cholesterol LDL cholesterol (which has been called "bad cholesterol") and HDL cholesterol (which has been called "good cholesterol"). The LDL-cholesterol is the type of cholesterol that is associated with atherosclerosis and heart disease. The HDL-cholesterol seems to protect the body from developing heart disease. A simple blood test can determine what a person's cholesterol level is. Changes in diet are often the most effective way to lower or maintain a healthy cholesterol level. One of the most important changes to make is to lower the amount of fat in the diet. Food packages, from the commissary, now have the percentage of fat and grams of fat on the label, which makes it easier to keep track of the amount of fat in the diet. Weight loss, even in the slightly overweight patient, can make a big difference in cholesterol level. The Diet for Health, when followed properly, should help with weight loss. A routine exercise program not only helps with weight loss, but also helps to lower overall risk of heart disease. Drug therapy is not a substitute for diet and exercise but should be considered to be an extension of the therapy. In some patients who are at high risk, diet, exercise and drug therapy may need to be started at the same time.

HIGH TRIGLYCERIDES

Studies have shown that elevated levels of triglycerides are associated with cardiovascular disease. Many, but not all, patients with high triglyceride levels also have high LDL-cholesterol levels and/or low HDL-cholesterol levels. Very high triglyceride levels (greater than 500) have been associated with inflammation of the pancreas (pancreatitis). High levels of triglycerides can sometimes cause the blood to thicken causing a problem with clotting. High triglyceride levels usually respond well to non-drug therapy, such as changes in diet and increased exercise. Triglyceride is ingested in the diet from fats and sugars, is also made in the body in the liver and is important in the body for energy and fuel storage. High triglyceride levels may be caused by overproduction in the liver or decreased removal by the body. Triglyceride levels have been shown to be increased in certain disease states, in times of extreme stress, and by certain drugs.

Reducing other risks of cardiovascular disease

A healthy diet, regular exercise, and weight loss in overweight people can improve overall health and decrease the risk of heart disease as well as lowering lipid levels. In addition to hyperlipidemia, there are other risk factors for heart disease that should be controlled:

1. Control high blood pressure
2. Control high blood sugar
3. Stop smoking
4. Limit alcohol intake
5. Reduce stress

HYPERTENSION (HTN)

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider

The pathways do not replace sound clinical judgement nor are they intended to strictly apply to all patients

*PREVENT CVD calculator found on CMC web Tools & EHR Note builder Guidelines tab

1 Adults 18-85 years of age. Refer to **Table 1** for HTN classification.

2 Implement lifestyle interventions, discontinue or minimize interfering drugs or substances, and screen for secondary causes of high blood pressure (**Table 4**).

3 Does the patient have one of the following conditions: History of cardiovascular disease (stroke, heart failure, or myocardial infarction), diabetes (DM), Albuminuria (Albumin/ Creatinine ratio >30 mg/g creatinine), or chronic kidney disease (CKD) (excluding end stage renal disease and renal transplant)?

No / **Yes**

4 Calculate 10-yr PREVENT CVD risk*

PREVENT CVD risk <7.5% or cannot be calculated

PREVENT CVD risk ≥7.5%

6 Initiate lifestyle interventions x 3-6 months and recheck blood pressure. At goal of <130/80?

Yes / **No**

5 Is the patient ≥ 65 years with high burden of comorbidity, limited life expectancy, and dependency in activities of daily living?

No / **Yes**

8 Assess risk vs benefits and consider patient preference before initiating medications. Treat based on tolerability.

7 **Target BP < 130/80**

9 Initiate first line antihypertensive if not at target. Refer to **Table 2 & 3** for compelling indications.
- Without significant co-morbidities: amlodipine, hydrochlorothiazide, lisinopril, or losartan

10 **Schedule follow-up in:**
- Nonpharmacological therapy only: follow up in 3-6 months
- Pharmacological therapy initiated: follow up in 1 month, obtain BP readings weekly

11 **At follow-up visit, is patient at BP goal?**

No / **Yes**

12 **<u>Patient is compliant:</u>** increase dose or add another drug (HCTZ, lisinopril, amlodipine or losartan). Follow-up based on box 10.

<u>Patient is noncompliant</u>: Counsel patient regarding IMPORTANCE of compliance and consider changing status of medications to NONKOP. Follow-up based on box 10.

If adverse effects are present, change drug class or add drug from another class and reduce dose of offending agent.

13
- Continue current drug regimen
- Continue to encourage lifestyle modifications
- Obtain annual laboratories (Appendix A)
- Order microalbumin annually if patient is not on an ACEI or ARB (angiotensin receptor blocker)
- Follow-up in chronic care clinic at least annually

14 **<u>If still not at BP goal, may consider:</u>**
- Intense individualized counseling
- DOT for a short period
- Obtaining a pharmacotherapy consult
- Additional BP agents (e.g., beta-blocker, aldosterone antagonist, or others). See **Table 3.**

Follow-up based on box 10 or as clinically indicated.

<u>If at BP goal: Refer to box 13</u>

Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee. Approved August 1995; Reviewed 1/08, 5/11, 7/17; Revised 10/98, 4/02, 4/03, 1/04, 1/06, 5/09, 5/14, 9/20, 5/25, 1/26

Table 1: Classification of Hypertension

BP Classification	SBP mmHg[1]	DBP mmHg[2]	Lifestyle Modification	Initial Therapy
Normal	<120	**and** <80	Encourage	No antihypertensive indicated
Elevated	120-129	**and** <80	Yes	No antihypertensive indicated, reassess in 3-6 months
Stage 1 Hypertension	130-139	80-89	Yes	Calculate risk with PREVENT CVD calculator; see algorithm on page 1
Stage 2 Hypertension	≥140	≥90	Yes	Antihypertensive therapy indicated

Table 2: Drug Selection in Patients with or Without Compelling Conditions

Patient Type	Initial Drug
A. When hypertension is the main condition:	• Amlodipine • Lisinopril or losartan
B. When hypertension is associated with other conditions:	
• Hypertension and diabetes	• Amlodipine, HCTZ, lisinopril, or losartan
• Hypertension and albuminuria	• Lisinopril or losartan
• Hypertension and CKD*	• Lisinopril or losartan
• Hypertension and clinical coronary artery disease	• Lisinopril or losartan and/or beta blocker
• Hypertension and stroke history	• Lisinopril or losartan and/or hydrochlorothiazide
• Hypertension and symptomatic heart failure with reduced ejection fraction	• Lisinopril or losartan + carvedilol or metoprolol succinate + diuretic + spironolactone†

Abbreviations:
CKD = chronic kidney disease
HCTZ = hydrochlorothiazide

*CKD defined as eGFR <60 mL/min/1.73m^2 or albuminuria ≥30 mg/g
†NYHA II-IV and who have LVEF of 40% or less provided eGFR >30 mL/min/1.73 m2 and K+<5.0 mEq/dL

Table 3: Formulary Oral Antihypertensive Agents

Drug Class	Formulary agents	Comments
First-line agents		
Thiazide diuretics	• HCTZ 12.5-50 mg • Triamterene/HCTZ 37.5 mg/ 25 mg • Metolazone 5 mg	• Recommended in history of stroke/ TIA, with or without lisinopril • Avoid in gout unless patient is on gout medications • Monitor for hyponatremia, hypokalemia, hypercalcemia, and uric acid levels
ACE inhibitor	Lisinopril 2.5-40 mg	• Recommended in CKD and albuminuria • Recommended in history of stroke/ TIA with or without a thiazide diuretic • Monitor potassium and renal function, especially in CKD patients or in those on potassium supplements or potassium-sparing drugs • Do not use in pregnancy or patients with history of angioedema with ACE-I • Do not combine with angiotensin II receptor blocker (i.e., losartan) or direct renin inhibitor
ARB	Losartan 25-100 mg	• Recommended in CKD and albuminuria • Recommended in history of stroke/ TIA with or without a thiazide diuretic • Monitor potassium and renal function, especially in CKD patients or in those on potassium supplements or potassium-sparing drugs • Do not use in pregnancy or patients with history of angioedema with ARB • Do not combine with angiotensin converting enzyme inhibitor (i.e., lisinopril) *or* direct renin inhibitor
Dihydropyridine CCB	Amlodipine 5-10 mg	• Associated with dose-related pedal edema • Can use in patients with HFrEF
Second-line Agents		
Non-dihydropyridine CCB	• Diltiazem XR 180-240 mg • Verapamil SR 180-240 mg	• Avoid use with beta-blockers due to increased risk of bradycardia/ heart block. • Avoid in patients with HFrEF
Loop diuretic	Furosemide 20-40 mg	Preferred diuretics in symptomatic HF and preferred over thiazides in moderate–severe CKD (GFR <30 mL/min)
Aldosterone antagonists	Spironolactone 25 mg	• Preferred agents in aldosteronism and resistant hypertension • Avoid use with potassium supplements, potassium-sparing diuretics, or significant renal dysfunction • Associated with risk of gynecomastia and impotence
Beta blockers	• Carvedilol 3.125-25 mg • Metoprolol succinate 25-200 mg • Propranolol 10-40 mg	• Not recommended as first-line unless the patient has ~~I~~CHD or HF • Metoprolol succinate is preferred in patients with bronchospastic airway disease requiring a beta blocker • Carvedilol or metoprolol succinate is preferred beta-blocker in patients with HFrEF • Avoid propranolol in patients with reactive airway disease • Avoid use with non-dihydropyridine CCB due to increased risk of bradycardia/heart block • Avoid abrupt cessation • Contraindicated in bradycardia and heart block
Alpha-1 blocker	Terazosin 1-10 mg	• May be used second-line in patients with concomitant BPH • Associated with orthostatic hypotension, especially in older adults
Direct vasodilators	• Hydralazine 25-50 mg • Minoxidil 2.5-10 mg	• Use with a diuretic due to retention of sodium and water • Use with a beta blocker due to reflex tachycardia • Hydralazine is associated with lupus-like syndrome at high doses • Minoxidil is associated with hirsutism and requires a loop diuretic. Minoxidil can induce pericardial effusion.
Alpha-2 agonists	Guanfacine 1-2 mg	• Reserved as last-line due to significant CNS adverse effects, especially in older adults • Avoid abrupt cessation

Abbreviations:
ACE-I = angiotensin converting enzyme inhibitor
ARB = angiotensin II receptor blocker
BPH = benign prostatic hyperplasia
CCB = calcium channel blocker
CKD = chronic kidney disease
CNS = central nervous system
CHD = coronary heart disease
GFR = glomerular filtration rate
HCTZ = hydrochlorothiazide
HF = Heart failure
HFrEF = Heart failure with reduced ejection fraction
IHD = Ischemic Heart Disease
TIA = Transient Ischemic Attack

Table 4: Secondary Causes of Hypertension (HTN)

Drugs and Substances	**Comments**
• Alcohol • Recreational drugs (e.g., cocaine, methamphetamine, etc.)	• Limit alcohol to ≤1 drink daily for women and ≤2 drinks for men • Discontinue use of recreational drugs
Caffeine	• Associated with acute increase in blood pressure • Limit caffeine to <300 mg/day (less than four cups of coffee) • Avoid caffeine in patients with uncontrolled hypertension
Non-steroidal anti-inflammatory drugs (NSAIDs)	• Avoid systemic NSAIDs when possible • Consider alternative analgesics (e.g., acetaminophen) depending on indication
Decongestants (e.g., phenylephrine)	• Use for the shortest duration possible, and avoid in severe or uncontrolled hypertension • Consider alternative therapies (e.g., nasal saline, intranasal corticosteroids, antihistamines)
Antidepressants (e.g., venlafaxine, duloxetine)	Monitor blood pressure, adjust antihypertensives, or consider alternative agents (e.g., Selective Serotonin Reuptake Inhibitors – sertraline, fluoxetine, paroxetine) depending on indication
Atypical antipsychotics (e.g., clozapine, olanzapine)	• Discontinue or limit use when appropriate • Consider alternative agents associated with lower risk of weight gain, diabetes mellitus, and dyslipidemia (e.g., aripiprazole, ziprasidone)
Oral contraceptives	• Use low-dose ethinyl estradiol (e.g., Low-ogestrel) agents • Avoid use in uncontrolled hypertension
Systemic corticosteroids (e.g., prednisone)	• Avoid or limit use when possible • Consider alternative modes of administration (e.g., inhaled, topical) when feasible
• Angiogenesis inhibitor (e.g., bevacizumab) • Tyrosine kinase inhibitors (e.g., sunitinib, sorafenib)	Initiate or intensify antihypertensive therapy
Medical Conditions	**Consider in Resistant Hypertension**
• Primary aldosteronism (prevalent in up to 20% of resistant HTN cases, and 5-10% in general HTN population)	• Symptoms include muscle cramps or weakness • Patients may also present with arrythmias (and hypokalemia) • Consider an oral sodium loading test for diagnosis • Screening recommended in all patients with resistant hypertension
• Sleep apnea (prevalent in ≥80% of resistant HTN cases)	• Symptoms include snoring, breathing pauses during sleep, daytime sleepiness • Most common in obese patients • Consider a sleep study referral
• Renovascular disease (prevalent in 5-34% of patients with HTN)	• This is suspected in patients with hypertension of abrupt onset or worsening or increasingly difficult to control hypertension • Consider specialist referral for a bilateral selective renal intra arterial angiography for diagnosis.
• Other secondary causes (less common): coarctation of the aorta, mineralocorticoid excess states, Cushing's Syndrome, pheochromocytoma, thyroid or parathyroid disease, congenital adrenal hyperplasia, acromegaly, renal parenchymal disease.	

Detection and Confirmation:

Patients should be seated in a chair with their backs supported, and their arms bared and supported at heart level. Patient should sit with feet flat on the floor and legs uncrossed.

- Patients should have emptied their bladder and refrained from smoking, exercising, or ingesting caffeine during the 30 minutes prior to the reading.
- Blood pressure (BP) measurement should begin after the patient has been at rest for at least 5 minutes.
- Patient should not talk immediately before or during the blood pressure measurement.
- Appropriate cuff size must be used to ensure accurate readings. The bladder within the cuff should encircle at least 80% of the arm. A large adult cuff should be kept in all clinics.
- Measurement of BP with a mercury sphygmomanometer is the preferred method. However, a recently calibrated aneroid manometer or a validated electronic device can be used.
- Systolic BP and diastolic BP should be recorded.
- Two or more readings separated by 2 minutes should be obtained and averaged for proper confirmation. Verification in the contralateral arm is recommended (if values are different, the higher value should be used). If these two readings differ by more than 5 mm Hg, additional readings should be obtained two weeks apart.
- In some cases, supine BP may be measured. Older persons may present with neurogenic orthostatic hypotension associated with supine hypertension.

Recommendation for Follow-up Based on Initial Blood Pressure Readings

Initial Blood Pressure (mm Hg)*

Systolic	Diastolic	Follow-up Recommended**
<120	<80	Recheck as clinically indicated
120-129	<80	Reassess in 3-6 months
130-139	80-89	• 10-yr PREVENT CVD risk <7.5%: Nonpharmacological therapy only. Reassess in 3-6 months • High risk condition or 10-yr PREVENT CVD risk ≥7.5%: Initiate pharmacological therapy. Check BP weekly and reassess in 1 month.
≥140	≥90	• Reassess in 1 month after initiating antihypertensives and checking BP weekly. • For those with higher pressures (e.g., 180/120 mm Hg), evaluate and treat per Hypertensive Emergency/Urgency pathway.

*If systolic and diastolic categories are different, follow up should be for the shorter time (e.g., 145/79 mm Hg should be evaluated within one month).

** Modify the schedule for follow up according to reliable information about past blood pressure measurements, other cardiovascular risk factors, or target organ disease. Provide advice on therapeutic lifestyle modifications.

Physical Exam:

- Measurement of weight, height, and waist circumference.
- Fundoscopic examination for hypertensive retinopathy (i.e., arteriolar narrowing, focal arteriolar constrictions, arteriovenous crossing changes, hemorrhages and exudates, disc edema).
- Examination for the neck for carotid bruits, distended veins, or enlarged thyroid gland.
- Examination of the heart for abnormalities in the rate and rhythm, increased size, precordial heave, clicks, murmurs and third and fourth heart sounds.
- Examination of the lungs for rales and evidence for bronchospasm.
- Examination of the abdomen for bruits, enlarged kidney, masses and abnormal aortic pulsation.
- Examinations of the extremities for diminished or absent peripheral arterial pulsations, bruits, and edema.
- Neurological assessment.

Medical History:

- Known duration and levels of elevated blood pressure.
- Patient history or symptoms of coronary heart disease (CHD), heart failure, cerebrovascular disease, peripheral vascular disease, renal disease, diabetes mellitus, dyslipidemia, gout, or sexual dysfunction.
- Family history of high blood pressure, premature CHD, stroke, diabetes, dyslipidemia, or renal disease.
- Symptoms suggestive of hypertension (headache, nose bleeds, dizziness, abnormal physical exam).
- History of recent changes in weight, leisure time physical activity, and smoking or tobacco use.
- Dietary assessment including intake of sodium, alcohol, saturated fat and caffeine.
- History of all prescribed and over-the-counter medications, herbal remedies, and illicit drugs.
- Results and adverse effects of past antihypertensive therapy.
- Psychosocial and environmental factors that may influence hypertensive control.

Baseline and Annual Laboratory Tests:
Routine laboratory tests recommended prior to initiating therapy and annually to determine end organ damage and other risk factors include:

- CBC
- Chemistry profile to include LFTs, serum creatinine, fasting blood sugar and fasting lipid profile
- TSH (baseline)
- Urinalysis
- Microalbumin to test for albumin to creatinine ratio (annually if not on ACE inhibitor or angiotensin receptor blocker)
- EKG

Cardiovascular Risk Factors:

- Hypertension
- Obesity (Body Mass Index $\geq$ 30 kg/m^2)
- Physical Inactivity
- Dyslipidemia
- Diabetes Mellitus
- Microalbuminuria (Albumin/ Creatinine ratio >30 mg/g creatinine) or estimated GFR < 60 mL/min
- Older age
- Family history of premature cardiovascular disease (male < 55 or females < 65)
- Preventing Risk of Disease Events (PREVENT) CVD risk calculator provides an estimated 10-year and 30-year risk of developing 1st cardiovascular disease (CVD) event, including MI (myocardial infarction), or stroke, fatal or nonfatal.
  - Risk Estimates are based on 3.2 million individuals with baseline examinations from 1992 to 2022 and include a diverse sample of racial and ethnic groups.
  - Applicable in adults aged 30-79 without known CVD. Out-of-range values should be managed as clinically indicated. Risk can still be estimated with the closest in-range value but may represent an over- or under-estimate.
  - Do not use the PREVENT calculator for adults with known CVD, evidence of severe subclinical CVD (e.g., left ventricular ejection fraction <40%, coronary artery calcium ≥300), positive genetic testing for a variant known to be pathogenic for an inherited cardiovascular condition, end-stage kidney disease, or limited life expectancy (<1 year).

Determining a Blood Pressure Goal:

- Adults with known cardiovascular disease (CVD) or 10-yr PREVENT CVD risk of ≥ 7.5: a BP goal of <130/80 mmHg is strongly recommended by the 2025 American Heart Association/ American College of Cardiology (AHA/ACC) guidelines.

- Adults with diabetes mellitus (DM) or chronic kidney disease (CKD*) (excluding end stage renal disease or renal transplant): The 2025 ACC/AHA guideline considers adults with hypertension at increased risk if they have diabetes, CKD or an estimated 10-year CVD risk of ≥7.5% according to PREVENT and therefore recommends a BP goal <130/80 mmHg.

- Adults ≥ 65: the 2025 ACC/AHA guidelines recommend a systolic BP goal of 130 mmHg for those who are noninstitutionalized ambulatory community-dwelling older adults. When evaluating these patients, it is important to consider their preference, comorbidities, life expectancy, and tolerability of antihypertensives to determine an appropriate regimen and BP goal. Those who have limited life expectancy or require assistance in daily activities may not be able to tolerate an intensive BP goal.

*CKD defined as eGFR <60 mL/min/1.73m^2 or albuminuria ≥30 mg/g

Background:
The 2017 ACC/AHA HTN guidelines reclassified BP into 4 new categories: normal, elevated, stage 1, and stage 2 (see Table 1, page 2). This change was due to data from various studies showing a higher risk of stroke and coronary heart disease (CHD) in patients with systolic blood pressure (SBP)/diastolic blood pressure (DBP) >120/80:

- Framingham Heart Study found that 55-year old adults (who were then normotensive in the study) have a **90% probability of developing HTN in their lifetime** and a 60% probability of receiving anti-HTN meds.
- Framingham Heart Study found that individuals with blood pressure values in the range of 130-139/85-89 mmHg have a **2-fold** increased risk of cardiovascular disease (CVD) versus a person with BP <120/80.
- Meta-analysis of 61 studies indicated that risk of death from CVD and stroke increases linearly with increasing BP beginning as low as 115/75 mmHg and for each increment of 20/10 mmHg the risk of CVD **DOUBLES.**
- **Risk was lowest with SBP 90-115 mmHg and was significantly lower than the risk for SBP 115-129 mmHg. Modest increases in either systolic or diastolic blood pressure above 130/85 mmHg were associated with large increases in hazard ratios, especially for coronary death, heart failure, ischemic stroke, intracerebral hemorrhage, and peripheral arterial disease (Rapsomaniki E et al; Lancet 2014)**

Management of Patient with Elevated Blood Pressure (SBP 120-129; DBP<80):
The main purpose of the *elevated* blood pressure category is to identify persons who are at risk of developing hypertension and hypertension-related long-term complications in the future. It is important that healthcare providers identify patients with elevated blood pressure early and manage their condition. **EDUCATION IS THE KEY HERE! This is the opportunity to counsel patients on the serious complications of HTN and to promote healthy habits and lifestyle changes so that an actual diagnosis of HTN may be avoided.**

Therapeutic Lifestyle Modifications:**
Lifestyle modifications are currently the gold standard in the management of patients with elevated BP. Suggested modifications and the extent of systolic blood pressure reduction are as follows:

Modification	Recommendation	Approximate SBP Reduction
Weight reduction	Encourage patient to maintain normal body weight (BMI 18-24.9)	1 mmHg/1 kg weight loss
Diet	Consider Diet for Health and encourage adherence. Encourage consumption of fruits, vegetables, whole grains, and low-fat products.	3-11 mmHg
Dietary sodium restriction	Discourage adding extra salt to food and commissary foods with high sodium content (e.g., instant noodle soup, chips).	5-6 mmHg
Physical activity	Encourage patient to engage in aerobic physical activity and resistance training to lower BP: 3 to 5 sessions a week, lasting on average 30 minutes per session, and involving moderate physical activity.	4-8 mmHg

**Set realistic goals for your patients and discuss the value of self-rewarding and goal setting. Encourage patients to make gradual changes to their lifestyle, as they are more likely to comply with one change at a time.

HYPERTENSION URGENCY & EMERGENCY

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients

1

Blood pressure (BP) > 180 mm Hg systolic and/or > 110 mm Hg diastolic ?

Yes

2

Obtain History and Perform Physical Exam

- Obtain BP both arms
- Evaluate heart, lungs, and neck veins for evidence of CHF
- Examine optic fundi for hemorrhages, exudates or papilledema;
- Determine all pulses especially if aortic dissection is suspected;
- Perform abdominal exam for bruits / renal artery stenosis
- **Perform neurological exam**
- **Elevate head at 45° angle**
- **Establish intravenous line if indicated**
- **Obtain EKG**
- **Obtain labs:** CMP, CBC, Urinalysis

**Signs of target organ damage: hypertensive encephalopathy, intracranial hemorrhage, unstable angina pectoris, acute myocardial infarction, acute left ventricular (LV) failure with pulmonary edema, dissecting aortic aneurysm, acute renal failure or eclampsia.*

3

Is there target organ damage* or optic disc edema?

Yes

No

4

Hypertension Emergency

Transfer to nearest Emergency Room

Call 911 and follow unit protocol. For UTMB, if ambulance is not immediately available, call 911.

Call Utilization Review/Utilization Management

5

Markedly Elevated BP/ Hypertension Urgency

(patient may experience symptoms of headache, shortness of breath, anxiety, or epistaxis)

- Short-acting antihypertensives (e.g.: clonidine) are not recommended. Please see II.D.1 under provider education
- Address causes of elevated BP such as anxiety, pain, drug-induced, edema, etc. Refer to Table 4 in Hypertension disease management guideline (HTN DMG) for secondary causes of HTN.
- Check compliance to antihypertensives

6

- Counsel patients with poor compliance.
- Consider increasing the dose of existing antihypertensive medications, reinstituting previous medications which may have expired, or adding a new antihypertensive medication
- If the patient has not been previously diagnosed with hypertension, refer to HTN DMG.

7

Follow-Up:

- Counsel the patient to return to medical if any symptoms develop
- Check BP three times weekly
- Schedule follow-up within 1-2 weeks

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.

Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee. Approved August 1995; Reviewed 1/08, 5/11, 7/17; Revised 10/98, 4/02, 4/03, 3/04, 5/14, 11/20, 5/25

PROVIDER EDUCATION

I. Hypertension emergencies:

A. Defined as severe elevations in blood pressure (BP), >180/110 mm Hg, complicated by evidence of impending or progressive target organ damage.

B. Patient should be transferred to the nearest Emergency Department (ED) as immediate blood pressure reduction is required to limit target organ damage.

C. Blood pressure does not need to reach the normal range immediately.

II. Hypertension urgencies

A. Defined as severe elevations in BP (>180/110) **WITHOUT** progressive target organ damage.

B. Does not require emergency therapy. Many of these patients have withdrawn from or are noncompliant with antihypertensive therapy.

C. Conditions such as withdrawal syndrome, anxiety, pain, nausea, edema, etc. that may lead to significant elevation in BP should be addressed.

D. <u>Rationale for not using short-acting antihypertensives (such as clonidine) to lower BP over hours:</u>

1. While the JNC7 guidelines suggested that some patients may benefit from treatment with an oral, short- acting agent (captopril, labetalol, or clonidine) followed by hours of observation, the guidelines also found no evidence that failure to aggressively lower BP in the emergency room was associated with any increased short -term risk, and that the term "urgency" has led to overly aggressive management of many patients with severe, uncomplicated hypertension.
2. The 2017 ACC/AHA HTN guidelines recommended reinstitution or intensification of antihypertensives and treatment of anxiety as applicable. There is no indication for referral to the ED, immediate reduction in BP in the ED, or hospitalizations.
3. The landmark 1967 Veteran Affairs Cooperative Trial demonstrated the long-term benefits of treating patients with chronic hypertensive urgency, which accrued over a period of months to years, not hours.
4. In a large retrospective cohort study of over 50,000 patients diagnosed with HTN urgency at outpatient clinics, only 0.7% were referred to the hospital for BP management. The referred patients were younger, were more likely African American, had higher BP values, and were more likely to have history of HTN and chronic kidney disease. When comparing 852 patients who were sent home to 426 patients who were sent to the hospital in a propensity-matched analysis, no significant difference in major adverse cardiac events were found at 7 days, 8 to 30 days, or 6 months. Sixty percent of patients at the hospital received a one-time dose antihypertensive, most commonly with labetalol or clonidine (Patel et al, JAMA 2016).

E. <u>Role of furosemide in HTN urgencies:</u>

1. Ensure the patient has no signs or symptoms of HTN emergency such as acute LV failure with pulmonary edema; otherwise, this is considered HTN emergency and the patient should be transferred to the nearest ED.
2. The antihypertensive effect of furosemide in HTN urgencies has not been well documented.
3. Furosemide is useful in patients with volume overload, but the risk of volume depletion in patients with reduced or normal volume status should be considered.
4. For edema, the initial oral dose is usually 20-40 mg once daily, then titrating as needed to an effective dose.

HYPOGLYCEMIA

1

Patient presents with signs and symptoms of hypoglycemia (generally blood glucose < 70 mg/dL, see Table 2)

1. Patient with known diabetes or insulinoma – go to box #2
2. Patient not known to have diabetes – go to box #2 to treat hypoglycemia and then treat underlying disease such as drugs (e.g., pentamidine, salicylates, ethanol), end stage liver disease, renal disease, endocrine deficiencies, non-beta cell tumors, prior gastric surgery, or inherited metabolic disorders

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

Underlying infections should be ruled out for episodes of hypoglycemia - especially recurring hypoglycemia.

2

Is the patient conscious and cooperative?

No

Yes

3

Notify unit provider & establish IV access.

4

Has IV access been established after at least 2 attempts ?

No

Yes

5

If unable to establish IV access, administer Glucagon (1 mg/cc) – 1mL IM or SQ (located in the crash cart).

Dose may be repeated one time in 15 minutes (see box 8).

6

Administer 50mL of dextrose 50% IVP x1

7

Have symptoms resolved?

No

Yes

8

Administer Glucagon (1 mg/cc) – 1mL IM or SQ (located in the crash cart).

Investigate other etiologies for mental status change and consider transfer to a higher level of care.

9

Discharge the patient when BG levels remain > 70 mg/dL. Before discharging the patient, it is important to consider medical staff availability, inmate housing, and duration of effect of the agent being used for the treatment of hypoglycemia.

Ingestion of a snack or meal shortly after glucose levels are raised is advisable. Response to IV dextrose may be transient.

Schedule follow up with unit provider for evaluation and possible medication adjustment.

10

Treat orally & notify unit provider.

Administer 1-2 tubes of oral glucose gel (1 packet contains 15 grams of glucose) or glucose-containing fluids, candy, or food. In general, 15-20 g oral glucose will be adequate. Recheck blood glucose (BG) in 15 minutes and repeat above until BG > 70 mg/dl.

Ingestion of a snack or meal shortly after BG concentration is raised is advisable if given oral glucose, because **response is transient (typically <2 hours)**.

Discharge the patient when BG levels remain > 70 mg/dL. Before discharging the patient, it is important to consider medical staff availability, inmate housing, and duration of effect of the agent being used for the treatment of hypoglycemia.

Consider scheduling patient who has had recurrent episodes for follow up appointment with unit provider for evaluation and possible medication adjustment.

Nurses: DMGs are to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.**

Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee, January 2006. Reviewed 5/10, 1/13. Revised 9/16, 3/21, 5/25.

I. Definitions:

A. Hypoglycemia - The American Diabetes Association has determined that a blood glucose of **≤ 70 mg/dL** can be used as the cut-off value in the classification of hypoglycemia. Hypoglycemia can be further classified by severity (Table 1).

Table 1. Classification of hypoglycemia

	Criteria	**Notes**
Level 1	Glucose < 70 mg/dL and ≥ 54 mg/dL	
Level 2	Glucose < 54 mg/dL	Neuroglycopenic symptoms begin to occur Immediate action required to resolve the event
Level 3	A severe event characterized by altered mental and/or physical status requiring assistance for treatment	Characterized by cognitive impairment that may or may not be recognized. Can progress to loss of consciousness, seizure, coma, or death

B. Documented symptomatic hypoglycemia – an event during which typical symptoms of hypoglycemia are accompanied by a measured blood glucose of ≤ 70 mg/dL.

C. Asymptomatic hypoglycemia – an event not accompanied by typical symptoms of hypoglycemia but with a measured blood glucose of ≤ 70 mg/dL. This is also called hypoglycemia unawareness (loss of warning symptoms of hypoglycemia). It is often precipitated by recurrent hypoglycemia in type 1 diabetes and advanced type 2 diabetes. Incidence increases with age and duration of diabetes. If the diagnosis of hypoglycemia has been made, consideration of targeting higher glucose levels in the short term should be given. A minimum of a three-week period of avoiding hypoglycemia should be attempted in efforts to return to an awareness of hypoglycemia. An A1c goal of ≤ 8% should be considered for the elderly diabetic population.

D. Probable symptomatic hypoglycemia – an event during which symptoms typical of hypoglycemia are not accompanied by a plasma glucose determination but presumed to be caused by a blood glucose of ≤ 70 mg/dL.

E. Pseudo-hypoglycemia - an event during which the person with diabetes reports any of the typical symptoms of hypoglycemia, but with a blood glucose level of > 70 mg/dL. This phenomenon commonly occurs when patients have been accustomed to hyperglycemia and undergo intensification of their glucose control. This syndrome is self-limiting and usually takes 2-4 weeks for the brain to readjust to their improved and thus relatively reduced circulating glucose levels.

Table 2. Symptoms of hypoglycemia

Neurogenic Symptoms (caused by falling glucose levels)	**Neuroglycopenic Symptoms** (caused by brain neuronal glucose deprivation)
Shakiness Trembling Anxiety Nervousness Palpitations Clamminess Sweating Dry mouth Hunger Pallor Pupil dilation	Abnormal mentation Irritability Confusion Difficulty in thinking Difficulty in speaking Ataxia Paresthesias Headaches Stupor Seizures Coma Death (if untreated)

II. Risk Factors
- A. Type 1 diabetes and advanced type 2 diabetes
- B. Medication (insulin or oral agents) excess
- C. Decreased influx of exogenous glucose (e.g., skipped or missed meals or snacks)
- D. Increased glucose utilization (e.g., increase in exercise)
- E. Reduced insulin clearance (e.g., renal failure)
- F. Age

III. Treatment
- A. Hypoglycemia should be treated with fast-acting carbohydrates if blood glucose is < 70 mg/dL
  1. Pure glucose is preferred but any form of carbohydrate will raise blood glucose
  2. Added fat may impair and then prolong the acute glycemic response
  3. Carbohydrate sources high in protein should be avoided as they may increase insulin response without increasing plasma glucose concentrations in type 2 diabetes
  4. Once glucose returns to normal, the patient should be counseled to eat a meal or snack to prevent recurrent hypoglycemia
- B. In patients who are unconscious or uncooperative, IV access should be attempted. Dextrose 50% administered via IV push is indicated in patients with IV access. Glucagon is indicated for patients in which IV access cannot be established and who are unable or unwilling to consume carbohydrates by mouth.

IV. Prevention
- A. Address hypoglycemia at each diabetes clinic visit
  1. Is the patient having episodes of hypoglycemia, how frequently are they occurring, and are they severe?
  2. What is the relationship of hypoglycemia to drug administration, meals, and exercise? (Table 3)
- B. Educate the patient on symptoms of hypoglycemia and what to do when they occur.
- C. In patients with recurrent episodes of hypoglycemia or a severe episode of hypoglycemia, consider:
  1. Increasing the frequency of glucose monitoring
  2. Adjusting the patient's medication regimen (Table 3)
  3. Increasing glycemic targets for at least several weeks in insulin-treated patients with hypoglycemia unawareness, one level 3 hypoglycemic event, or a pattern of unexplained level 2 hypoglycemia to partially reverse hypoglycemia unawareness and reduce risk of future episodes
  4. Ordering bedtime snacks
  5. Evaluating the patient's other medications (e.g., non-selective beta blockers) to determine if there is a medication that may be masking the symptoms of hypoglycemia making it difficult for the patient to identify hypoglycemic episodes for early intervention and self-management

Table 3. Pharmacokinetics of Insulin*

Insulin	Onset of Action	Peak Action	Effective Duration
Regular Insulin	30 to 60 min	2 to 3 hours	8-10 hours
NPH Insulin	2 to 4 hours	4 to 10 hours	12 to 18 hours
Insulin glargine (Lantus)	3 to 4 hours	Peakless	~24 hours

*The pharmacokinetics of insulin preparations may be used to determine which insulin to adjust <u>when</u> a patient is experiencing symptoms of low or high blood glucose.

Examples:

1. If patient is symptomatic of hypoglycemia around 9am and he or she injected NPH and regular insulin at 4am, most likely it is the NPH that needs to be adjusted as it is peaking 5 hours after injection.
2. If patient is symptomatic of hypoglycemia or hyperglycemia after dinner, the regular insulin will need to be adjusted as its onset of action is faster than the NPH.

LIVER CIRRHOSIS

Alert Symptoms
⇒Abdominal Pain
⇒Mental Status Change
⇒Fever
⇒Oliguria/Anuria
⇒Anasarca
⇒Rapid weight gain or loss
⇒Hematochezia
⇒Hematemesis / Melena

The pathway does not replace sound clinical judgment nor is it intended to strictly apply to all patients.

1

Initial Management of Cirrhosis

- Complete baseline evaluation and offer preventive measures including indicated vaccinations (HBV, HAV, pneumococcal, annual influenza and Covid-19) and HBV/HCV screening (box A)
- Enroll in Cirrhosis CCC and follow up every 3- 6 months
- Refer to Liver or ESLD clinic for UTMB (box B), GI clinic for TTech and/or appropriate specialty clinic for treatment as indicated based on etiology (e.g., UTMB virology - HIV, HCV/HBV)

2

Compensated

Lab abnormalities suggestive of cirrhosis:
low platelets but ≥ 70,000, elevated bilirubin but < 2.0,
PT prolongation < 2 sec., low albumin but ≥ 3.0.

3

Decompensated

Evidenced by

- Ascites
- Varices or variceal bleed
- SBP
- PLT < 70K, Alb < 3.0, bili > 1.5, PT prolongation > 2 sec
- Jaundice
- Encephalopathy
- HRS or HPS
- HCC
- Childs-Pugh ≥ 7

*Consider MRIS, hospice or transplant evaluation as indicated (MELD ≥ 22 or recurrent ascites, bleed, or encephalopathy requires MRIS referral, MELD > 30 hospice referral)

4

HCC Screening

- Ultrasound (US) + AFP every 6 months.
- Consider Triple Phase Liver CT and see Liver Mass Referral Guideline if:
  - Lesion ≥ 10 mm on ultrasound or
  - AFP > 20 ng/ml (non-HCV) or > 60 ng/ml (chronic HCV) or
  - Doubling of AFP from previous value or
  - History of HCC

5

Variceal Screening

All patients with cirrhosis should be referred for EGD at the time of diagnosis. Use of NSBB may be initiated based on endoscopy findings (see Table 3).

6

Laboratory & Clinic Surveillance

Cirrhosis CCC Q 6 months if compensated or every 3 months if decompensated.
Complete physical exam, review for symptoms, medication review, CBC with diff & PLT, CMP, PT/INR, blood pressure, pulse, weight, temperature, mental status screening, MELD score.

7

Esophageal Varices & Portal HTN

(see table 3)

Primary prophylaxis - see Variceal Surveillance (box 5)
Secondary prophylaxis

- First Line - propranolol and EVL
- Second line - TIPS or shunt

8

Ascites / Edema

(see table 4)

- Sodium restriction
- Diuretics
- Paracentesis
- TIPS or shunt for refractory cases

9

SBP

(see table 5)

Secondary prophylaxis

- Bactrim DS 1 tab daily
- Alternate - Ciprofloxacin 500mg daily

Treatment

- Admit to hospital for evaluation and IV antibiotics

10

Hepatorenal Syndrome

(see table 6)

- Treatment per specialty clinic

11

Hepatic Encephalopathy

(see table 7)

- Identify and treat precipitating factors
- First line - lactulose
- Second line - lactulose plus rifaximin or neomycin

12

HCC

- Ultrasound Q6 months
- Treatment per specialty clinic: surgical resection, RFA, PEI, TACE, chemotherapy, symptomatic treatment

CCC - chronic care clinic, EGD – esophagogastroduodenoscopy, EVL - endoscopic variceal ligation, HCC - hepatocellular carcinoma, HPS - hepatopulmonary syndrome, HE - hepatic encephalopathy, HRS - hepatorenal syndrome, MELD - model for end-stage liver disease, NSBB - nonselective beta blocker, PEI - percutaneous ethanol injection, RFA - radiofrequency ablation, SBP - spontaneous bacterial peritonitis, TACE - transarterial chemoembolization, TIPS - transjugular intrahepatic portosystemic shunt.

Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee. Approved: 7/2013 Revised: 9/2022

Box A. Initial Management

Baseline Evaluation

- Complete H&P
- Vitals including weight
- Labs: CBC with diff and plts, PT/INR, CMP, alpha-fetoprotein, A1c if diabetic
- Screening: HIV, anti-HBsAb, anti-HBc, HBsAg, anti-HAV, anti-HCV with reflex
- Calculate MELD Score (CMC homepage-Tools-Calculators)

Preventive Health Measures

- Vaccinations - HBV, HAV, pneumococcal, annual influenza and Covid-19
- Patient education on disease state, avoidance of hepatotoxic and nephrotoxic medications, treatment, and compliance

Box B. UTMB Specialty Referral Criteria

Expedited GI clinic referral:

- Ascites as only complaint

Expedited ESLD VCL or GI clinic referral:

- History of bleed from varices OR
- Difficult to control ascites* OR
- Resistant encephalopathy* OR
- Resistant diuresis with increasing BUN/Creatinine OR
- An INR increase of 0.5 within 1-3 months
- MELD Score ≥12
- Decompensated Cirrhosis

Urgent ESLD VCL or GI clinic referral:

- MELD Score ≥20

Urgent GI Referral:

- Significant melena

911:

- Hematochezia/ hematemesis

*Direct admit

TABLE 1: Child-Turcotte-Pugh (CTP) Calculator

	POINTS*		
	1	**2**	**3**
Encephalopathy	None	Grade 1-2 (or precipitant—induced)	Grade 3-4 (or chronic)
Ascites	None	Mild / Moderate (diuretic - responsive)	Severe (diuretic - refractory)
Bilirubin (mg/dL)	< 2	2 - 3	> 3
Albumin (g/dL)	> 3.5	2.8 - 3.5	< 2.8
PT (sec prolonged) or INR	< 4 < 1.7	4 - 6 1.7 - 2.3	> 6 > 2.3

*CTP score is obtained by adding the score for each parameter
CTP class: A = 5 - 6 points, B = 7 - 9 points, C = 10 - 15 points

TABLE 2: West Haven Criteria for Semi-quantitative Grading of Mental Status (Hepatic Encephalopathy [HE])

Grade 0	No detectable symptoms
*Minimal (or covert) Encephalopathy (MHE)	Mildest form of the HE continuum. Subtle neurocognitive abnormalities primarily affect attention, vigilance, response inhibition, and executive function which are not recognizable on standard neurological or mental status examination but are evident on psychometric testing. MHE may predict the development of overt HE and is associated with poor survival.
Grade 1	Trivial lack of awareness Euphoria or anxiety Shortened attention span Impaired performance of addition
Grade 2	Lethargy or apathy Minimal disorientation for time or place Subtle personality change Inappropriate behavior Impaired performance of subtraction Asterixis
Grade 3	Somnolence to semi-stupor, but responsive to verbal stimuli Confusion Gross disorientation
Grade 4	Coma (unresponsive to verbal or noxious stimuli)

* Not an official stage on the West Haven Scale.

TABLE 3: ESOPHAGEAL VARICES & PORTAL HYPERTENSION	
EVALUATION & TREATMENT	• Nonselective beta-blockers (NSBB) propranolol and carvedilol are the preferred pharmacologic agents for prevention of bleeding and may be continued indefinitely or until patient experiences refractory ascites, hypotension leading to systolic blood pressure <90 mm Hg, hepatorenal syndrome, spontaneous bacterial peritonitis, sepsis. **(Decision to initiate NSBB should be guided by EGD and ESLD specialty clinic).** ◦ Recommended Dose: ◦ Propranolol: 20-40 mg twice daily with maximum daily dose of 320 mg in patients without ascites or 160 mg in patients with ascites ◦ Carvedilol 3.125 mg twice daily with maximum dose of 6.25 mg twice daily (except in patients with hypertension) ◦ NSBBs Therapy Goals: Heart rate 55-60 beats/minute and systolic BP not below 90 mmHg • Primary Prophylaxis ◦ Small varices –Primary prophylaxis for small varices is only indicated in patients with CTP B or C cirrhosis or red wales. For CTP A or absence of wales, surveillance at 1 year is indicated. ◦ Medium/large varices – propranolol or carvedilol if patient unable to take propranolol. NSBB is appropriate for large varices unless red wales or stigmata of recent bleeding are seen. Endoscopic variceal ligation (EVL) may be preferred in patients at high risk of hemorrhage or those who have contraindications or intolerance to beta-blockers. (Decision to perform EVL would be made by ESLD specialty clinic). • Secondary Prophylaxis ◦ Combination of EVL and propranolol (1st line therapy) ◦ TIPS may be considered in certain patients with recurrent hemorrhage despite EVL plus maximal doses of propranolol. (Decision to perform EVL or TIPS would be made by ESLD specialty clinic.) • Role of proton pump inhibitors (PPI): ◦ PPIs are not used to treat varices but may be considered if acid reflux symptoms are present. ◦ Varices bleed by rupturing from within the vessel through thinning of the wall rather than from erosion from acid in the lumen.
MONITORING	Surveillance • Patients on primary prophylaxis with propranolol (no history of hemorrhage) - repeat EGD is not necessary. • Patients treated with EVL - surveillance EGD every 6-12 months.

TABLE 4: ASCITES / EDEMA	
EVALUATION & TREATMENT	• Swelling starts first in the feet/ankles then progresses to the thighs, scrotum, and even penis. In some patients, edema presents with abdominal swelling, after swelling is present to the knees. Edema above the rib cage is not due to cirrhosis. • Consider paracentesis for new onset ascites with fluid analysis (cell count and differential, albumin, total protein concentration, and culture. A Serum to Ascitic Albumin Gradient (SAAG) of $\geq$ 1.1 gm/dL indicates portal hypertension with 97% accuracy. – Paracentesis may be performed at Estelle-E2, Young-GC, Hospital Galveston-HG, and Montford-HP. For patients requiring frequent or routine paracentesis, consider requesting a housing change to an appropriate TDCJ facility. • Salt restriction (< 2 gm/day) • Diuretic therapy ◦ For minimal to mild edema: – Furosemide 20 mg daily or – Spironolactone 100 mg daily. Daily doses less than 50 mg are insufficient for controlling edema and should not be used. ◦ For moderate edema or greater: – Furosemide 40mg with Spironolactone 100 mg. Also useful in patients who do not respond to or have hyperkalemia with spironolactone monotherapy. – Titrate diuretic therapy every 5-7 days. This 40 mg:100 mg ratio of furosemide:spironolactone can be further increased to a maximum daily dose of 160 mg of furosemide and 400 mg daily of spironolactone – Amiloride 10-40 mg daily may be substituted for spironolactone if tender gynecomastia is present but may be less effective. Nonformulary approval is required. – If the above program does not work, metolazone 5 mg can be added once per week, increasing to 5 mg M-W-F, then 5 mg M-F, and 5 mg daily. Renal function and electrolytes must be monitored closely when using > 2 diuretics. Consider BMP every 1-2 weeks until stable, then monthly. – Monitor body weight and diuretic complications (BMP every 1-2 weeks during titration) which include uncontrolled or recurrent encephalopathy, serum sodium < 120 mmol/L despite fluid restriction, Scr > 2.0 mg/dL, K > 6.0. – TED hose (knee-high) may be considered for lower leg edema. Patients with thigh swelling or who demonstrate pitting over the thighs need thigh-high TED hose. If the hose will not stay up or if there is abdominal wall swelling, consider referral to Brace & Limb for fitted compression garments (hose up to the waist). Compression hose and garments may help prevent hospitalization for chronic edema and cellulitis. • Tense ascites (massive and/or painful) - consider large volume paracentesis (LVP) followed by sodium restriction and diuretic therapy. If greater than 5 L of ascitic fluid removed replace with 6-8 g of albumin per liter removed. Caution as LVP and aggressive diuresis can precipitate HRS.

Continued on page 4

TABLE 4: ASCITES / EDEMA CONTINUED	

EVALUATION & TREATMENT	• Refractory Edema or Ascites
	  ◦ Fluid overload unresponsive to sodium restriction and high-dose diuretics or recurs rapidly after therapeutic paracentesis.
	  ◦ Often due to inadequately titrated diuretics or diuretic complications.
	  ◦ Refer to ESLD clinic and consider serial paracentesis. TIPS or peritoneovenous shunt may be necessary.

MONITORING	Weight and CMP every 90 days or sooner during diuretic titration or with paracentesis.

TABLE 5: SPONTANEOUS BACTERIAL PERITONITIS (SBP)	

EVALUATION & TREATMENT	• May be asymptomatic; however, most common symptoms include fever, abdominal pain, abdominal tenderness and altered mental status. Laboratory abnormalities suggestive of infection include worsening Scr, elevated WBC, and acidosis.
	• Diagnosis is confirmed by paracentesis with $\geq$ 250 PMNs/mm^3 and/or positive ascitic bacterial culture.
	• Acute treatment requires hospitalization and IV antibiotic (cefotaxime or ceftriaxone).
	• Outpatient prophylaxis of SBP
	  ◦ All patients with a history of prior SBP should receive indefinite prophylaxis with one of the following:
	  - First line - sulfamethoxazole/trimethoprim DS one tab daily
	  - Second line - ciprofloxacin 500 mg po once daily. (Reserved for sulfa allergy or renal insufficiency.)

MONITORING	Signs/symptoms and vitals (temperature) at each encounter. CMP and CBC every 90 days or more frequently if clinically indicated.

TABLE 6: HEPATORENAL SYNDROME (HRS)	

TREATMENT	• HRS should be considered in patients with cirrhosis and ascites with a creatinine level above 1.5 mg/dL or CrCl <40 mL/min. It is a diagnosis of exclusion. The following should be ruled out and treated.
	  ◦ Sepsis
	  ◦ Volume depletion
	  ◦ Vasodilators
	  ◦ Organic renal failure
	• There are two types of HRS
	  ◦ HRS-AKI (hepatorenal syndrome with acute kidney injury) - rapidly progressive acute renal failure usually occurring in hospitalized patients. Typically characterized by onset < 2 weeks, two-fold increase in creatinine, and clearance < 20 mL/min. Poor prognosis (median survival 2 weeks).
	  ◦ HRS-NAKI (hepatorenal syndrome with nonacute kidney injury) - slower onset typically seen in outpatients with refractory ascites. Often precipitated by over-diuresis, GI bleed, or infection. Median survival 6 months.
	• Hospitalization and specialty care required. Precipitating factors should be treated. Diuretics should be discontinued, and intravascular volume expanded with albumin. The only definitive therapy for HRS is transplant.

MONITORING	CMP every 90 days or more frequently if clinically indicated.

TABLE 7: HEPATIC ENCEPHALOPATHY (HE)	

EVALUATION & TREATMENT	• Varied presentation. May present with sleep disturbances, changes in personality or behavior, sporadic lack of awareness, shortened attention span, slowed mental functioning, asterixis, lethargy, apathy, disorientation, slurred speech, bizarre behavior, stupor, and eventual coma.
	• Identification and treatment of precipitating factors should be instituted (GI hemorrhage, infection, renal or electrolyte imbalance, dehydration, psychoactive medications, constipation, poor compliance with medications). HE is a clinical diagnosis and serum ammonia levels are not routinely indicated.
	• Pharmacologic Prophylaxis (indefinite)
	  ◦ First line - lactulose starting at 30 mL BID - TID. Titrate to achieve 3-4 loose stools per day. Consider DOT or pill window dosing for suspected poor compliance.
	  ◦ Second line – rifaximin 550 mg-600 mg po BID or neomycin 500-1000 mg BID plus lactulose.
	  ◦ For patients with a history of renal impairment, rifaximin may be considered prior to a trial of neomycin.
	• Patients with acute or significant changes in mental status - consider transport to higher level of care.
	  ◦ An additional supplemental dose of po lactulose 15 mL given between scheduled TID dosing can maximize the acidifying effect of lactulose without causing a greater number of stools and may be considered.
	  ◦ In the infirmary setting, a tepid tap water enema may be considered and is preferred over lactulose enema. Administer 2000 mL and repeat until returns are clear.

MONITORING	Mental status screening at each encounter.

Table 8. Common Medications used in ESLD

Medication	Formulary Status	Indication	Dosing	Side Effects / Comments
Amiloride 5 mg tab	NF	Ascites / edema	5 mg to 10 mg once daily	Hyperkalemia, hyponatremia, acidosis, GI upset
Ciprofloxacin 500 mg tab	NF	SBP Prophylaxis	500 mg once daily	Rash, nausea, vomiting, diarrhea Reserved for sulfa allergy or renal insufficiency.
Furosemide 20 mg, 40 mg tab	F	Ascites / edema	40 mg to 160 mg daily. Doses over 80 mg daily should be divided twice daily.	Electrolyte disturbances including hypokalemia and hyponatremia, increased serum creatinine, photosensitivity, rash, dizziness, hypotension, hyperuricemia
Lactulose 10 gm/15 mL syr	F	Hepatic Encephalopathy	Start at 30 mL BID - TID. Titrate to achieve 3-4 loose stools per day.	Can cause electrolyte imbalance, abdominal discomfort, cramping, nausea, flatulence.
Metolazone 5 mg tab	F	Ascites / edema	Titrate slowly up to 5 mg daily	Electrolyte disturbances including hypokalemia and hyponatremia, increased serum creatinine, photosensitivity, rash, dizziness, hypotension, hyperuricemia
Neomycin 500 mg tab	NF	Hepatic Encephalopathy	500 mg to 1000 mg BID	Nausea, nephrotoxicity, ototoxicity. Avoid in AKI or CKD.
Propranolol 10 mg, 20 mg, 40 mg tab	F	Esophageal varices	Initial dose 20 mg BID. Titrate to a maximally tolerated dosage (heart rate 55-60 beats/minute).	Hypotension, bradycardia, fatigue. Caution in decompensated CHF, sinus bradycardia, heart block, severe asthma or COPD.
Rifaximin 200 mg tab	NF	Hepatic Encephalopathy	600 mg (3 x 200 mg tabs) po BID	Reserved for breakthrough HE despite optimized lactulose and neomycin.
Spironolactone 25 mg tab	F	Ascites / edema	100 mg to 400 mg daily	Gynecomastia, hyperkalemia, rash, renal dysfunction
Sulfamethoxizole / trimethoprim 800 mg/160 mg tab	F	SBP Prophylaxis	1 double strength tablet once daily	GI upset, rash, uticaria, blood dyscrasia, hyperkalemia, crystalluria

Table 9. Medications which should be used with caution or contraindicated in ESLD

Medication	Formulary Status	Dosing / Comments
Acetaminophen	F	May be used up to a maximum daily dose of 2,600 mg.
Acetaminophen / codeine	F*	Up to 2,600 mg acetaminophen daily. Impaired hepatic conversion of codeine (prodrug) to its active form may result in decreased analgesic effect.
Aminoglycosides (Gentamicin, Tobramycin)	F	Should be avoided whenever possible in the treatment of bacterial infection due to the potential side effects of nephrotoxicity or reduced renal perfusion.
Angiotensin Converting Enzymes Inhibitors (ACEI) / Angiotensin Receceptor Blockers (ARBs)	F	ACEI / ARBs should generally be avoided in patients with both cirrhosis and ascites due to the potential side effects of nephrotoxicity or reduced renal perfusion.
Anticonvulsants Carbamazepine Divalproex Phenytoin Primidone	F	Phenytoin, carbamazepine, and divalproex are all extensively metabolized by the liver, highly protein bound, and potentially hepatotoxic. They should generally be avoided in cirrhosis due to increased risk of toxicities, including thrombocytopenia. Divalproex is contraindicated with severe hepatic impairment. Primidone is also heavily metabolized by the liver and can accumulate in cirrhosis precipitating hepatic encephalopathy. If anticonvulsant therapy is indicated, levetiracetam may be considered. Levetiracetam requires dose adjustment in renal impairment.

*Formulary restrictions apply

Table 9 Cont. Medications which should be used with caution or contraindicated in ESLD

Medication	Formulary Status	Dosing / Comments
Antidepressants SSRI's Celexa (citalopram) Prozac (fluoxetine) Zoloft (sertraline) SNRI's Effexor (venlafaxine) Cymbalta (duloxetine) Serotonin Receptor Modulator Desyrel (trazodone)	F	• Most psychotropic drugs are hepatically metabolized, increasing the potential for accumulation and adverse effects in patients with hepatic impairment • Duloxetine should be avoided in all patients with hepatic impairment • Citalopram should be limited to a max of 20 mg daily in hepatic impairment • Venlafaxine XR dosing should be reduced by 50% or more in hepatic impairment • Specific dose adjustments are not provided for fluoxetine, sertraline, or trazodone. Consideration may be given to using lower doses of fluoxetine and sertraline, and trazodone should be used with caution in hepatic impairment
Benzodiazepines	F*	Should generally be avoided in cirrhosis as benzodiazepines may trigger or aggravate hepatic encephalopathy.
Morphine sulfate	F*	Initiate at low doses and titrate slowly. Morphine is extensively metabolized by the liver and accumulation occurs in cirrhosis. Renal insufficiency may result in accumulation of toxic metabolites.
NSAIDS	F	NSAIDS should generally be avoided in patients with cirrhosis due to increased risk of variceal hemorrhage, impaired renal function, risk of hepato-renal syndrome, and diuretic resistance. Low to moderate doses may be used cautiously but must be administered with a proton pump inhibitor (omeprazole 20-40 mg daily) and monitored closely for adverse effects.
Proton Pump Inhibitors (PPI) (omeprazole)	F	Avoid chronic PPI use in patients with an unclear indication. PPI use in patients with cirrhosis may increase the risk of SBP, hepatic encephalopathy, and C. difficile infection.

Information for the Provider

I. Screening for Cirrhosis

A. Key History Questions

1. Have you ever been diagnosed with HCV, HAV, HCV, or other liver disorder?
2. Have you ever been jaundiced?
3. Have you used drugs intravenously?
4. Have you shared instruments for body piercing or tattooing?
5. Have you ever had a blood transfusion? If so what year? How many bags?
6. Any liver disease in your family?
7. Before TDCJ, how much alcohol did you drink?
8. Do you bleed excessively or bruise easily?
9. Have you ever had an imaging study (ultrasound, MRI or CT) of the liver? Why?
10. Have you had a liver biopsy, EGD, or colonoscopy? When? Where? Why?
11. Have you ever had your legs or stomach swell with fluid? When?
12. Have you ever had anemia, bloody stools, or black tarry stools? When?
13. Have you ever had periods of confusion or fuzzy thinking? When?

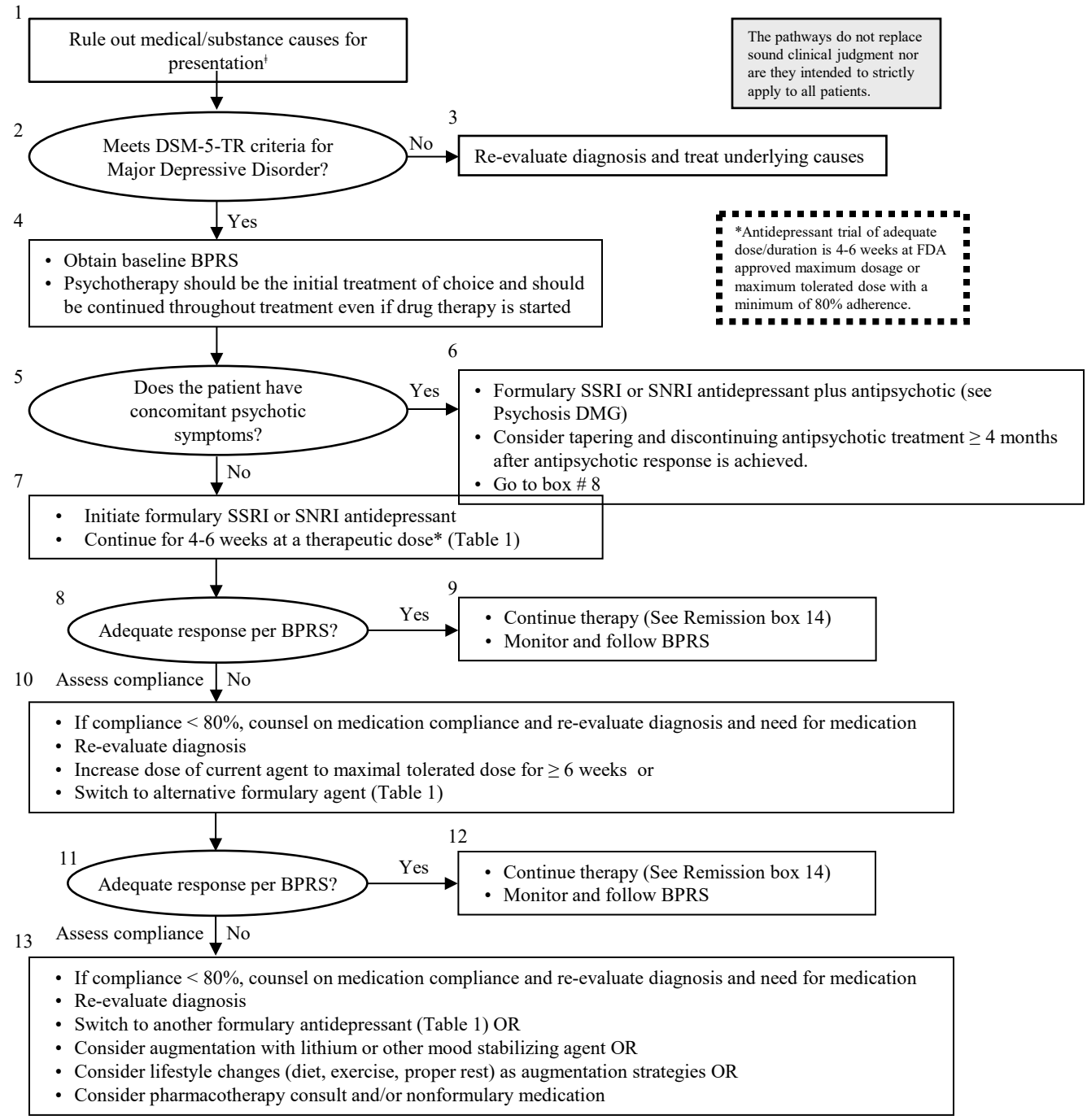
B. Key Physical Findings

1. Always list age, height, weight, and BMI at each visit. Check last visit and note change.
2. Skin/Hands/Nails: jaundice, thin skin, bruises, petechiae, palmar and peri-nail bed erythema, curved nails, Dupuytren's contractures, spider angiomas, venous pattern over abdomen (caput medusa), especially upper abdomen. Varicose veins may account for edema. Acanthosis nigricans in collar area, axilla, groin, under breasts, or belt area is a sign of insulin resistance, pre-diabetes (consider non-alcoholic fatty liver disease, NAFLD).
3. Check for neck vein distention and hepato-jugular reflux. Liver edge and tenderness.
4. Loss of shoulder and pelvic muscle strength.
5. Gynecomastia: off or on spironolactone.
6. Liver enlargement by percussion: 2 cm or less below the xiphoid. 7-11 cm in a line. 2-10 cm to the right of the xiphoid. May be below the ribcage if patient has a low diaphragm due to pulmonary disease.
7. Peripheral edema: pitting over the tibia from ankle to knee. May have enlargement by history of upper leg or pitting. May have penile or scrotal edema. May have pitting over abdomen.
8. Ascites: best test is shifting dullness.
9. Encephalopathy: asterixis, accentuated by closing eyes with arms outstretched. Minimal encephalopathy: tremor of hands when outstretched with eyes closed.

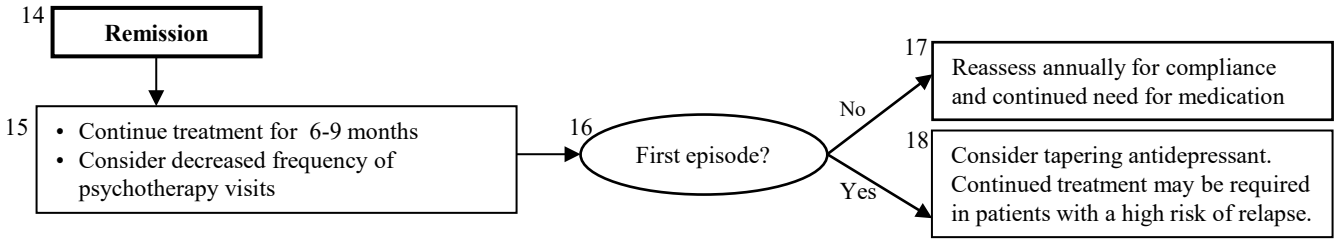
C. Key Laboratory Findings

1. CBC with differential: WBC and Platelets decline as the spleen enlarges from congestion in portal hypertension. Anemia may be present due to bleeding.
2. PT/INR elevation.
3. Metabolic panel for low albumin, elevated BUN and serum creatinine, electrolyte imbalance.
4. Liver panels so that you can see if bilirubin is elevated in unconjugated, conjugated, or protein bound (delta) fractions. Elevation in AST, ALT, and/or alkaline phosphatase.
5. HAV antibody, HBV surface antigen and antibody, HBV core antibody, HCV antibody.
6. Order a panel to look for congenital liver disease or other causes of liver disease: ceruloplasmin, iron, iron binding capacity, ferritin, alpha-1 antitrypsin, ANA, SMA, AMA.
7. MELD score

MAJOR DEPRESSIVE DISORDER (MDD)



‡Medical causes for depression may include endocrine, infectious, or neurologic disorders, vitamin deficiencies, fibromyalgia, etc.



Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee, Approved 1/99, revised 5/02, 2/03, 4/03, 11/05, 5/07, 1/11, 9/11, 3/13, 7/16, 5/17, 5/18, 5/23, 1/26

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.

Medication Selection

Patients should be evaluated for use of formulary agents when possible. Providers should consider history of response, contraindications, comorbidities, compliance, and potential for adverse effects and drug interactions when making treatment decisions. When medications are changed, patients should be monitored closely for worsening symptoms and adverse effects.

Table 1: Formulary Antidepressants

Drug Class	Generic Name	Brand Name	Initial Daily Dosage (Range)	Therapeutic Range (ng/mL)	Monitoring
Selective Serotonin Reuptake Inhibitors (SSRIs)	Escitalopram 10 mg, 20 mg tablets	Lexapro®	10 mg (10 – 20 mg) Do not exceed 10 mg in elderly	N/A	• Emergence of suicidal ideation or behavior • Escitalopram, fluoxetine and sertraline have also been associated with QTc prolongation. EKG monitoring is encouraged if risk factors for QTc prolongation are present.[a]
	Fluoxetine 20 mg capsule	Prozac®	20 mg (20 – 80 mg)		
	Sertraline 50 mg, 100 mg tablets	Zoloft®	50 mg (50 – 200 mg)		
Serotonin Norepinephrine Reuptake Inhibitor (SNRI)[b]	Venlafaxine XR 37.5 mg, 75 mg, 150 mg capsules	Effexor XR®	75 mg (150-225 mg)	N/A	• Emergence of suicidal ideation or behavior • Dose-related increases in systolic blood pressure and pulse
	Duloxetine 30, 60 mg capsules	Cymbalta®	30-60 mg (60-120 mg)		
Other[c]	Trazodone 50 mg, 100 mg tablets	Desyrel®	100 – 150 mg (300 – 600 mg)	N/A	• Emergence of suicidal ideation or behavior • Priapism

[a] Risk factors for QTc prolongation include age > 65 years old, use of other concomitant QTc prolonging medications, baseline hypokalemia or hypomagnesemia, or pre-existing cardiovascular impairment

[b] venlafaxine functions as an SNRI at doses ≥ 150 mg/day. Titration to such doses may offer enhanced efficacy in the treatment of MDD when compared to lower doses, at which this agent functions more like an SSRI.

[c] Generally not recommended as first line or second line therapy for treatment of depression. Due to its sedating effect, trazodone in conjunction with an antidepressant may be used in treating sleep difficulties related to depression.

SEROTONIN SYNDROME – a life-threatening condition caused by excessive serotonergic activity in the nervous system

- May occur with the use of one or more serotonergic medications (ex: antidepressants, buspirone, linezolid, lithium)
- Symptoms: fever, agitation, sweating, shivering, muscle rigidity, confusion

BRIEF PSYCHIATRIC RATING SCALE (BPRS) - Instructions for the Clinician

The Brief Psychiatric Rating Scale (BPRS) is a widely used instrument for assessing psychopathology at baseline and longitudinally as an outcome measurement when treatment is introduced. The BPRS is a scale measuring positive symptoms, general psychopathology and affective symptoms. It has proven particularly valuable for documenting the efficacy of treatment in patients who have moderate to severe psychopathology. The BPRS has been well validated in the clinical literature and is reportedly the most studied psychometric instrument currently in use.

The BPRS should be administered by a clinician who is knowledgeable concerning psychiatric disorders and is able to interpret the constructs used in the assessment. The individual's behavior over the previous 2-3 days should also be considered and can be reported by the patient's caregivers or teachers. It should be utilized at baseline and then at each visit as long as the patient is prescribed a psychotropic medication.

The BPRS utilized in the electronic medical record (EMR) consists of a range of 23 symptom constructs covering a broad array of potential psychopathology. The assessment typically takes 10-20 minutes or less for the interview and scoring.

Instructions for Use and Scoring:
Each item is rated on a seven-point scale (1=not present to 7=extremely severe). Zero (0) is entered if the item is not assessed. The scores of the 23 items should be summed and recorded. The total score should be compared to the total score from one evaluation to the next as a measure of response to treatment. In addition, a single subscale (symptom) or cluster of subscales (e.g., grandiosity, elevated mood, excitement, distractibility) can be followed over time.

Brief Psychiatric Rating Scale (BPRS)

Patient Name _____ Patient Number _____ Date_____

Facility _____ Practitioner _____

Enter the score for the term that best describes the patient's condition.

0 = Not assessed, 1 = Not present, 2 = Very mild, 3 = Mild, 4 = Moderate, 5 = Moderately severe, 6 = Severe, 7 = Extremely severe

Score		
____	1.	SOMATIC CONCERN - Preoccupation with physical health, fear of physical illness, hypochondriasis.
____	2.	ANXIETY - Worry, fear, over-concern for present or future, uneasiness
____	3.	EMOTIONAL WITHDRAWAL - Lack of spontaneous interaction, isolation deficiency in relating to others.
____	4.	CONCEPTUAL DISORGANIZATION - Thought processes confused, disconnected, disorganized, disrupted.
____	5.	IMPULSIVENESS
____	6.	MOTOR HYPERACTIVITY - Increase in energy level evidenced in more frequent movement and/or rapid speech. Do not rate if restlessness is due to akathisia.
____	7.	MANNERISMS AND POSTURING - Peculiar, bizarre, unnatural motor behavior (not including tic).
____	8.	GRANDIOSITY - Exaggerated self-opinion, arrogance, conviction of unusual power or abilities.
____	9.	DEPRESSIVE MOOD - Sorrow, sadness, despondency, pessimism.
____	10	HOSTILITY - Animosity, contempt, belligerence, disdain for others.
____	11.	SUSPICIOUSNESS - Mistrust, belief others harbor malicious or discriminatory intent.
____	12.	HALLUCINATORY BEHAVIOR - Perceptions without normal external stimulus correspondence.
____	13.	MOTOR RETARDATION - Slowed, weakened movements or speech, reduced body tone.
____	14.	UNCOOPERATIVENESS - Resistance, guardedness, rejection of authority.
____	15.	UNUSUAL THOUGHT CONTENT - Unusual, odd, strange, bizarre thought content.
____	16.	BLUNTED AFFECT - Reduced emotional tone, reduction in formal intensity of feelings, flatness.
____	17.	EXCITEMENT - Heightened emotional tone, agitation, increased reactivity.
____	18.	DISORIENTATION - Confusion or lack of proper association for person, place or time.
____	19.	ELEVATED MOOD - A pervasive, sustained and exaggerated feeling of well-being, cheerfulness, or euphoria implying a pathological mood. Optimism that is out of proportion to the circumstances.
____	20.	SUICIDALITY - Expressed desire, intent, or actions to harm or kill self.
____	21.	BIZARRE BEHAVIOR - Reports of behaviors which are odd, unusual, or psychotically criminal. Not limited to interview period. Include inappropriate sexual behavior and inappropriate affect.
____	22.	SELF-NEGLECT - Hygiene, appearance, or eating behavior below usual expectations, below socially acceptable standards or life threatening.
____	23.	DISTRACTIBILITY - Degree to which observed sequences of speech and actions are interrupted by stimuli unrelated to the interview. Distractibility is rated when the individual shows a change in the focus of attention as characterized by a pause in speech or a marked shift in gaze. Individual's attention may be drawn to noise in adjoining room, books on a shelf, interviewer's clothing, etc.

CHECKLIST FOR NON-ALCOHOLIC FATTY LIVER DISEASE

The protocol does not replace sound clinical judgment nor is it intended to strictly apply to all patients.
Patients with a diagnosis of non-alcoholic fatty liver disease (NAFLD) should be referred to GI Specialty Clinic.

DISEASE STATE MANAGEMENT	
ACHIEVED?	GOAL
☐ Yes ☐ No	<u>Type 2 Diabetes</u> Is diabetes at goal? • HbA1c ≤ 7% or consider less stringent goal < 8% based on patient-specific factors • Nonformulary pioglitazone may be considered for biopsy-proven NASH patients with GI consultation If not, refer to Diabetes algorithm
☐ Yes ☐ No	<u>Hyperlipidemia</u> Lipids already evaluated with the Hyperlipidemia algorithm? • Statins are safe to use in patients with NAFL or NASH without decompensated cirrhosis If not, refer to Hyperlipidemia algorithm
☐ Yes ☐ No	<u>Immunizations</u> Received hepatitis A, hepatitis B, pneumococcal, and annual influenza vaccine? • If not, administer the indicated vaccines
☐ Yes ☐ No	<u>Routine Monitoring</u> Routine monitoring completed? • Complete CMP, CBC, and non-invasive assessment scores for liver fibrosis annually • Liver ultrasound annually if abnormal baseline ultrasound and as-needed if normal baseline ultrasound with worsening non-invasive assessment scores
LIFESTYLE MODIFICATIONS	
ACHIEVED?	GOAL
☐ Yes ☐ No	<u>Weight</u> Goal weight achieved? • BMI 18.5 to 24.9 kg/m^2 • Waist circumference < 40 inches in men or < 35 inches in women • If overweight, set goal of 3-5% weight loss (7-10% in NASH patients)
☐ Yes ☐ No	<u>Physical Activity</u> Goal physical activity achieved? • Minimum of 30 minutes of moderate activity 5 days per week
☐ Yes ☐ No	<u>Diet</u> Diet modifications implemented? • Encourage reduced-calorie diet to meet weight loss goal • Limit high-fructose beverages and processed foods • Limit alcohol intake

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Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee, Approved 9/2022.

SECONDARY COMPLICATIONS	
PRESENT?	
☐ Yes ☐ No	Complications of Cirrhosis Has NAFLD progressed to compensated or decompensated cirrhosis? • Decompensated cirrhosis – esophageal varices, ascites, SBP, hepatorenal syndrome, hepatic encephalopathy, hepatocellular carcinoma • Consider specialist referral for liver cirrhosis or advanced fibrosis based on imaging or non-invasive assessment scores If present, refer to Cirrhosis algorithm and consider GI specialist referral

I. Definitions

a) Non-alcoholic fatty liver disease (NAFLD)
   i. Evidence of > 5% hepatic steatosis by imaging or histology in the absence of secondary causes of hepatic fat accumulation such as significant alcohol consumption. A broad term encompassing the spectrum of fatty liver disease, from fatty liver to cirrhosis.

b) Non-alcoholic fatty liver (NAFL)
   i. Hepatic steatosis without evidence of liver injury. Low risk of progression to cirrhosis.

c) Non-alcoholic steatohepatitis (NASH)
   i. Hepatic steatosis with liver injury and inflammation with or without fibrosis. Increased risk of progression to cirrhosis and hepatocellular carcinoma.

II. Risk Factors

a) Obesity
b) Type 2 Diabetes Mellitus
c) Hyperlipidemia
d) Insulin resistance
e) Metabolic Syndrome

III. Diagnosis

a) Obtain liver ultrasound
b) Screen for significant alcohol consumption and other causes of chronic liver disease
c) Obtain CMP, CBC, BMI, waist circumference, A1c, lipid panel, TSH, A1AT, ANA, ferritin, ceruloplasmin to evaluate risk factors and rule out other causes of liver disease
d) Consider liver biopsy for patients at high risk for advanced fibrosis and NASH based on non-invasive assessment scores

IV. Non-invasive Assessments for Liver Fibrosis

a) NAFLD Fibrosis Score
   i. Calculated based on age, BMI, presence of diabetes, ALT, AST, albumin, and platelet count
   ii. Score < -1.455 = low risk for advanced fibrosis
   iii. Score -1.445 to 0.675 = indeterminate risk
   iv. Score > 0.675 = high risk for advanced fibrosis

b) Fibrosis-4 Score
   i. Calculated based on age, AST, ALT, and platelet count
   ii. Score < 1.45 = low risk for advanced fibrosis
   iii. Score 1.45 to 3.25 = indeterminate risk
   iv. Score > 3.25 = high risk for advanced fibrosis

Formulary Substitutions for Commonly Prescribed Non-Formulary Medications

Patients should be evaluated for use of formulary agents whenever possible. Clinicians should consider history of response, contraindications, co-morbidities, medication compliance, and potential for adverse effects and/or drug-drug interactions when making treatment decisions. When medications are changed, patients should be monitored more closely for signs of worsening symptoms and adverse effects. The recommendations listed below are not intended to replace sound clinical judgment.

Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee 7/08; Revised 5/11, 11/14, 11/17, 11/18, 11/19, 11/20, 11/22, 9/23, 9/24, 1/25, 9/25. Reviewed 11/21

Name of Non-Formulary Medication	Dose Range & Frequency	Name of Formulary Medication	Dose Range & Frequency and Dosages Available	Comments/Approximate Equivalent (Non-Formulary to Formulary)
Anti-Diabetic Medications				
Aspart (Novolog®, Fiasp®)		Regular (Novolin R®) 100 units/mL vial, 10 mL		Unit to unit conversion
Glulisine (Apidra®)				
Lispro (Admelog®, Humalog®, Lyumjev®)				
Regular (Humulin R®)				
Degludec (Tresiba®)		Lantus® 100 units/mL		Unit to unit conversion. Consider 20% dose reduction when switching from Toujeo® .
Glargine (Toujeo®, Basaglar®, Semglee®)				
NPH (Humulin®)		NPH (Novolin N®) 100 units/mL vial		Unit to unit conversion
Aspart Protamine 70/ Aspart 30 (Novolog Mix 70/30®)		NPH (Novolin N®) 100 units/mL vial, 10 mL + Regular (Novolin R®) 100 units/ml vial, 10 mL		Add up the total units and give 70% to 75% as NPH or reduce dose by 20%. Administer 2/3 of dose in am and 1/3 of daily dose in pm
Lispro Protamine 75/ Lispro 25 (Humalog Mix 75/25®)				
Lispro Protamine 50/ Lispro 50 (Humalog Mix 50/50®)				Add up the total units and give 50% as NPH. Administer 2/3 of dose in am and 1/3 of daily dose in pm.
NPH 50/ Regular 50 (Humulin 50/50®)				
Glimepiride (Amaryl®)	1 - 8 mg QD	Glipizide (Glucotrol®) 5 mg, 10 mg tablets	5-40 mg daily in single or divided doses	2 mg QD to 5 mg QD
Glyburide (Diabeta®)	5 – 20 mg in single or divided doses			5 mg QD to 5 mg QD
Glyburide micronized (Glynase PresTab®)	1.5 - 12 mg in single or divided doses			3 mg to 5 mg QD

Name of Non-Formulary Medication	Dose Range & Frequency	Name of Formulary Medication	Dose Range & Frequency and Dosages Available	Comments/Approximate Equivalent (Non-Formulary to Formulary)
Anti-Glaucoma Medications				
Bimatoprost (Lumigan®) 0.03% Ophthalmic Solution	1 gtt in affected eye q PM	Latanoprost (Xalatan®) 0.005% Ophthalmic solution	1 gtt in affected eye(s) q PM	
Latanoprostene bunod (Vyzulta®) 0.24% Ophthalmic Solution	1 gtt in affected eye q PM			
Tafluprost (Zioptan®) 0.0015% Ophthalmic Solution	1 gtt in affected eye q PM			
Travoprost (Travatan®) 0.004% Ophthalmic Solution	1 gtt in affected eye q PM			
Betaxolol (Betoptic®) 0.5% Ophthalmic Solution	1-2 gtts in affected eye BID	Timolol (Timoptic®) 0.5% Ophthalmic Solution	1 gtt in affected eye BID	
Carteolol (Occupress®) 1% Ophthalmic Solution	1 gtt in affected eye BID			
Levobunolol (Betagan®) 0.25% and 0.5% Ophthalmic Solution	0.25% - 1-2 gtts in affected eye BID 0.5% - 1-2 gtts in affected eye QD			
Metipranolol (OptiPranolol®) 0.3% Ophthalmic Solution	1 gtt in affect eye BID			
Timolol (Timoptic-XE®) 0.25% and 0.5% ophthalmic Gel Forming Solution	1 gtt in affected eye QD			
Apraclonidine (Iopidine®) 1% Ophthalmic solution	1 gtt in affected eye TID	Brimonidine (Alphagan®) 0.2% ophthalmic solution 10mL	1 gtt in affected eye TID	
Brinzolamide (Azopt®) 1% Ophthalmic Suspension	1 gtt in affected eye TID	Dorzolamide (Trusopt®) 2% Ophthalmic Solution	1 gtt in affected eye TID	
Dorzolamide 2 % Ophthalmic + Timolol 0.5% Ophthalmic Solution (Cosopt®)	1 gtt in affected eye BID	Dorzolamide (Trusopt®) 2% Ophthalmic Solution + Timolol (Timoptic®) 0.5% Ophthalmic Solution	1 gtt in affected eye BID and 1 gtt in affected eye BID	
Anti-Hyperlipidemic Medications				
Fluvastatin (Lescol®)	20-80 mg QD	Pravastatin (Pravachol®) 10 mg, 20 mg, 40 mg tablets	10-80 mg QD	**Non-formulary to Pravastatin: Atorvastatin** 80 mg QD to 40 mg QD: 10 mg QD
Lovastatin (Mevacor®)	10-80 mg QD	Atorvastatin (Lipitor®) 10 mg, 20 mg, 40 mg, 80 mg tablets	10-80 mg QD	80 mg QD to 80 mg QD: 20 mg QD
Pitavastatin (Livalo®)	1-4 mg QD			2 mg QD to 40 mg QD: 10 mg QD
Rosuvastatin (Crestor®)	5-40 mg QD			5 mg QD to 80 mg QD: 20 mg QD
Simvastatin (Zocor®)	5-80 mg QD			20 mg QD to 40 mg QD: 10 mg QD
Gemfibrozil (Lopid®) 600mg	600 mg BID	Fenofibrate (Tricor®)	48-145 mg QD	600 mg BID to 48-145 mg QD

Name of Non-Formulary Medication	Dose Range & Frequency	Name of Formulary Medication	Dose Range & Frequency and Dosages Available	Comments/Approximate Equivalent (Non-Formulary to Formulary)
Anti-Hypertensive Medications				
Felodipine (Plendil®)	2.5 - 10 mg QD	Amlodipine (Norvasc®) 5 mg, 10 mg tablets	2.5 - 10 mg QD	5 mg QD to 5 mg QD
Isradipine (DynaCirc CR®)	5 - 20 mg QD			5 mg QD to 5 mg QD
Levamlodipine (Conjupri®)	2.5 – 5 mg QD			5 mg QD to 10 mg QD
Nicardipine SR (Cardene SR®)	30 - 60 mg BID			30 mg BID to 5 mg QD
Nifedipine (Procardia XL®)	30 - 120 mg QD			30 mg QD to 5 mg QD
Nisoldipine (Sular®)	10 - 40 mg QD			10 mg QD to 5 mg QD
Benazepril (Lotensin®)	10 - 40 mg QD	Lisinopril (Prinivil®) 2.5 mg, 5 mg, 10 mg, 20mg, 40 mg tablets	10 - 40 mg daily	10 mg QD to 10 mg QD
Captopril (Capoten®)	25 - 50 mg BID-TID			25 mg BID to 10 mg QD
Enalapril (Vasotec®)	2.5 - 40 mg QD			5 mg QD to 10 mg QD
Fosinopril (Monopril®)	10 - 40 mg QD			10 mg QD to 10 mg QD
Moexipril (Univasc®)	7.5 - 30 mg QD			7.5mg QD to 10 mg QD
Perindopril (Aceon®)	4 - 8 mg QD			4 mg QD to 10 mg QD
Quinipril (Accupril®)	10 - 40 mg QD			10 mg QD to 10 mg QD
Ramipril (Altace®)	2.5 - 20 mg QD			2.5 mg QD to 10 mg QD
Trandolapril (Mavik®)	1 - 8 mg QD			2 mg QD to 10 mg QD
Aliskiren (Tekturna®)	150 - 300 mg QD			150 mg QD to 10 mg QD
Azilsartan (Edarbi®)	40 - 80 mg QD	Losartan (Cozaar®) 25 mg, 50 mg, 100 mg	25 – 100 mg QD	40 mg QD to 50 mg QD
Candesartan (Atacand®)	8 - 32 mg QD			8 mg QD to 25 mg QD
Eprosartan (Teveten®)	400 - 800 mg QD			400 mg QD to 25 mg QD
Irbesartan (Avapro®)	150 - 300 mg QD			150 mg QD to 50 mg QD
Olmesartan (Benicar®)	20 - 40 mg QD			20 mg QD to 50 mg QD
Telmisartan (Micardis®)	20 - 80 mg QD			20 mg QD to 25 mg QD
Valsartan (Diovan®)	80 - 320 mg QD			80 mg QD to 50 mg QD
Acebutolol (Sectral®)	100 - 1200 mg in divided doses	Metoprolol succinate (Toprol XL®) 25 mg, 50 mg, 100 mg, and 200 mg Tablets	25 – 100 mg QD	Acebutolol 100 mg BID to Metoprolol succinate 50 mg QD: Propranolol 20 mg BID: Carvedilol 3.125 mg BID: Sotalol 80 mg BID
		Propranolol (Inderal®) 10 mg, 20 mg, 40 mg tablets	40 - 160 mg in divided doses	
Atenolol (Tenormin®)	25 – 100 mg QD	Coreg (Carvedilol®) 3.125 mg, 6.25 mg, 12.5 mg, 25 mg tablets	3.125-25 mg BID	Atenolol 25 mg QD to Metoprolol succinate 50 mg QD: Propranolol 20 mg BID: Carvedilol 3.125 mg BID: Sotalol 80 mg BID
Betaxolol (Betopic®)	5 - 20 mg QD	Sotalol (Betapace®) 80 mg, 120 mg, 160 mg tablets	80-160 mg BID	Betaxolol 5 mg QD to Metoprolol succinate 50 mg QD: Propranolol 20 mg BID:

Name of Non-Formulary Medication	Dose Range & Frequency	Name of Formulary Medication	Dose Range & Frequency and Dosages Available	Comments/Approximate Equivalent (Non-Formulary to Formulary)
				Carvedilol 3.125 mg BID: Sotalol 80 mg BID
Bisoprolol (Zebeta®)	2.5 - 10 mg QD			Bisoprolol 2.5 mg QD to Metoprolol Succinate 50 mg QD: Propranolol 20 mg BID: Carvedilol 3.125 mg BID: Sotalol 80 mg BID
Metoprolol tartrate (Lopressor®)	25 mg, 50 mg, 100 mg in divided doses			Metoprolol tartrate 25 mg BID to Metoprolol succinate 50 mg QD: Propranolol 20 mg BID: Carvedilol 3.125 mg BID: Sotalol 80 mg BID
Nadolol (Corgard®)	40 - 120 mg QD			Nadolol 40 mg QD to Metoprolol succinate 50 mg QD: Propranolol 20 mg BID: Carvediolol 3.125 mg BID: Sotalol 80 mg BID
Penbutolol (Levatol®)	10 - 40 mg QD			Penbutolol 10 mg QD to Metoprolol succinate 50 mg QD: Propranolol 20 mg BID: Carvedilol 3.125 mg BID: Sotalol 80 mg BID
Pindolol (Visken®)	5 – 20 mg divided BID			Pindolol 5 mg BID to Metoprolol succinate 50 mg QD: Propranolol 20 mg BID: Carvedilol 3.125 mg BID: Sotalol 80 mg BID
Propranolol long-acting (Inderal LA®)	60 – 180 mg QD			Propranolol LA 60 mg QD to Metoprolol succinate 50 mg QD: Propranolol 20 mg BID: Carvedilol 3.125 mg BID: Sotalol 80 mg BID
Timolol (Blocadren®)	10 - 20 mg divided BID			Timolol 10 mg BID to Metoprolol succinate 50 mg QD: Propranolol 20 mg BID: Carvedilol 3.125 mg BID: Sotalol 80 mg BID
Doxasozin (Cardura®)	1 - 16 mg Q HS	Terazosin (Hytrin®) 1 mg, 2 mg, 5 mg, 10 mg capsules	1 - 20 mg Q HS	1 mg Q HS to 1 mg Q HS
Prazosin (Minipress®)	3 - 20 mg in 2 - 3 doses/day			1 mg TID to 1 mg Q HS

Name of Non-Formulary Medication	Dose Range & Frequency	Name of Formulary Medication	Dose Range & Frequency and Dosages Available	Comments/Approximate Equivalent (Non-Formulary to Formulary)
Clonidine (Catapress®)	0.1 - 0.8 mg TID	Guanfacine (Tenex®) 1 mg, 2 mg tablets	1 - 3 mg QD	0.1 mg TID to 1 mg QD
Anticoagulant Medications				
Apixaban (Eliquis®)	2.5 – 5 mg BID	Rivaroxaban (Xarelto®) 15mg, 20mg	15 – 20 mg QD	Apixaban 5 mg BID to rivaroxaban 20 mg QD
Dabigatran (Pradaxa®)	150 mg BID			Dabigatran 150 mg BID to rivaroxaban 20 mg QD
Antiviral Medication				
Acyclovir (Zovirax®)	800 – 4000 mg in divided doses	Valacyclovir (Valtrex®) 500mg, 1000mg tablets	500 – 1000 mg BID	
Anti-Retroviral Medications				
Single-Entity Anti-Retroviral Medications				
Cobicistat (Tybost®, COBI)	150 mg QD	Ritonavir (Norvir®, RTV) 100 mg	100 mg QD	COBI 150 mg to RTV 100 mg QD
Doravirine (Pifeltro®, DOR)	100 mg QD			Please obtain non-formulary approval.
Enfuvirtide (Fuzeon®, T20)	90 mg SQ BID			Please obtain non-formulary approval. An expedited referral to Virology is recommended.
Emtricitabine (Emtriva®, FTC)	200 mg QD	Lamivudine (Epivir®, 3TC) 150 mg, 300 mg	150 mg BID or 300 mg QD	FTC 200 mg QD to 3TC 300 mg QD
Etravirine (Intelence®, ETR)	200 mg BID			Please obtain non-formulary approval.
Maraviroc (Selzentry®, MVC)	150 mg BID (concomitant CYP3A inhibitors) 600 mg BID (concomitant CYP3A inducers) 300 mg BID (other concomitant drugs)			Please obtain non-formulary approval. An expedited referral to Virology is recommended.
Nevirapine XR (Viramune®, NVP)	400 mg QD	Nevirapine (Viramune®) 200 mg	200 mg BID or 400 mg QD	Switch from extended release to immediate release.
Raltegravir (Isentress HD®, RAL)	600 mg BID	Raltegravir (Insentress ®, RAL) 400 mg	400 mg BID	Isentress HD® to RAL 400 mg BID
Tenofovir Alafenamide Fumarate (Vemlidy®, TAF)	25 mg QD	Tenofovir (Viread®, TDF) 300 mg	300 mg QD	TAF 25 mg QD to TDF 300 mg QD
Tipranavir (Aptivus®, TPV)	500 mg BID + ritonavir (Norvir®, RTV) 200 mg BID			Please obtain non-formulary approval.
Combination Anti-Retroviral Medications				

Name of Non-Formulary Medication	Dose Range & Frequency	Name of Formulary Medication	Dose Range & Frequency and Dosages Available	Comments/Approximate Equivalent (Non-Formulary to Formulary)
Efavirenz+Emtricitabine+ Tenofovir Disoproxil Fumarate (Atripla®)	600 mg + 200 mg + 300 mg QD	Efavirenz (Sustiva®, EFV) 600 mg + Emtricitabine + Tenofovir disoproxil fumarate (Truvada®, FTC/TDF)	600 mg + 200 mg/ 300 mg QD	Atripla® to EFV 600 mg + FTC 200 mg/TDF 300 mg QD
Bictegravir+Emtricitabine+ Tenofovir alafenamide (Biktarvy®)	50 mg + 200 mg + 25 mg QD			Biktarvy® is available through prior authorization. Include prior authorization criteria in special instructions: new intake on Biktarvy®.
Lamivudine+ Tenofovir Disoproxil Fumarate (Cimduo®, Temixys®)	300 mg + 300 mg QD	Lamivudine (Epivir®, 3TC) 300mg + Tenofovir (Viread®, TDF) 300mg	300 mg +300 mg QD	Cimduo® or Temixys® to 3TC 300 mg + TDF 300 mg QD
Zidovudine+Lamivudine (Combivir®)	300 mg BID + 150 mg BID	Zidovudine (Retrovir®, AZT) 300 mg + Lamivudine (Epivir®, 3TC) 150 mg	300 mg + 150 mg BID	Combivir® to AZT 300 mg + 3TC 150 mg BID
Emtricitabine+Rilpivirine+ Tenofovir (Complera®)	200 mg+25 mg +300 mg QD	Rilpivirine (Edurant®, RPV) 25 mg + Emtricitabine + Tenofovir disoproxil fumarate (Truvada®, FTC/TDF)	25 mg + 200 mg/ 300 mg QD	RPV available through prior authorization: Complera® to RPV 25 mg + FTC 200 mg/TDF 300 mg QD
Emtricitabine+tenofovir alafenamide (Descovy®)	200 mg + 25 mg QD	Emtricitabine + Tenofovir disoproxil fumarate (Truvada®, FTC/TDF)	200 mg/ 300 mg QD	Descovy® to FTC 200 mg/TDF 300 mg QD
Doravirine+Lamivudine+ Tenofovir Disoproxil Fumarate (Delstrigo®)	100 mg + 300 mg + 300 mg QD	Lamivudine (Epivir®, 3TC) 300 mg + Tenofovir (Viread®, TDF) 300 mg	100 mg + 300 mg + 300 mg QD	Please request non-formulary approval for doravirine: Delstrigo® to DOR 100 mg + 3TC 300 mg + TDF 300 mg QD
Dolutegravir + Lamivudine (Dovato®)	50 mg + 300 mg QD	Dolutegravir (Tivicay) 50 mg + Lamivudine (Epivir, 3TC) 300 mg	50 mg + 300 mg QD	Dovato® to DTG 50 mg + 3TC 300 mg
Atazanavir+Cobicistat (Evotaz®)	300 mg+ 150 mg QD	Atazanavir (Reyataz®, ATV) 300 mg + ritonavir (Norvir®, RTV) 100 mg	300 mg + 100 mg QD	Evotaz® to ATV 300 mg + RTV 100 mg
Tenofovir Alafenamide+ Elvitegravir+Cobicistat+ Emtricitabine(Genvoya®)	10 mg + 150 mg + 150 mg + 200 mg QD	Continue Genvoya® on intake patients		Genvoya® is available through prior authorization. Include prior authorization criteria in special instructions: new intake on Genvoya® or Stribild®.
Dolutegravir+Rilpivirine (Juluca ®)	50 mg +25 mg QD	Dolutegravir (Tivicay®, DTG) 50 mg + Rilpivirine (Edurant®, RPV) 25 mg	50 mg + 25 mg QD	RPV available through prior authorization: Juluca® to DTG 50 mg + RPV 25 mg
Emtricitabine+Rilpivirine+ Tenofovir Alafenamide (Odefsey®)	200mg + 25mg + 25mg QD	Rilpivirine (Edurant®, RPV) 25 mg + Emtricitabine + Tenofovir disoproxil fumarate (Truvada®, FTC/TDF)	25 mg + 200 mg/ 300 mg QD	RPV available through prior authorization: Odefsey® to RPV 25 mg + FTC 200 mg/TDF 300 mg QD

Name of Non-Formulary Medication	Dose Range & Frequency	Name of Formulary Medication	Dose Range & Frequency and Dosages Available	Comments/Approximate Equivalent (Non-Formulary to Formulary)
Darunavir+Cobicistat (Prezcobix®)	800mg + 150mg QD	Darunavir (Prezista®, DRV) 800 mg + Ritonavir (Norvir®, RTV) 100 mg	800 mg + 100 mg QD	Prezcobix® to DRV 800 mg + RTV 100 mg QD
Tenofovir+Elvitegravir+ Cobicistat+Emtricitabine (Stribild®)	300 mg + 150 mg + 150 mg + 200 mg QD	Converted to Prior Authorization Genvoya®		Stribild® converted to Genvoya® available through prior authorization for new intake patients. See Genvoya®.
Efavirenz+Lamivudine+ Tenofovir Disoproxil Fumarate (Symfi®)	600 mg + 300 mg + 300 mg QD	Efavirenz (Sustiva®, EFV) 600 mg + Emtricitabine + Tenofovir disoproxil fumarate (Truvada®, FTC/TDF)	600 mg + 200 mg/ 300 mg QD	Symfi® to EFV 600 mg + FTC 200 mg/TDF 300 mg QD
Efavirenz+Lamivudine+ Tenofovir Disoproxil Fumarate (Symfi Lo®)	400 mg + 300 mg + 300 mg QD	Efavirenz (Sustiva®, EFV) 600 mg + Lamivudine (Epivir®, 3TC) 300 mg + Tenofovir (Viread®, TDF) 300 mg	600 mg + 300 mg + 300 mg QD	Symfi Lo® to EFV 600 mg + 3TC 300 mg + TDF 300 mg QD
Darunavir+Cobicistat+ Emtricitabine+Tenofovir Alafenamide Fumarate (Symtuza®)	800 mg + 150 mg + 200 mg + 10 mg QD	Darunavir (Prezista®, DRV) 800 mg + Ritonavir (Norvir®, RTV) 100 mg + Emtricitabine + Tenofovir disoproxil fumarate (Truvada®, FTC/TDF)	800 mg + 100 mg + 200 mg/ 300 mg QD	Symtuza® to DRV 800 mg + RTV 100 mg + FTC 200 mg/TDF 300 mg QD
Abacavir+Dolutegravir+ Lamivudine (Triumeq®)	600 mg + 50 mg + 300 mg QD	Abacavir + Lamivudine (Epzicom®, ABC/3TC) + Dolutegravir (Tivicay®, DTG) 50 mg	600 mg/ 300 mg + 50 mg + 300 mg QD	Triumeq® to ABC 600 mg/ 3TC 300 mg + DTG 50 mg QD
Abacavir+Lamivudine+ Zidovudine (Trizivir®)	300 mg+ 150 mg+300 mg BID	Abacavir (Ziagen®, ABC) 300 mg + Lamivudine (Epivir®, 3TC) 150 mg + Zidovudine (Retrovir®, AZT) 300 mg	300 mg + 150 mg + 300 mg BID	Trizivir® to ABC 300 mg + 3TC 150 mg + AZT 300 mg BID
Gastrointestinal Medications				
Cimetidine (Tagamet®)	300 – 1600 mg/day in single doses or divided BID - QID	Famotidine (Pepcid®) 20 mg tablet Calcium Carbonate (Tums®) 500 mg	20 – 80 mg single or divided doses 1 tablet BID - TID	
Nizatidine (Axid AR®)	150 – 300 mg/day in single or divided doses			
Dexlansoprazole (Dexilant®)	30-60 mg QD	Omeprazole (Prilosec®) 20 mg capsule	20-40 mg single or divided doses	60 mg QD to 20 mg QD
Esomeprazole (Nexium®)	20-40 mg QD			20 mg QD to 20 mg QD
Lansoprazole (Prevacid®)	15-30 mg QD			30 mg QD to 20 mg QD
Pantoprazole (Protonix®)	20-40 mg QD			40 mg QD to 20 mg QD
Rabeprazole (Aciphex®)	20-40 mg QD			20 mg QD to 20 mg QD
Miscellaneous				
Calcium carbonate (Titralac®) 420 mg chewable tablet	1 tablet QID	Calcium carbonate (Tums®) 500 mg chewable tablet	1 tablet QID	Tritralac® contains 168 mg elemental calcium Tums contains 200 mg elemental calcium

Name of Non-Formulary Medication	Dose Range & Frequency	Name of Formulary Medication	Dose Range & Frequency and Dosages Available	Comments/Approximate Equivalent (Non-Formulary to Formulary)
Ferrous gluconate (Fergon®) 325 mg tablet	2 tablets QD	Ferrous sulfate (Feosol®) 325 mg tablet	1 tablet QD	Fergon® tablet contains 36 mg elemental iron Feosol® tablet contains 65 mg elemental iron
Docusate calcium (Surfak®) 240 mg capsule	240 mg QD	Docusate sodium (Colace®) 100 capsules	100 mg BID or 200 mg QD	
Tolterodine (Detrol®, Detrol LA®)	1 – 2 mg IR BID 2 – 4 mg ER QD	Solifenacin (Vesicare®) 5 mg, 10 mg tablets	5 – 10 mg QD	Convert to solifenacin 5 mg QD, may increase to 10 mg QD based on response
Oxybutynin (Ditropan®, Ditropan XL®)	10 – 20 mg QD in divided doses 5 – 30 mg ER QD			
Respiratory Medications				
Tiotropium (Spiriva®)	1 capsule QD	Aclidinium (Tudorza® Pressair®) 400mcg/actuation, 60 actuations	1 inhalation BID	
Ipratropium (Atrovent®) 17 mcg, 200 puffs	2 puff QID			
Atrovent / ipratropium (Combivent®)	2 puffs QID	Albuterol (Proventil HFA®) 90 mcg, 200 puffs Aclidinium (Tudorza® Pressair®) 400mcg/actuation, 60 actuations	2 puffs QID prn SOB 1 inhalation BID	
Beclomethasone (QVAR®) Redihaler	40-320 mcg BID	Ciclesonide (Alvesco®) 80 mcg, 60 metered actuations Ciclesonide (Alvesco®) 160 mcg, 60 metered actuations	1 – 2 inhalations BID	Convert based on whether the patient was dosed at low, medium, or high dose; then convert to Alvesco® dosing listed below: Low dose (inhalations) = Alvesco® 80 mcg, 1 inhalation BID; Medium dose (inhalations) = Alvesco® 160 mcg, 1 inhalation BID; High dose (inhalations) = Alvesco® 160 mcg, 2 inhalations BID. Alvesco® does not have labeled indication for COPD Qvar Redihaler® is the preferred steroid inhaler in patients on antiretroviral therapy. Non-formulary approval is required.
Budesonide (Pulmicort Turbuhaler®)	180 – 1200 mcg/day divided BID			
Flunisolide (Aerospan®)	500 – 2000 mcg/day divided BID			
Fluticasone HFA (Flovent®)	88 – 880 mcg/day divided BID			
Mometasone (Asmanex Twisthaler®)	200 – 400 mcg/day given once daily or divided BID			
Triamcinolone (Azmacort®)	300 – 1500 mcg/day divided 2 – 4 times/day			

Name of Non-Formulary Medication	Dose Range & Frequency	Name of Formulary Medication	Dose Range & Frequency and Dosages Available	Comments/Approximate Equivalent (Non-Formulary to Formulary)
Very High Potency Topical Steroids				
Betamethasone dipropionate, augmented (Diprolene®) 0.05%				
Clobetasol diprionate (Temovate®) 0.05%				
Fluocinonide (Vanos®) 0.1%				
Halobetasol propionate 0.05% (Ultravate®)				
High Potency Topical Steroids				
Amcinonide (Cyclocort®) 0.1%		Fluocinonide (Lidex®) 0.05% ointment 15 gm tube 0.05% cream 15 gm tube		
Betamethasone dipropionate (Diprolene®) 0.05%				
Betamethasone valerate (Valesone®) 0.1%				
Clobetasol priopionate (Impoyz®) 0.025%				
Desoximetasone (Topicort®) 0.25%				
Diflorasone diacetate (Florone®) 0.05%				
Fluticasone priopionate (Cutivate®) 0.005%				
Halcinonide (Halog®) 0.1%				
Halobetasol priopionate (Bryhali®) 0.01%				
Mometasone furoate (Elocon®) 0.1%				
Triamcinolone acetonide (Kenalog®) 0.5%				
Intermediate Potency Topical Steroids				
Betamethasone valerate (Beta-Val®) 0.1%		Mometasone (Elocon®) 0.1% 60mL solution Triamcinolone acetonide (Kenalog®) 0.025% ointment 15 gm tube 0.1% cream 15 gm tube 0.1% cream 80 gm tube		
Clocortolone pivalate (Cloderm®) 0.01%				
Fluocinolone acetonide (Synalar®) 0.025%				
Flurandrenolide (Cordran®) 0.05%				

Name of Non-Formulary Medication	Dose Range & Frequency	Name of Formulary Medication	Dose Range & Frequency and Dosages Available	Comments/Approximate Equivalent (Non-Formulary to Formulary)
Fluticasone propionate (Cutivate®) 0.05%				
Hydrocortisone butyrate (Locoid®) 0.1%				
Hydrocortisone probutate (Pandel®) 0.1%				
Hydrocortisone valerate (Westcort®) 0.2%				
Prednicarbate (Dermatop®) 0.1%				
Low Potency Topical Steroids				
Alcometasone dipropionate (Aclovate®) 0.05%		Hydrocortisone (Hytone®) 1% cream 30 gm tube, unit dose packets Triamcinolone acetonide (Kenalog®) 0.025% cream		
Desonide (DesOwen®) 0.05%				
Fluocinolone (Synalar®) 0.01% solution				

OPIOID DISCONTINUATION

1

- Counsel the patient on signs and symptoms of opioid withdrawal
- Evaluate patient's withdrawal symptoms with the Clinical Opiate Withdrawal Scale (COWS); refer to page 5. The COWS can be found in the EHR under Notebuilder Templates
- If the patient has been taking the opioid short-term on an as needed basis, or if they have been noncompliant, the opioid should be discontinued.
- Do not discontinue methadone or buprenorphine in a pregnant patient
- If patient on buprenorphine or methadone for medication assisted treatment (MAT) upon intake, see Buprenorphine and Methadone Discontinuation for MAT DMG for information on tapering these agents

2 Does the patient have underlying cardiac disease, i.e., CAD, heart failure, or history of arrhythmias?

Yes → 3
- Transfer patient to a 24-hour medical facility.
- Order baseline EKG and repeat as clinically indicated.
- Go to box #6.

No

4 Does the patient have acute psychiatric issues warranting crisis management or psychiatric admission?

Yes → 5
- Transfer patient to an inpatient psychiatric facility.
- Go to box #6.

No

6 Has the patient's opioid been prescribed for acute pain, or are they a new intake with unclear duration of use?

Yes → 7 Rapid Taper: Decrease the total daily opioid dose by 20-50% of the first dose, then reduce by 10-20% daily until discontinued.

No

8 Has the patient been receiving daily opioids for < 1 year?

Yes → 9 Fast Taper: Decrease the total daily opioid dose by 10-20% per week until discontinued.

No

10 Has the patient been receiving daily opioids for ≥ 1 year?

Yes → 11 Slow Taper: Decrease the total daily opioid dose by 10% per month until discontinued.

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

12 Is patient having moderately severe withdrawal symptoms (score of ≥25 on the COWS)?

Yes → 13
- Transfer patient to 24-hour medical facility, if patient is not already transferred.
- Administer clonidine 0.1 mg TID up to 0.3 mg TID for 7 days; taper over additional 3 days. Maximum total daily dose should not exceed 1 mg/day.
- Monitor vital signs before every administration of clonidine. Clonidine should be held if systolic blood pressure (SBP) < 90mmHg, diastolic blood pressure (DBP) < 60mmHg, or pulse rate (PR) < 50 bpm.
- Provide supportive care for pain, nausea, vomiting, and diarrhea as clinically indicated.
- If patient is experiencing significant withdrawal symptoms, the taper may be paused or slowed as needed.

No

14
- Monitor vital signs as clinically indicated.
- Provide supportive care for pain, nausea, vomiting, and diarrhea as clinically indicated

15 Monitor patient for severe complications, i.e., signs of dehydration and acute mental status changes. If present, transfer to higher level of care.

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.

Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee, October 2008. Reviewed 01/11. Revised 9/14, 7/20, 3/24, 7/25

I. Considerations for opioid discontinuation
   A. Risks of long-term opioid treatment may outweigh the potential benefits
      1. Adverse effects: sedation, decreased concentration and memory, drowsiness, mood changes, constipation, dry mouth, abdominal pain, nausea, and osteopenia
      2. Potential for abuse and/or misuse of medications
      3. Overdose: Risk of overdose is significantly increased in patients receiving doses ≥ 50 MME/day (morphine milligram equivalents) without necessarily adding benefits for pain control or function. Refer to Table 1 to calculate MME. MME is the amount of morphine an opioid dose is equal to and is often used as a gauge of abuse and overdose potential. Doses ≥ 90 MME/day are considered high and should be avoided without carefully justifying the clinical decision to prescribe such dose.

Table 1. Calculating morphine milligram equivalents (MME)

Opioid (mg/day)*	Conversion Factor
Fentanyl transdermal patch (mcg/hr) (Duragesic®)	2.4
Methadone (Dolophine®) 1-20 mg/day	4
Methadone (Dolophine®) 21-40 mg/day	8
Methadone (Dolophine®) 41-60 mg/day	10
Methadone (Dolophine®) ≥60-80 mg/day	12
Morphine (MS Contin®)	1
Oxycodone (Xtampza ER®)	1.5
Oxymorphone (Opana®)	3

***Note:** This table is not intended to be used to convert patients from one opioid to another. Please refer to the Chronic Cancer Pain DMG for steps to calculate equianalgesic opioid doses if needed.

   B. Tapering to a reduced dose or tapering and discontinuing long-term opioid therapy should be considered in the following situations:
      1. Resolution or healing of the painful condition (e.g., cancer remission)
      2. Inability to achieve or maintain anticipated pain relief or functional improvement despite reasonable dose escalation
      3. Intolerable adverse effects at the minimum dose that produces effective analgesia
      4. Inappropriate use of medications
      5. Deterioration in physical, emotional, or social functioning attributed to opioid therapy
      6. Concurrent use of sedating medications (e.g., benzodiazepines)
      7. Comorbid medical conditions that increase risk for adverse outcomes (e.g., lung disease, sleep apnea, hepatic impairment, renal impairment, advanced age)
   C. Tapering and discontinuation may be preferred over abrupt discontinuation in patients receiving high doses (e.g., ≥ 90 MME/day) for long periods of time (> 1 year) due to an increased risk of withdrawal effects
      1. Abrupt discontinuation may also result in increased pain, drug seeking behavior, serious psychological distress and suicidal ideation

II. Opioid withdrawal
   A. Definition - clinical syndrome produced by discontinuation of an opioid drug from an opioid-dependent patient
   B. Onset of symptoms - initial signs and symptoms may occur in a few hours or up to 48 hours after cessation or reduction in dosage of an opioid, depending upon the half-life of the drug concerned. Withdrawal of longer-acting opioids produces a withdrawal syndrome with a more delayed onset, milder severity and prolonged duration. Methadone withdrawal typically begins 36 to 48 hours after the last dose, peaks after about 3 days, and gradually subsides over a period of 3 weeks or longer depending on the dose and duration of use.

C. Symptoms
   1. Usually are self-limiting and generally non-life threatening, unless there is a concurrent serious medical condition
   2. Milder symptoms may include restlessness, mydriasis, lacrimation, rhinorrhea, sneezing, piloerection, yawning, perspiration, restless sleep and aggressive behavior
   3. More severe symptoms may include muscle spasms, back aches, abdominal cramps, hot and cold flashes, insomnia, nausea, vomiting, diarrhea, tachypnea, hypertension, hypotension, tachycardia, bradycardia and cardiac arrhythmias

D. Management
   1. Educate the patient on signs and symptoms of withdrawal
   2. Monitor the following:
      a. Vital signs as clinically indicated
      b. Signs of dehydration, acute mental changes and aggravation of underlying cardiac disease
   3. Provide supportive care if needed
      a. Pain - ibuprofen, acetaminophen
      b. Nausea and vomiting - promethazine
      c. Diarrhea - loperamide
      d. Clonidine may be used to alleviate severe symptoms
         i. Usual Dose - 0.1 mg PO TID up to 0.3 mg PO TID (0.006 mg/kg/day in divided doses, maximum 1 mg/day). Severity of withdrawal symptoms and baseline blood pressure should be considered when initiating clonidine
         ii. Continue effective dose for 7 days, then taper and discontinue over the next 3 days
         iii. Vital signs should be checked before every administration of clonidine
            - Clonidine should be held if SBP <90mmHg, DBP <60mmHg, or PR< 50 bpm

III. Opioid tapering

A. A taper is not necessary for patients who have been taking an opioid as needed on a short-term basis, or those who have been noncompliant.

B. Patients should be stratified into one of 3 tapers based on duration of opioid use (Table 3)
   1. Rapid taper: patients taking an opioid for acute pain (e.g., post-operative pain) or if they are a new intake with an unclear opioid history
      a. Decrease the total daily opioid dose by 20-50% of the first dose, then reduce by 10-20% daily until discontinued.
   2. Fast taper: patients receiving opioids daily for less than 1 year
      a. Decrease the total daily opioid dose by 10-20% per week until discontinued
   3. Slow taper: patients receiving opioids daily for $\geq$ 1 year
      a. Decrease the total daily opioid dose by 10% per month until discontinued

C. Tapering plans should be individualized based on patient response. If withdrawal effects are significant, the taper may be paused or slowed as clinically indicated.

D. The longer the duration of previous opioid therapy, the longer the taper may take.

E. Once the smallest available dose is reached, the interval between doses can be extended until the patient is receiving the smallest dose once daily.

Table 2. Opioid taper examples

Rapid Taper (over days)	**Fast Taper (over weeks)**	**Slow Taper (over months)**
Prior dose: morphine 60 mg/day Day 1: 45 mg/day Day 2: 30 mg/day Day 3: 15 mg/day then stop	Prior dose: morphine 90 mg/day Week 1: 75 mg/day Week 2: 60 mg/day Week 3: 45 mg/day Week 4: 30 mg/day Week 5: 15 mg/day then stop	Prior dose: morphine 90 mg/day Month 1: 75 mg/day Month 2: 60 mg/day Month 3: 45 mg/day Month 4: 30 mg/day Month 5: 15 mg/day then stop

Clinical Opiate Withdrawal Scale

The Clinical Opiate Withdrawal Scale (COWS) is an 11-item scale. This tool can be used in both inpatient and outpatient settings to rate common signs and symptoms of opiate withdrawal. The summed score for the complete scale can be used to help determine the stage or severity of opiate withdrawal and assess the level of physical dependence on opioids.

For each item, write in the number that best describes the patient's signs or symptoms.

Score:
- Mild = 5-12
- Moderate = 13-24
- Moderately severe = 25-36
- Severe ≥ 37

Patient Name: _____ Patient MRN #: _____
Current Vitals (BP, RR, HR):_____ Date:_____ Time:_____
Observer: _____

Signs & Symptoms	Score
Resting Pulse Rate: (record beats per minute) *Measured after patient is sitting or lying down for one minute* 0 = pulse rate 80 or below 1 = pulse rate 81–100 2 = pulse rate 101–120 4 = pulse rate greater than 120	
Sweating: over past ½ hour not accounted for by room temperature or patient activity 0 = no report of chills or flushing 1 = subjective report of chills or flushing 2 = flushed or observable moistness on face 3 = beads of sweat on brow or face 4 = sweat streaming off face	
Restlessness: observation during assessment 0 = able to sit still 1 = reports difficulty sitting still, but is able to do so 3 = frequent shifting or extraneous movement of legs/arms 5 = unable to sit still for more than a few seconds	
Pupil size 0 = pupils pinned or normal size for room light 1 = pupils possibly larger than normal for room light 2 = pupils moderately dilated 5 = pupils so dilated that only the rim of the iris is visible	
Bone or joint aches: if patient was having pain previously, only the additional component attributed to opiate withdrawal is scored 0 not present 1 mild/diffuse discomfort 2 patient reports severe diffuse aching of joints/muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	
Cont. next page	

COWS cont.

Signs & Symptoms	Score
Runny nose or tearing: not accounted for by cold symptoms or allergy 0 = none present 1 = nasal stuffiness or unusually moist eyes 2 = nose running or tearing 4 = nose constantly running or tears streaming down cheeks	
GI upset: over last ½ hour 0 = no GI symptoms 1 = stomach cramps 2 = nausea or loose stool 3 = vomiting or diarrhea 5 = multiple episodes of diarrhea or vomiting	
Tremor: observation of outstretched hands 0 = no tremor 1 = tremor can be felt, but not observed 2 = slight tremor observable 4 = gross tremor or muscle twitching	
Yawning: observation during assessment 0 = no yawning 1 = yawning once or twice during assessment 2 = yawning three or more times during assessment 4 = yawning several times/minute	
Anxiety or irritability 0 = none 1 = patient reports increasing irritability or anxiousness 2 = patient obviously irritable or anxious 4 = patient so irritable or anxious that participation in the assessment is difficult	
Gooseflesh skin 0 = skin is smooth 3 = piloerrection of skin can be felt or hairs standing up on arms 5 = prominent piloerrection	
Total Score	

*COWS adapted from National Institute on Drug Abuse. http://www.drugabuse.gov/nidamed-medical-health-professionals

Suspected Opioid Overdose

The pathways do not replace sound clinical judgement nor are they intended to strictly apply to all patients

1. Nursing Standing Delegation Orders for Administration of Naloxone for Opioid Overdose will be followed. Please refer to UTMB/CMC Nursing Services Policy Manual or Texas Tech Nursing Policy Manual, Suspected Opioid Overdose.
2. If signs of opioid overdose are suspected (Box A, Box B), 911 will be activated and the provider will be notified.
3. Naloxone (Narcan®) nasal spray - one spray (4 mg) in one nostril - will be administered to the patient.
4. If patient has not responded (e.g., presence of respirations, response to external stimuli) in 2 minutes, another dose of naloxone nasal spray will be administered in the alternate nostril. Provider will be notified of the patient's condition.
5. Naloxone administration may precipitate withdrawal symptoms (Box C). Abrupt withdrawal may result in adverse cardiovascular (CV) effects in patient with pre-existing CV disease. Please refer to Opioid Discontinuation DMG.
6. At any time, the provider will be notified for any changes in the patient's condition.

Box A.

Overdose Risk Factors

- High-dose prescription opiates
- Lung, kidney, or liver disease
- Mixing opioids with other drugs
  - Benzodiazepines
  - Gabapentin
  - Promethazine
  - Stimulants

Box B.

Opioid Overdose Signs and Symptoms

- Unresponsive or less responsive
- Depressed mental status or decreased mentation
- Pinpoint pupils
- Slow/shallow breathing (< 8 breaths per minute)
- Cold skin
- Blue nails or lips
- Choking or gurgling sounds

Box C.

Withdrawal Symptoms

- Diarrhea
- Fever
- Lacrimation
- Rhinorrhea
- Mydriasis
- Muscle Aches
- Insomnia
- Agitation
- Nausea
- Vomiting

Box D.

Naloxone Nasal Spray 4 mg

- Opioid antagonist indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression.
- It is intended for immediate administration as emergency therapy in settings where opioids may be present.
- It is not a substitute for emergency medical care.
- It will not reverse the effects of synthetic cannabinoids (K-2 or "Spice").
- Due to the duration of action of naloxone relative to the opioid, repeat doses may be necessary.
- Repeat doses may be necessary if partial agonists or mixed agonists/antagonists such as buprenorphine or pentazocine are present.
- Effectiveness of the nasal spray may be reduced in patients with nasal septal defects, mucosal damage (e.g., cocaine users), obstruction, trauma, epistaxis, or the common cold.

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider**.

Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee. Approved November 2018. Reviewed 11/22.

Chronic Cancer Pain

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

1

1. Provider should complete a thorough history and physical including a comprehensive pain assessment (pg. 2) to determine location, quality, type and intensity.
2. Provide patient with pain management education (see pg. 5).
3. Initiate Non-Pharmacological Therapy as available and indicated (pg. 2).

2 Patient in Cancer Pain Crisis?

Yes → 3 See Oncologic Emergency (pg. 5)

No

4

Mild Pain (Scale:1-3)

OPIOID NAÏVE:

First line therapy*:
- Acetaminophen 650mg up to Q 4 hours
- Ibuprofen 400-800mg up to QID
- Naproxen 250-500mg BID

Second line therapy:
- Meloxicam 7.5-15mg once daily

Failure of first- & second-line therapy:
- Consider addition and titration of adjunctive therapy according to pain syndrome (Table 2, pg. 3)

OR

CURRENTLY PRESCRIBED ANALGESIC:
- Consider continuation of current analgesic regimen and increase dose if pain is not controlled.
- Assess pain control & opioid side effects at each visit.
- If pain goals are not met, reassess and consider adjunctive therapy.

5

Moderate Pain (Scale:4-6)

OPIOID NAÏVE:

First line therapy:
APAP/codeine 300/30mg - 1 or 2 tablets BID to QID

Second line therapy:
Morphine elixir 10mg or 20 mg BID to QID

Failure of first- or second-line therapy:
- Consider addition and titration of adjunctive therapy according to pain syndrome (Table 2, pg 3).

OR

CURRENTLY PRESCRIBED OPIOID:
- Increase total daily scheduled opioid dose 25-50%. Administer as morphine ER in 2 divided doses at 12-hour intervals.
- Provide short acting rescue opioids at 10-15% of total daily scheduled dose. Give in divided doses BID-QID as needed.
- If pain goals are not met, reassess and consider adjunctive therapy.

6

Severe Pain (Scale:7-10)

OPIOID NAÏVE:

First line therapy:
Morphine IR Elixir 10mg/5ml
Morphine ER Tabs 15mg, 30mg, 60mg

Outpatient:
- For very severe pain, consider infirmary bed placement for initial titration; otherwise,
- Start morphine elixir 10mg BID-QID for the first 24-48 hours to establish pain control.
- If pain is expected to be continuous, convert to morphine ER 15-30mg every 12 hours. Give morphine elixir 10mg-20mg as needed for breakthrough pain up to QID.

Inpatient:
- Start morphine elixir at 10mg every 4 hours. Reassess pain relief 60 minutes post dose and every 4 hours. Repeat dose & titrate as needed.
- Once stable for 24 hours, calculate total daily dosage of morphine and convert to long-acting morphine ER. Give in 2 divided doses at 12-hour intervals .
- Provide short acting rescue opioids at 10-15% of total daily scheduled dose. Give in divided doses as needed.

OR

CURRENTLY PRESCRIBED OPIOID:
- Increase total daily scheduled opioid dose 50-75%. Administer as morphine ER divided Q12H.
- Give morphine elixir 10mg-20mg as needed for breakthrough pain up to QID.

7

- Outpatient: Reassess pain at least every 30 days during dose titration.
- Inpatient: Reassess pain within 1 hour of rescue administration and every 4 hours for the first 24 hours following a dose adjustment. Repeat the rescue dose after 1 hour if pain remains above 7 (See Pain Scale on pg. 2). Consider increasing rescue dose upon next administration.
- Adjust scheduled opioid dose if using more than 3 rescue doses per day. Base new dose on pain rating and total daily morphine (scheduled + rescue).
- Adjunctive therapy should be considered according to pain syndrome (Table 2, pg. 3).
- Assess pain control & opioid side effects at each visit.

8 Persistent pain despite adequate dose & titration?

Yes → 9

Step up therapy to next pain severity as needed (mild, moderate to severe).

If pain not adequately controlled despite appropriate dose increase or intolerable side effects, consider consultation with oncologist or pain specialist.

No → 10 Continue therapy and follow up within a month as needed.

Drug	Max Daily Dose
Acetaminophen (APAP)	4000mg
APAP/codeine 300/30mg	13 tablets
Ibuprofen[1]	3200mg
Meloxicam[1]	15mg
Naproxen[1]	1500mg

1. See NSAID adverse effects and cautions (pg. 3).
2. Begin prophylactic bowel regimen when starting opioids (Table 5, pg. 6)

Nurses: DMGs are to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.**

Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee, July 2010. Revised 1/13, 11/17, 5/18, 5,22.

I. History & Physical – evaluate oncologic treatment, radiation, surgery and pre-existing chronic pain

II. Pain Assessment

A. Qualify pain (C.O.L.D.E.R.)

1. **C** = character or quality of pain
   a. Somatic pain in skin, muscle, or bone that is well localized and is often described as aching, stabbing, throbbing, or pressure.
   b. Visceral pain in organs that is poorly localized and is often described as gnawing, cramping, or aching.
   c. Neuropathic pain that is often described as sharp, tingling, burning, shooting, or stabbing and /or associated with numbness.
2. **O** = onset of pain
3. **L** = location of pain including referral pattern and radiation
4. **D** = duration of pain
5. **E** = exacerbation, what factors aggravate or worsen pain
6. **R** = remission, what factors alleviate or improve pain

B. Use pain rating scale to assess intensity of pain

1. Evaluate pain currently and within last 24 hours
2. Evaluate pain at rest and with movement

Figure 1. Mosby Pain Rating Scale

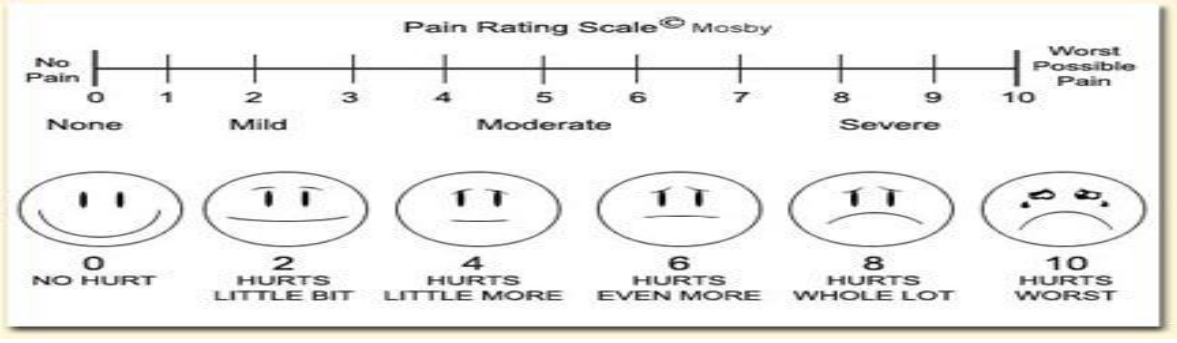


Table 1. Non-Communicative Rating Scale

Verbal/Vocal		Body Movement		Facial		Touching	
0	Positive	0	Moves easily	0	Smiling	0	No touching
2-4	Whimper/moans	5	Neutral, shifting, pacing	2-4	Neutral	5	Rubbing, patting
5-7	Repetitive comment, crying	10	Tense, not moving	5-7	Frown, grimace	10	Clenched, tight muscles
8-10	Screaming			8-10	Clenched teeth		

C. Identify associated symptoms such as nausea, vomiting or sleep disturbance

D. Identify potential etiology - cancer, cancer therapy (XRT, chemotherapy, surgery), or not cancer related

E. Determine if pain interferes with activities

F. Observe pain response during physical exam and movement during clinic visit to assess level of pain and interference with daily activities.

G. Current and past pain medication use – reason for use, length of therapy, effectiveness, side effects, and reason for discontinuation.

III. Psychosocial Assessment – psychiatric history, risk factors for aberrant use or diversion, risk factors for under-treatment of pain

IV. Management

A. Treat underlying causes

B. Non-Pharmacologic Interventions

1. Consider assistive devices for bed, bath, and walking if indicated
2. Consider physical therapy (PT) if indicated. PT techniques may be useful in teaching patients to control pain, by moving in a safe, structured way.
3. Consider thermal therapy with heat (by hot towels) or ice. Note: Appropriate measures should be used to reduce risk to skin.

C. Pharmacologic Therapy
1. Stepwise approach including simple analgesics, opioid combinations, and opioid analgesics *plus or minus* adjunctive therapy.
2. NSAIDs
   a. If two NSAIDs are tried in succession without efficacy, use another approach to analgesia
   b. If NSAIDs are effective but treatment is limited by toxicities that are not deemed serious, consider trial of another NSAID that is less renally excreted (e.g., Meloxicam).
   c. Adverse effects - Toxicity of some anti-cancer treatment may increase the risk profile of NSAIDs
      i. Renal - Discontinue NSAID if BUN or creatinine doubles or if hypertension develops or worsens
      ii. GI – If patient develops gastric upset or nausea, consider discontinuing NSAID, changing agents, or adding protective therapy such as famotidine or omeprazole. If patient develops ulcer or gastrointestinal hemorrhage, discontinue the NSAID.
      iii. Cardiac - Discontinue NSAIDs if hypertension develops or worsens
   d. Monitoring
      i. Baseline blood pressure, BUN, creatinine, CBC, fecal occult blood
      ii. Repeat as clinically indicated every 3 months
   e. Caution – NSAIDs are antipyretics and may mask fever. Use caution in patients on myelosuppressive chemotherapy. NSAIDs may have antiplatelet effects that can increase the risk of bleeding in patients who are thrombocytopenic or on myelosuppressive chemotherapy and likely to become thrombocytopenic. Consider non-NSAIDs such as acetaminophen.
3. Adjunctive therapy (Table 2)
   a. Consider addition of adjunctive therapy according to pain syndrome
   b. Titrate dose to adequate response or intolerable side effects.

Table 2: Adjunctive Therapy

Pain Descriptor	**Cancer Pain Syndrome** (Drug Class)	**Selected Drugs**	**Additional Information**
Aching, dull, localized tenderness	**Bone** **(**NSAIDS)	Ibuprofen 400-800 mg QID	-Max daily dose 3200 mg -May cause GI upset
		Meloxicam 7.5-15 mg daily	-Max daily dose 15 mg -May cause GI upset
		Naproxen 250-500 mg BID	-BID dosing -Max daily dose 1500 mg -May cause GI upset
Deep, boring, referred, poorly localized	**Visceral** **(**Corticosteroids) *Also used for spinal cord and nerve compression	Prednisone 10 – 80 mg daily	-May increase blood glucose -May cause GI upset -Increased appetite -May cause CNS symptoms -May cause osteopenia
Burning, tingling, shooting, lancinating, chronic neuralgias	**Neuropathic** **(**Duloxetine or Venlafaxine) *Refer to Neuropathic Pain DMG	Duloxetine 60 mg daily Or Venlafaxine ER 75 to 300 mg daily	-Duloxetine - Max daily dose is 60 mg daily -Venlafaxine – Max daily dose is 225 mg daily -Potential for causing dose related increases in blood pressure and heart rate. -Duloxetine has been associated with orthostatic hypotension and syncope -Use caution with Mental Health conditions and other Mental Health medications. -Potential for abuse -Dosage base on renal and hepatic function.
Colic-cramping abdominal pain, bladder spasms	**Smooth muscle spasms** **(**Anticholinergics)	Oxybutynin 5-10 mg TID	-Used for bladder spasms and retention -Max daily dose 30 mg

V. Opioid analgesics

A. General Principles

1. The appropriate dose is the dose that relieves the patient's pain throughout the dosing interval without causing unmanageable side effects.
2. For continuous pain, provide pain medication on a regular schedule with supplemental doses for breakthrough pain.
3. Consider converting from short acting opioids to extended-release opioids for control of chronic persistent pain when 24 hour opioid requirement is stable.
4. Provide rescue doses of short acting opioids for pain not relieved by sustained release opioids including breakthrough pain or acute exacerbations of pain, activity, or position related pain or pain at the end of dosing interval.
5. Rescue (breakthrough) Dosing – usually provided as 10-15% of the 24-hour total daily scheduled dose as needed.

B. Dose Titrations

1. If 3 or more rescue doses are needed in a 24-hour period, an increase in dose may be necessary.
2. Calculate dosage increase based upon total daily opioid dose around the clock including scheduled and prn doses. Example, Total 24-hour opioid requirement, morphine 15mg SR BID (30mg) + 3 x 10mg breakthrough doses = 60mg or new opioid dose of 30mg SR BID. As an alternative to calculating the total daily dose needed use the following guide:

   Pain < 4 Increase dose by 25%
   Pain 4-7 Increase dose by 25% to 50%
   Pain >7 Increase dose by 50% to 100
3. The rapidity of dose escalation should be related to the severity of the symptoms.
4. If patient is experiencing unmanageable side effects and pain is < 4, consider downward dose titration by approximately 25% and reevaluate. Monitor to ensure pain control without escalation.

C. Switching opioids

1. Switch from fixed combination opioids to single entity opioid when acetaminophen dose > 4000mg/day.
2. Conversion equation:

$$\frac{\text{Equianalgesic dose (route) current opioid}}{\text{24-hour dose (route) current opioid}} = \frac{\text{Equianalgesic dose (route) new opioid}}{\text{24-hour dose (route) new opioid}}$$

3. To convert from one opioid to another:
   a. Total the amount of current opioid(s) taken in a 24-hour period that effectively controls pain.
   b. Calculate the equianalgesic dose of the new opioid (Table 3)
   c. If patient was effectively controlled, reduce the dose by 25-50% to allow for incomplete cross tolerance between different opioids. During the first 24 hours, titrate rapidly to analgesic effect. If previous dose was ineffective, may begin with 100% of equianalgesic dose or increase that by 25%.
   d. Lastly divide the total daily dose of new opioid needed by the number of doses per day to determine the individual dose (e.g., new 24-hour morphine dose of 60mg, may be given as 10mg elixir Q 4 hrs or morphine ER 30mg Q 12 hrs).

Table 3. Equianalgesic Opioid Dose Conversions

Opioid	Oral Dose (mg)	Parenteral (IV/SC) Dose	Conversion Factor IV : PO	Duration of Action (hrs)	Comments
Morphine	30	10	3	IR: 4hrs ER: 12hrs	
Oxycodone	20	NA	NA	IR: 4hrs ER: 12hrs	
Codeine	200	130	1.5	3-4hrs	
Hydrocodone	30-200	NA	NA	3-5hrs	
Methadone	3-20	10	2	4-8hrs	• Extremely long half life and should be used with caution to avoid accumulation. • Equianalgesic dosing with methadone is dose-dependent and subject to significant inter-patient variability. It is generally not recommended for pain management and should be used cautiously to avoid overdose.
Hydromorphone	7.5	1.5	5	2-3hrs	
Tramadol	50-100	NA	NA	3-7hrs	• Weak opioid agonist. Recommended max dose is 400mg daily to avoid CNS toxicity. • Risk of over dosage or suicide for patients who are addiction-prone, taking tranquilizers or antidepressant drugs. • Requires dose adjustment in renal & hepatic impairment.

D. Fentanyl patches
1. Use restricted to hospice patients or inpatients who are NPO without G-tube placement
2. Due to risk of fatal respiratory depression, use of fentanyl is not recommended for opioid-naïve patients.
3. Patches should only be used in patients with stable opioid requirements. Due to its long half life, the dose may be difficult to titrate if pain is not well controlled
4. Use cautiously with CYP450 3A4 inhibitors, which can increase fentanyl plasma concentrations
5. For dosages exceeding 100mcg, multiple patches can be used. Usual duration of action is 72 hours, but may be reduced to 48 hours for some patients.
6. Fever and heat from external sources (lamp, hot compress) accelerates drug release and should be avoided.
7. PRN morphine may be needed particularly during the first 8-24 hours after converting to the patch
8. Dose adjustments should be based on the average amount of additional (rescue) opioid required over the 72-hour period.

Converting to Fentanyl patch
* Calculate the total 24-hour morphine dose.
* Table 3 displays the range of 24-hour oral morphine doses that are recommended for conversion to each fentanyl dose. Titrate no more frequently than every 3 days after the initial dose and every 6 days thereafter until analgesic efficacy.
* Due to patient variability, the doses suggested in table 3 are a guide. Clinical judgment must be used to titrate to the desired response.

Table 4. Fentanyl Conversion

Oral Morphine (mg/24hours)	Parenteral Morphine (mg/24 hours)	Transdermal Fentanyl Equivalent (mcg/hr)
25-65	8-22	25
65-115	23-37	50
116-150	38-52	75
151-200	53-67	100
201-225	68-82	125
226-300	83-100	150

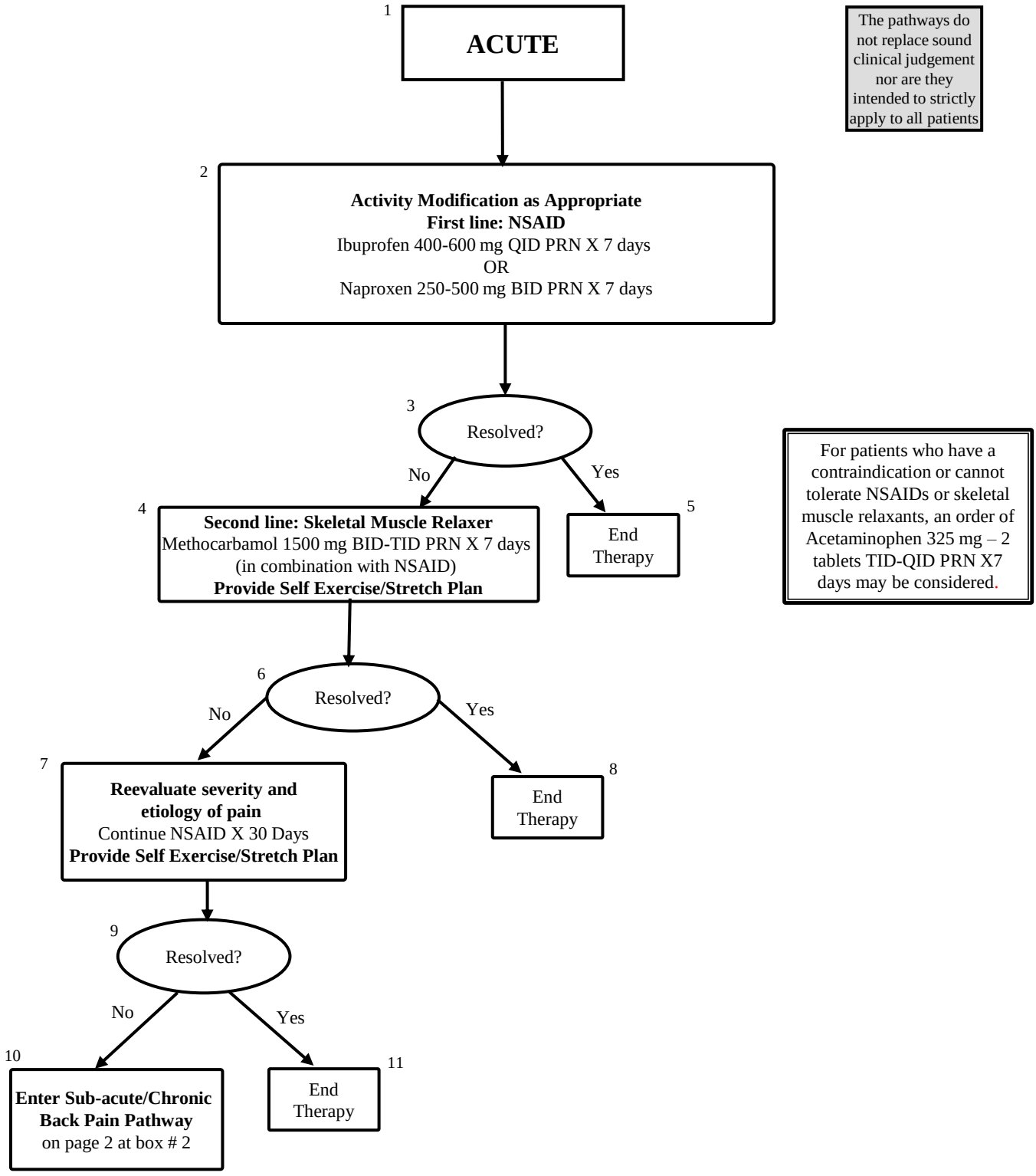
E. Patient Education
1. Relaxation and deep breathing techniques - These methods focus the patient's attention on performing a specific task, instead of concentrating on the pain.
2. Exercise - Aids in the correction of posture and may relieve symptoms in patients with nonspecific neck or lower back pain.
3. Encourage patients to report poor pain control or side effects.
4. Discuss treatment goals and expectations
5. Discuss treatment options, potential side effects, and management of adverse effects.
6. If prescribed, discuss long term use of opioid analgesics and concerns of addiction and need to increase dose if tolerance develops.

F. Referrals
1. Consider referral or consultation with pain specialist if pain is not controlled despite adequate dose, titration, and use of adjunctive therapies.
2. **Oncologic Emergency** - Severe uncontrolled pain is a medical emergency and should be evaluated & treated promptly (e.g., surgery, steroids, radiotherapy, antibiotics). Potential causes are listed below.
   a. Metastases – brain, epidural, leptomeningeal
   b. Infection
   c. Bone fracture or impending fracture of weight bearing bone
   d. Obstructed or perforated viscus
3. Consider mental health referral if patient appears to be depressed.

G. Monitoring and Assessment
1. Assess the five A's at each clinic visit.
   a. Adverse effects – minimize adverse effects
   b. Adherence to treatment & signs of aberrant drug related behavior
   c. Activity – optimize functional status, both physical and psychosocial
   d. Analgesic efficacy – optimize pain relief
   e. Affect – relationship between pain and mood
2. Use pain rating scales to assess intensity of pain (Figure 1 and Table 1)
3. Prior to changing therapy:
   a. Compare pain assessment scores for changes
   b. Ensure analgesics are given as prescribed
   c. Evaluate need for adjunctive medications
   d. Evaluate the appropriateness of dosing intervals
   e. Consider need for dose increase and upward titration to maximum daily dose as tolerated before changing drug therapy.

Table 5. Management of Opioid Side Effects	
Adverse Event	**Action**
Constipation	❑ Anticipate and treat prophylactically. Goal is 1 bowel movement every 1-2 days. ❑ Encourage increased fluids, fiber and physical activity (calcium polycarbophil / fiber tabs – 2 to 4 tabs BID) ❑ As a preventive measure a bowel regimen should be prescribed with the initial opioid prescription consisting of a stimulant laxative (bisacodyl 10-15mg HS) ❑ For acute treatment of constipation, additional agents may be provided as needed. - Milk of magnesia 15-60 ml daily or - Lactulose 15-30 ml BID or - If no bowel movement in 3 days, consider magnesium citrate or enema - Last line – consider use of prokinetic agent (metoclopramide 10-20mg QID)
Dizziness	❑ Usually resolves as body adjusts to medication. ❑ Encourage patient to contact provider if condition persists more than 1 week or is bothersome.
Nausea	❑ Take medication with food. ❑ Encourage patient to contact provider if condition persists more than 1 week or is bothersome.
Respiratory Depression	❑ Infrequent, but requires immediate medical attention. ❑ May occur from drug accumulation as a result of overaggressive titration, but can occur at any time.
Sedation	Sedation Scale: Level 3 or higher – consider intervention 4 = Somnolent, minimal or not response to physical stimulation 3 = Frequently drowsy, easily arousable, drifts off to sleep during conversation 2 = Slightly drowsy 1 = Awake and alert ❑ Sedation can be reduced or avoided with slow titration. Consider dose reduction with slower titration. ❑ Rule out other causes such as concomitant CNS depressants, CNS pathology, hypercalcemia, dehydration, sepsis, or hypoxia.
Sweating	❑ Relatively uncommon. Consider dose reduction with slower titration.
Vomiting	❑ May resolve as body adjusts to medication. Hold the next dose. Increase fluids as appropriate. Progressive alimentation. ❑ Consider short term use of meclizine, metoclopramide or prochlorperazine.
Itching	❑ Itching is often self limiting but may be dose related. Consider antihistamine. ❑ Pseudoallergies caused by endogenous histamine release from the mast cells, include flushing, itching, sneezing, hives, sweating, exacerbation of asthma, and low blood pressure. ❑ A true allergy to opioids is rare and seems to be IgE mediated or T-cell mediated. Symptoms of a true opioid allergy include hives, maculopapular rash, erythema multiforme, pustular rash, severe hypotension, bronchospasm, and angioedema.
Urinary Hesitation	❑ Go back to previously tolerated dose with gradual titration. ❑ Consider fecal impaction as a potential cause for urinary retention. ❑ If the patient has the urge to urinate but is unable to void after 6 hours, immediate medical attention is required.

PAIN, BACK



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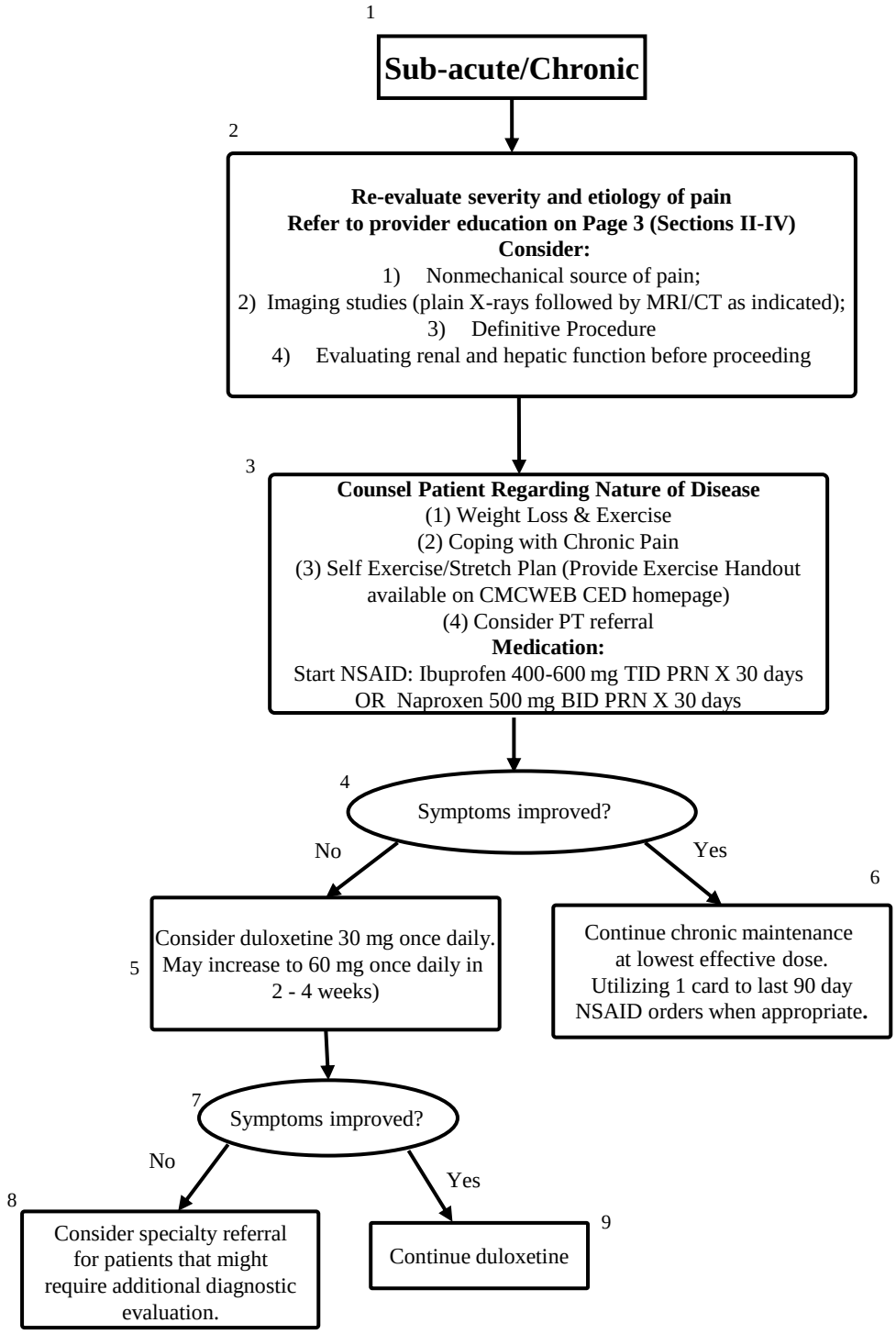
PAIN, BACK Page #2



The pathways do not replace sound clinical judgement nor are they intended to strictly apply to all patients

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I. Definitions
   A. Acute low back pain – pain lasting up to 4 weeks
   B. Subacute low back pain – pain lasting between 4 weeks and 12 weeks
   C. Chronic low back pain – pain lasting greater than 12 weeks

II. History & Physical - Observe pain response during physical exam and movement during entire clinic visit to assess level of pain and interference with daily activities.

III. Pain Assessment
   A. Qualify pain (C.O.L.D.E.R.)
      1. **C** = character or quality of pain
         a. Somatic pain in skin, muscle, or bone that is well localized and is often described as aching, stabbing, throbbing, or pressure.
         b. Visceral pain in organs that is poorly localized and is often described as gnawing, cramping, or aching.
         c. Neuropathic pain that is often described as sharp, tingling, burning, shooting, or stabbing and /or associated with numbness.
      2. **O** = onset of pain
      3. **L** = location of pain including referral pattern and radiation. Ex: dermatome /spinal nerve root distribution
      4. **D** = duration of pain
      5. **E** = exacerbation, what factors aggravate or worsen pain
      6. **R** = remission, what factors alleviate or improve pain
   B. Evaluate pain currently and within last 24 hours and evaluate pain at rest and with movement
   C. Identify potential etiology
   D. Determine if pain interferes with activities

IV. Psychosocial Assessment – psychiatric history, risk factors for aberrant use or diversion, risk factors for under-treatment of pain

V. Non-Pharmacologic Interventions
   A. Treat underlying causes
   B. Consider assistive devices for bed, bath, and walking if indicated
   C. Consider physical therapy (PT) if indicated. PT techniques may be useful in teaching patients to control pain, by moving in a safe and structured way

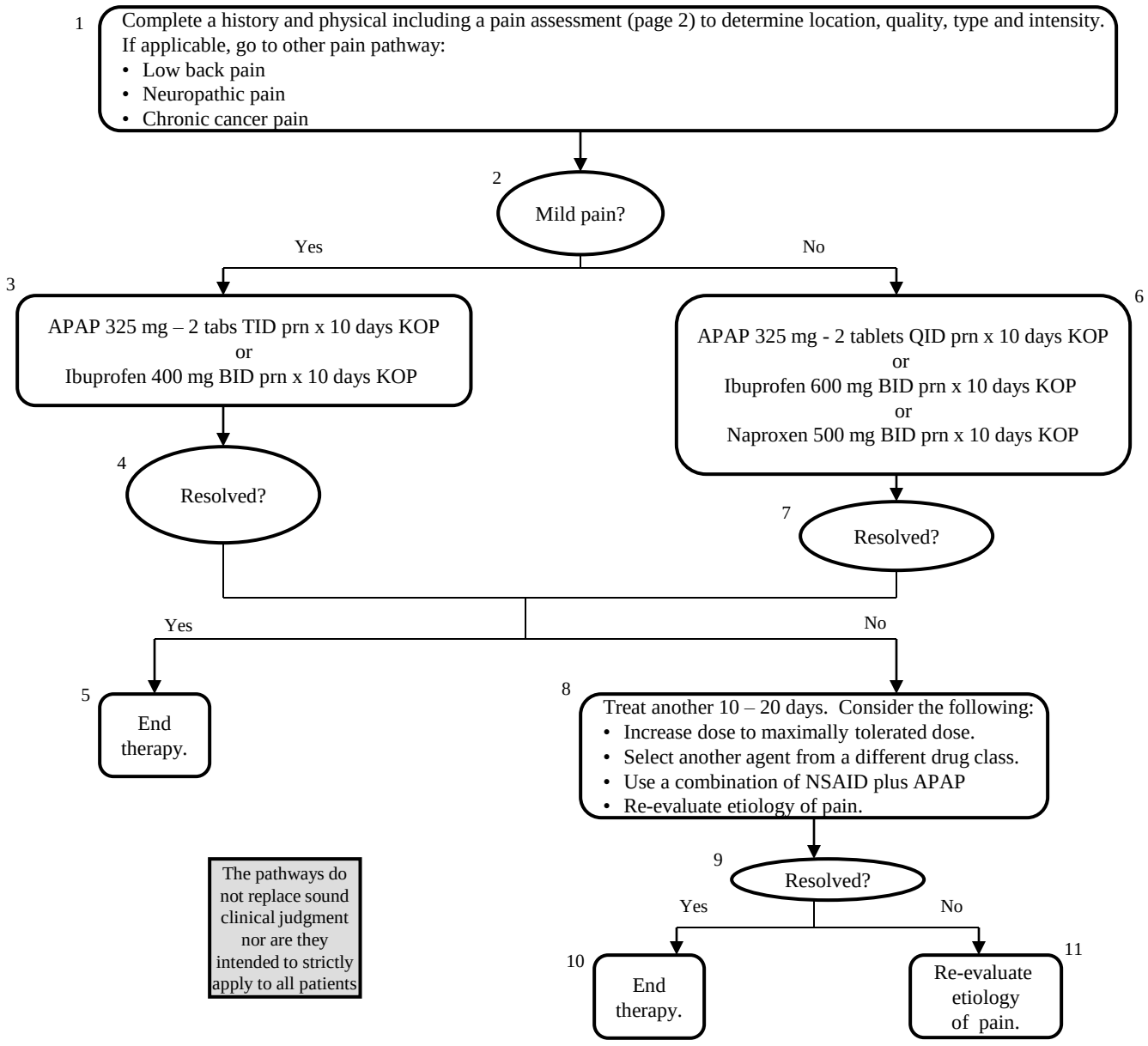
VI. Pharmacologic Therapy
   A. Stepwise approach: Use simple analgesics – If treatment is ineffective:
      1. Increase dose to maximally tolerated dose or
      2. Try another formulary NSAID or
      3. Select another agent from a different drug class
   B. First-Line Therapy: NSAIDs (e.g., naproxen, ibuprofen, meloxicam)
      1. All NSAIDs are considered equivalent. If two NSAIDS are tried in succession without efficacy, use another approach to analgesia.
      2. If NSAIDS are effective but treatment is limited by toxicities that are not deemed serious, consider trial of another NSAID (e.g., Meloxicam). Note: due to its slow onset, other NSAIDs are generally preferred.
      3. Averse effects
         a. Renal - Discontinue NSAID if BUN or creatinine doubles or if hypertension develops or worsens.
         b. GI – NSAIDs can cause an increased risk of serious gastrointestinal adverse events especially in the elderly, including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. If patient develops gastric upset or nausea, consider discontinuing NSAID, changing agents, or adding protective therapy such as famotidine or omeprazole. If patient develops ulcer or gastrointestinal hemorrhage, discontinue NSAID.
         c. Cardiac - NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may be increased in patients with cardiovascular disease or risk factors for cardiovascular disease.

4. Monitoring
    a. Baseline blood pressure, BUN, creatinine, CBC
    b. Repeat as clinically indicated every 3 months
5. Precautions
    a. Nonsteroidal anti-inflammatory drugs are associated with gastrointestinal and renal risks. Clinicians should therefore assess renovascular and gastrointestinal risk factors before prescribing NSAIDs and should recommend the lowest effective doses for the shortest periods necessary.
    b. For patients who are unable to take NSAIDs (i.e., due to allergy or other intolerance, chronic kidney disease, hypertension, peptic ulcer disease, or cardiovascular disease), a trial of acetaminophen may be considered.

C. Second-Line Agents and Adjunctive Therapy
1. Consider addition of adjunctive therapy according to pain duration
    a. Acute low back pain: Methocarbamol
    b. Subacute-chronic back pain: Duloxetine
2. Methocarbamol
    a. Methocarbamol is recommended to be used as an adjunct for patients with acute pain who do not have adequate response to nonpharmacologic therapy and NSAIDs.
    b. Methocarbamol is restricted to one 7-day supply per injury with a minimum 30-day period required between orders. It should be taken on an "as-needed" basis.
    c. Adverse effects: CNS effects and fall/injury risk; dizziness, drowsiness, confusion and sedation, increased risk of accidental injury (including falling and bone fracture) in older adults.
    d. Risk factors for increased adverse reactions include older adults (>65 years), continuous use within the prior 60 days, concurrent use of alcohol and other CNS depressants.
    e. Overdosage: deaths have been reported with an overdose of methocarbamol alone or in the presence of other CNS depressants, alcohol, or psychotropic drugs. Signs of methocarbamol toxicity include nausea, drowsiness, blurred vision, hypotension, seizures, and coma.
3. Duloxetine
    a. Duloxetine is recommended to be used as an adjunct for patients with sub-acute-chronic pain who do not have adequate response to nonpharmacologic therapy and NSAIDs.
    b. Duloxetine is started at 30 mg orally once daily, and after one week may be increased to 60 mg orally once daily (maximum dose), if tolerated.
    c. Use caution with Mental Health conditions and other Mental Health medications.
    d. Duloxetine should be taken every day, not on an "as-needed" basis. An adequate trial of duloxetine is for 12 weeks.
    e. Adverse effects: nausea, vomiting, xerostomia, drowsiness, fatigue, headache, abdominal pain.
    f. Contraindications: use of monoamine oxidase inhibitors (concurrently or within 14 days of discontinuing the MAO inhibitor), severe renal impairment (CrCl < 30 mL/min), uncontrolled narrow angle glaucoma, or hepatic impairment.
    g. Precautions: Duloxetine should not be abruptly discontinued, as withdrawal effects can occur. In order to minimize withdrawal symptoms, a gradual taper is recommended with doses higher than 30 mg and duration of use for more than 3 weeks. For patients taking the 60 mg capsule, it is recommended to decrease the dose to 30 mg daily for 1-2 weeks prior to stopping.
4. Acetaminophen
    a. Acetaminophen may be considered in patients with intolerance or a contraindication to NSAIDs or skeletal muscle relaxants.
    b. Acetaminophen should only be used on an "as-needed" basis; use with caution in patients with hepatic impairment or acute liver disease.

D. Refer to other pain pathways if needed
1. Mild to moderate pain
2. Neuropathic pain
3. Chronic cancer pain

TREATMENT OF MILD TO MODERATE PAIN



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Reviewed 3/01, 4/03, 1/07, 9/17; Revised 8/98, 12/98, 9/10, 1/13, 3/22.

I. History & Physical
A. Perform a physical exam. Identify and document pertinent positive and negative objective findings. Observe pain response during physical exam and movement during entire clinic visit to assess level of pain and interference with daily activities.

II. Pain Assessment
A. Qualify pain (C.O.L.D.E.R.)
1. **C** = character or quality of pain
a. Somatic pain in skin, muscle, or bone that is well localized and is often described as aching, stabbing, throbbing, or pressure.
b. Visceral pain in organs that is poorly localized and is often described as gnawing, cramping, or aching.
c. Neuropathic pain that is often described as sharp, tingling, burning, shooting, or stabbing and /or associated with numbness.
2. **O** = onset of pain
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4. **D** = duration of pain
5. **E** = exacerbation, what factors aggravate or worsen pain
6. **R** = remission, what factors alleviate or improve pain
B. Evaluate pain currently and within last 24 hours and evaluate pain at rest and with movement
C. Identify potential etiology
D. Determine if pain interferes with activities

III. Psychosocial Assessment – psychiatric history, risk factors for aberrant use or diversion, risk factors for under-treatment of pain

IV. Pharmacologic Therapy
A. Use simple analgesics – If treatment is ineffective:
1. Increase dose to maximally tolerated dose or
2. Select another agent from a different drug class or
3. May consider NSAID plus APAP combination
B. Refer to other pain pathways if needed
1. Low back pain
2. Neuropathic pain
3. Chronic cancer pain

Formulary Medications	**Usual Directions** †	**Max Daily Dose**	**Drug Class**
Acetaminophen (APAP) 325 mg *	1-2 tablets 2-4 times daily	4,000 mg/day	
Ibuprofen 200 mg *	1 tablet 2-4 times daily	3,200 mg/day	NSAID – propionic acid
Ibuprofen 400 mg	1 tablet 2-4 times daily	3,200 mg/day	NSAID – propionic acid
Ibuprofen 600 mg	1 tablet 2-4 times daily	3,200 mg/day	NSAID – propionic acid
Ibuprofen 800 mg	1 tablet 2-4 times daily	3,200 mg/day	NSAID – propionic acid
Naproxen 250 mg	1 tablet 2-3 times daily	1,500 mg/day	NSAID – propionic acid
Naproxen 500 mg	1 tablet 2 times daily	1,500 mg/day	NSAID – propionic acid
Meloxicam 7.5 mg	1 tablet once daily	15 mg/day	NSAID - oxicam
Meloxicam 15 mg	1 tablet once daily	15 mg/day	NSAID - oxicam

*Denotes Floor Stock Item
†Ranges should not be used in ordering medications.

NEUROPATHIC PAIN

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

1

1. Complete a detailed history and focused physical examination
2. Treat underlying cause(s) appropriately
3. Provide patient with pain management education

2

Initiate a first-line medication. Medication selection should be based on patient's comorbidities and the potential for side effects. Continue medication for 12 weeks to evaluate response.

Drug	Class	Initial Dose	Titration	Target Dose
Duloxetine	Antidepressant	60 mg daily	-	60 mg mg/day
Venlafaxine ER	Antidepressant	75 mg daily	75 mg q month	75 – 225 mg/day
Divalproex Sodium	Anticonvulsant	250 mg daily	250 mg q month	500 - 1250 mg/day
Carbamazepine*	Anticonvulsant	200 mg daily	200 mg q month	1000 – 1600 mg/day
Pyridoxine†	Other	50 mg daily	-	50- 100 mg/day

*See carbamazepine precaution on page 3

† For drug-induced neuritis (e.g., prescribe pyridoxine prophylactically with isoniazid)

3 Adequate pain relief?

No → 4 Titrate dose as outlined in box 2. Consider switching to an agent in a different class if patient does not respond to adequate trial.

Yes → 5 Continue therapy. Monitor for continued response and side effects.

4 → 6 Adequate pain relief?

Yes → 7 Continue therapy. Monitor for continued response and side effects.

No → 8

- Titrate dose as outlined in box 2.
- Consider combination therapy with an antidepressant and anticonvulsant if patient does not respond to an adequate trial of monotherapy
- Consider switching to a different combination if patient does not respond to first combination.

8 → 9 Adequate pain relief?

Yes → 10 Continue therapy. Monitor for continued response and side effects.

No → 11 Consider other therapeutic alternatives.

Nurses: DMGs are to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.**

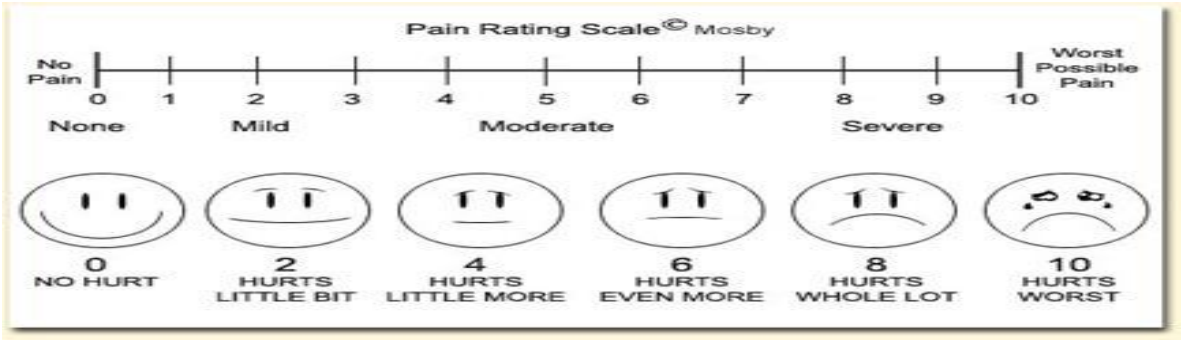
Prepared by the Correctional Managed Care Pharmacy and Therapeutics Committee. Approved January 2005; Reviewed 11/14; Revised 3/08, 5/11, 01/18, 5/18, 3/22.

Definitions:

- Pain: an unpleasant sensory and emotional experience associated with actual or potential tissue damage.
- Neuropathic pain: an injury or disease of the central and/or peripheral somatosensory nervous system. It has significant impact on quality of life and is often refractory to treatment.

I. Treatment Principles
  A. Treat underlying conditions
    1. Patients should be evaluated for underlying medical conditions that might be the cause of pain and those conditions should be managed appropriately.
    2. Common causes of neuropathic pain
      a. Disease processes
        i. Metabolic disorders: peripheral diabetic neuropathy
        ii. Viral infections: post-herpetic neuralgia, HIV, leprosy
        iii. Autoimmune disorders: multiple sclerosis, Guillain-Barre syndrome
        iv. Traumatic damage to the nervous system: spinal cord injury, amputation
      b. Iatrogenic causes
        i. Antiretrovirals: "d" drugs (e.g., zalcitabine = ddC, didanosine = ddI, stavudine = d4T)
        ii. Antibacterials: dapsone, isoniazid
        iii. Antineoplastics: vinblastine, cisplatin
      c. Nutritional deficiencies: vitamin B-12 deficiency
  B. Goals of therapy
    1. Define realistic goals and treatment expectations: to reduce, not necessarily eliminate pain
    2. Complete pain relief is unlikely to be achieved. Most therapies only result in 30-50% reduction in pain

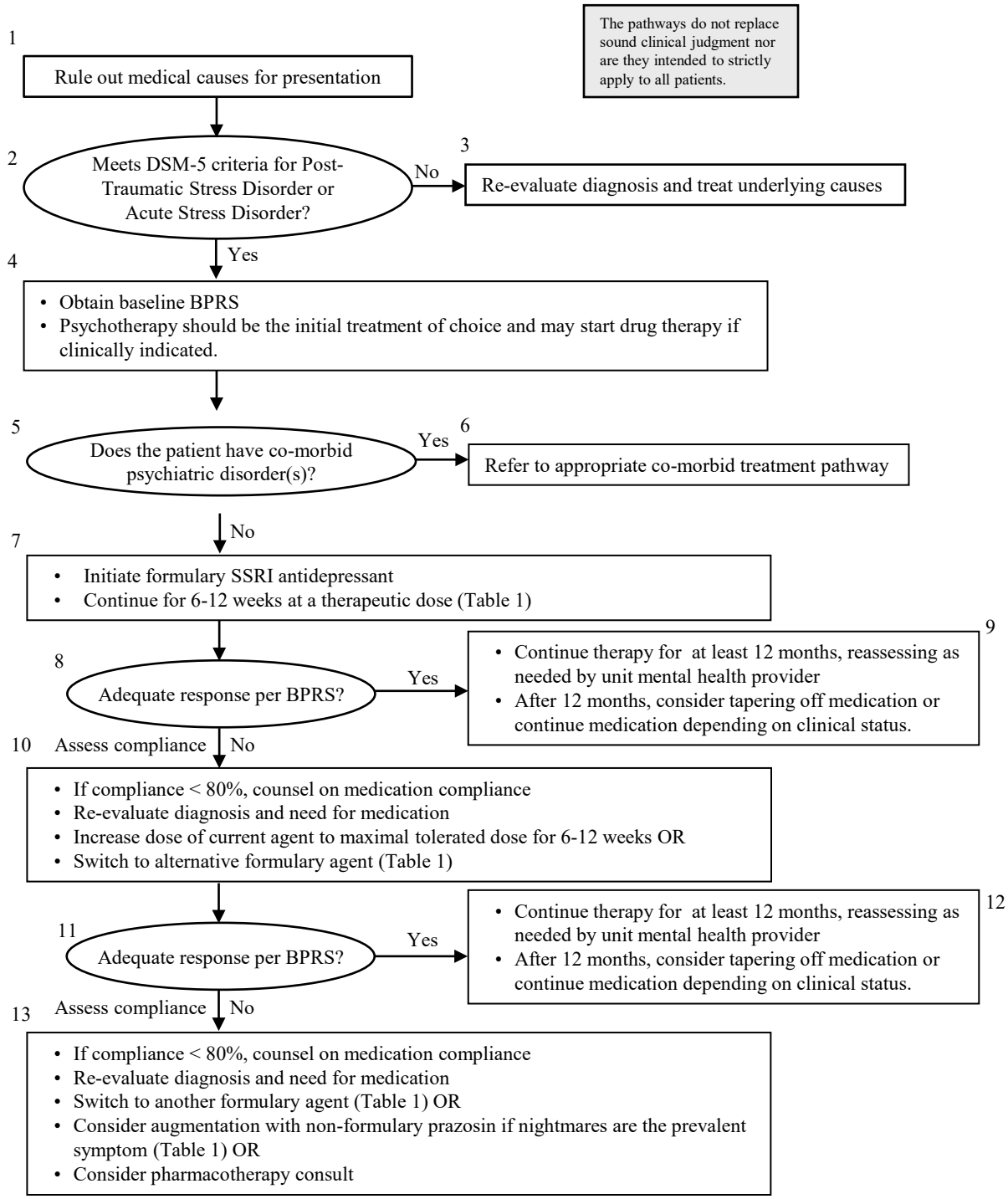
II. Patient Evaluation
  A. Assessment
    1. General history – predisposing factors
      a. Past medical history
      b. Family history
      c. Social history
    2. History of present illness (C.O.L.D.E.R.)
      a. C = character or quality of pain
      b. O = onset
      c. L = location of pain
      d. D = duration of pain
      e. E = exacerbation, what makes pain worse
      f. R = remission, what makes pain better
      g. Patient pain rating to establish baseline pain severity and assess treatment response



    3. Physical exam
      a. Vital signs
      b. Functional assessment
      c. Focused physical exam of part of body associated with pain
  B. Presentation
    1. Allodynia: pain due to a stimulus that does not normally provoke pain
    2. Hyperalgesia: an increase in the perception of pain generated by a stimulus that causes pain
    3. Paresthesia: the perception of sensations comparable to needle bites, tingling, itching, reduced or loss of sensitivity
    4. The perceived pain is usually spontaneous, manifesting itself without needing a stimulus

III. Management
  A. Treat underlying causes such as poor glycemic control in diabetics, nutritional deficiencies, and/or discontinue drug therapy, if possible, that may be causing neuropathic pain
  B. Pharmacologic therapy
    1. General treatment principles
      a. Antidepressants and anticonvulsants are the mainstays of therapy
        i. Serotonin noradrenergic reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), sodium channel blockers and gabapentinoids have demonstrated comparable efficacy
        ii. Evaluate selection of drugs based on co-morbidities (e.g., depression, anxiety, mood disorders), potential adverse effects, and intensity of pain
      b. Monotherapy is preferred
      c. If the patient is being seen by Mental Health, joint decision making should be employed to select a treatment option that may treat both the medical and mental health condition, and avoid duplicate therapy
      d. Allow adequate time between dose adjustments and reassess pain severity prior to dose increases
      e. An adequate trial is considered 12 weeks on a therapeutic dose of the medication
      f. Combination therapy may be considered for patients that do not respond to monotherapy
      g. Consider specialty referral for patients that might require additional diagnostic evaluation
    2. SNRI antidepressants: duloxetine and venlafaxine ER
      a. First-line agents for the treatment of neuropathic pain
      b. Preferred over other antidepressant treatments (TCAs) due to reduced side effect potential
      c. SNRI antidepressants should not be used concurrently with SSRI antidepressants or other SNRI medications
      d. Associated with increases in blood pressure and cardiac conduction abnormalities: use with caution in patients with cardiac disease
    3. Sodium channel blockers: carbamazepine and divalproex
      a. First-line agents for the treatment of neuropathic pain
      b. Genetic testing recommended for people with Asian ancestry and carbamazepine treatment
        i. Serious skin reactions (e.g., Stevens Johnson Syndrome) are more common in people with the HLA-B 1502 variant, a mutation found primarily in Asian patients. Reactions have been fatal.
        ii. Carbamazepine should not be prescribed for patients with Asian ancestry unless no other reasonable alternative exists. If so, patients must undergo genetic testing for the mutation before initiating the medication. Providers must obtain approval from their Regional or District Medical Director prior to ordering the test.
        iii. The risks versus benefits of carbamazepine therapy should be weighed in patients that test positive and discussed with the Regional or District Medical Director prior to initiating therapy.
        iv. Carbamazepine therapy may be continued in intake Asian patients or Asian patients already taking the medication for ≥ 3 months if they have not experienced adverse effects.
    4. Gabapentin: Reports of gabapentin drug abuse in the literature are increasing. Another disadvantage includes multiple daily dosing. For these reasons, gabapentin is a non-preferred agent in the correctional setting.

POST TRAUMATIC STRESS DISORDER and ACUTE STRESS DISORDER



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Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee,
Approved May 2002, revised 2/03, 9/05, 7/08, 5/11, 3/14, 5/18, 3/19, 5/24

Medication Selection
Patients should be evaluated for use of formulary agents when possible. Practitioners should consider history of response, contraindications, co-morbidities, medication compliance, and potential for adverse effects and/or drug-drug interactions when making treatment decisions. When medications are changed, patients should be monitored closely for worsening symptoms and adverse effects.

Table 1: PTSD Pharmacotherapy

Drug Class	Generic Name	Brand Name	Initial Dose (Dose Range) mg/day	Monitoring
Selective Serotonin Reuptake Inhibitors (SSRIs)	Citalopram 20 mg, 40 mg tablet	Celexa®	20 (20 – 40)	• Emergence of suicidal ideation or behavior • Citalopram: EKG at baseline and as clinically indicated if risk factors for QTc prolongation are present[a] • If QTc is > 450 msec for males or > 470 msec for females, do not initiate citalopram. If pt is on citalopram and QTc is > 500 msec, consider alternative treatment. • Fluoxetine has also been associated with QTc prolognation. EKG monitoring is encouraged if risk factors for QTc prolongation are present.[a]
	Fluoxetine 20 mg capsule	Prozac®	20 (20 –80)	
	*Sertraline 50 mg, 100 mg tablet	Zoloft®	50 (50 – 200)	
Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)[b]	*Venlafaxine XR 75 mg, 150 mg capsule	Effexor XR®	75 (75-225)	• Emergence of suicidal ideation or behavior • Dose-related increases in systolic blood pressure and pulse
	Duloxetine 30 mg, 60 mg capsules	Cymbalta®	30-60 (60-120)	
Other[c]	Prazosin 1 mg capsule	Minipres®	1 (1-15)	• Monitor supine, standing, and sitting BP; orthostatic hypotension • When discontinuing, taper over 1 week or more

[a] Risk factors for QTc prolongation include age > 65 years old, use of other concomitant QTc prolonging medications, baseline hypokalemia or hypomagnesemia, or pre-existing cardiovascular impairment.
[b] venlafaxine functions as an SNRI at doses ≥ 150 mg/day. At lower doses, venlafaxine functions more like an SSRI.
[c] Not a formulary agent but may be requested via non-formulary approval process if nightmares are a predominant symptom. Titrate gradually to limit risk of orthostasis.
*Sertraline and venlafaxine carries stronger evidence for its use in the management of PTSD

BRIEF PSYCHIATRIC RATING SCALE (BPRS) - Instructions for the Clinician
The Brief Psychiatric Rating Scale (BPRS) is a widely used instrument for assessing psychopathology at baseline and longitudinally as an outcome measurement when treatment is introduced. The BPRS is a scale measuring positive symptoms, general psychopathology and affective symptoms. It has proven particularly valuable for documenting the efficacy of treatment in patients who have moderate to severe psychopathology. The BPRS has been well validated in the clinical literature and is reportedly the most studied psychometric instrument currently in use.

The BPRS should be administered by a clinician who is knowledgeable concerning psychiatric disorders and is able to interpret the constructs used in the assessment. The individual's behavior over the previous 2-3 days should also be considered and can be reported by the patient's caregivers or teachers. It should be utilized at baseline and then at each visit as long as the patient is prescribed a psychotropic medication.

The BPRS utilized in the electronic medical record (EMR) consists of a range of 23 symptom constructs covering a broad array of potential psychopathology. The assessment typically takes 10-20 minutes or less for the interview and scoring.

Instructions for Use and Scoring:
Each item is rated on a seven-point scale (1=not present to 7=extremely severe). Zero (0) is entered if the item is not assessed. The scores of the 23 items should be summed and recorded. The total score should be compared to the total score from one evaluation to the next as a measure of response to treatment. In addition, a single subscale (symptom) or cluster of subscales (e.g., grandiosity, elevated mood, excitement, distractibility) can be followed over time.

Brief Psychiatric Rating Scale (BPRS)

Patient Name _____ Patient Number _____ Date_____

Facility _____ Practitioner _____

Enter the score for the term that best describes the patient's condition.

0 = Not assessed, 1 = Not present, 2 = Very mild, 3 = Mild, 4 = Moderate, 5 = Moderately severe, 6 = Severe, 7 = Extremely severe

Score		
____	1.	SOMATIC CONCERN - Preoccupation with physical health, fear of physical illness, hypochondriasis.
____	2.	ANXIETY - Worry, fear, over-concern for present or future, uneasiness
____	3.	EMOTIONAL WITHDRAWAL - Lack of spontaneous interaction, isolation deficiency in relating to others.
____	4.	CONCEPTUAL DISORGANIZATION - Thought processes confused, disconnected, disorganized, disrupted.
____	5.	IMPULSIVENESS
____	6.	MOTOR HYPERACTIVITY - Increase in energy level evidenced in more frequent movement and/or rapid speech. Do not rate if restlessness is due to akathisia.
____	7.	MANNERISMS AND POSTURING - Peculiar, bizarre, unnatural motor behavior (not including tic).
____	8.	GRANDIOSITY - Exaggerated self-opinion, arrogance, conviction of unusual power or abilities.
____	9.	DEPRESSIVE MOOD - Sorrow, sadness, despondency, pessimism.
____	10	HOSTILITY - Animosity, contempt, belligerence, disdain for others.
____	11.	SUSPICIOUSNESS - Mistrust, belief others harbor malicious or discriminatory intent.
____	12.	HALLUCINATORY BEHAVIOR - Perceptions without normal external stimulus correspondence.
____	13.	MOTOR RETARDATION - Slowed, weakened movements or speech, reduced body tone.
____	14.	UNCOOPERATIVENESS - Resistance, guardedness, rejection of authority.
____	15.	UNUSUAL THOUGHT CONTENT - Unusual, odd, strange, bizarre thought content.
____	16.	BLUNTED AFFECT - Reduced emotional tone, reduction in formal intensity of feelings, flatness.
____	17.	EXCITEMENT - Heightened emotional tone, agitation, increased reactivity.
____	18.	DISORIENTATION - Confusion or lack of proper association for person, place or time.
____	19.	ELEVATED MOOD - A pervasive, sustained and exaggerated feeling of well-being, cheerfulness, or euphoria implying a pathological mood. Optimism that is out of proportion to the circumstances.
____	20.	SUICIDALITY - Expressed desire, intent, or actions to harm or kill self.
____	21.	BIZARRE BEHAVIOR - Reports of behaviors which are odd, unusual, or psychotically criminal. Not limited to interview period. Include inappropriate sexual behavior and inappropriate affect.
____	22.	SELF-NEGLECT - Hygiene, appearance, or eating behavior below usual expectations, below socially acceptable standards or life threatening.
____	23.	DISTRACTIBILITY - Degree to which observed sequences of speech and actions are interrupted by stimuli unrelated to the interview. Distractibility is rated when the individual shows a change in the focus of attention as characterized by a pause in speech or a marked shift in gaze. Individual's attention may be drawn to noise in adjoining room, books on a shelf, interviewer's clothing, etc.

PREGNANCY WELLNESS

1

Initial evaluation: complete at the intake facility or upon discovery of pregnancy by facility provider:

1. Obtain history and physical as indicated per Health Appraisal of Incoming Inmates Correctional Managed Health Care Policy(CMHC) E-34.1 prior to OBGYN visit
2. Obtain baseline laboratories (*see Table 1 on Page 2*)*
3. Mental health intake screening
4. Update vaccines: Infection control nurse(ICN) to refer to immunization table and update if needed
5. Prescribe prenatal vitamins (Note: include prior authorization criteria in special instructions field: Pregnancy)
6. Diet: Regular diet with PM snack or Diet for Health with PM snack or other diet as clinically indicated
7. Refer to obstetrics clinic (service code PREG) and other specialists as clinically indicated
8. Refer to dental for a comprehensive treatment plan within 30 days of the diagnosis of pregnancy
9. All patients regardless of pregnancy risk category should be reassigned to Carole Young

*Some labs may be obtained by OBGYN provider

The pathways do not replace sound clinical judgment, nor are they intended to strictly apply to all patients

2

Prenatal Visits: Completed by OBGYN clinic provider or facility provider, as appropriate

1. Frequency of visits
   - A. Up to 28 weeks: every 4 weeks
   - B. 28-36 weeks: every 2 weeks
   - C. 36 weeks-delivery: weekly
2. Components of visits: vital signs, maternal weight, urine dipstick for glucose, protein, and UTI, gestational age by date/size, fundal height, fetal heart tones, fetal position, fetal movement
   - A. As indicated: refer for ultrasound (*see Table 2 on Page 3*), catheter urinalysis, fetal movement counts
3. Lab testing and screening as clinically indicated by gestational age (*see Table 1 on Page 2*)
4. Screening once each trimester for depression and anxiety using the Edinburgh Postnatal Depression Scale (EPDS)
   - A. Refer to mental health clinician if score ≥ 12

3

Post-partum Management: Completed by OBGYN clinic provider or facility provider, as appropriate

1. Patients will be seen by the OB provider at Carole Young 1 week after a vaginal delivery and 2 weeks after a C-section.
   - A. Patients can return to their unit of assignment if cleared by OB provider at this visit
2. If cesarean section with staple skin closure, remove staples 5-10 days post-surgery or as recommended by obstetrician at discharge
3. Complete postpartum exam should occur on or between 21 to 56 days after delivery(~6 weeks).
   - A. Components: weight, blood pressure, breast, abdomen, OGTT(oral glucose tolerance test) if gestational diabetes and pelvic exam (when indicated) per the Periodic Physical Examinations CMHC Policy E-34.2)
   - B. Individuals with a history of GDM (gestational diabetes mellitus) should have lifelong screening for the development of type 2 diabetes or prediabetes every 3 years.
     - Consider testing prior to 3 years for patients with the following: a family history of GDM or obese pre-pregnancy BMI
4. Screen for postpartum depression using the Edinburgh Postnatal Depression Scale (EPDS) at both the immediate postpartum visit at Carole Young and the complete postpartum exam at unit of assignment *(see EDPS scale on Page 11 and Page 12*)
   - A. Refer to mental health clinician if score ≥ 12

REFUSALS

1. All refusals must be documented on a Refusal of Treatment or Services form (HSM-82).
2. All refusals for obstetrical care should be communicated to the unit provider and/or obstetrical provider. If a patient is refusing to attend an obstetrical appointment, prenatal care should still be offered at the unit of assignment by the unit provider.

Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee May 2020. Revised 5/2025, 9/2025.

Table 1: Lab Tests and Screening
Initial Visit
ABO and RH type Prenatal Antibody screen Chemistry profile, including LFTs (Liver Function Tests) CBC with differential Syphilis Screening(IGG/IGM) Urine culture HIV testing Hepatitis serology (HbsAg, Anti-HBs, anti-HBc total antibody, anti-HCV and anti-HAV total antibody) Chlamydia Gonorrhea Pap smear (as indicated per CMHC Policy E-34.2) PPD skin test Rubella IgG Varicella titer (if not known) Fasting blood sugar Thyroid studies (as clinically indicated) Drug panel 5 Sickle cell screen (Black, Asian or Mediterranean if status unknown)
≥ 9 Weeks
Non-invasive prenatal testing (NIPT)
<14 weeks
Ultrasonography (if needed)
18-22 Weeks – ideally, but may be performed at any gestational age
Basic or Detailed anatomy ultrasound (see Table 2)
24-28 Weeks
CBC Glucose Challenge Test (1 hr glucose tolerance) D (Rh) Antibody Screen (when indicated) Anti-D immune globulin (RHIG) given (28 wks or greater) (when indicated)
28-32 Weeks
HIV Syphilis Screening(IGG/IGM)
32 Weeks
Non-Stress Testing (twice weekly) Examples of conditions in which non-stress testing is recommended: • History of fetal demise • Advanced maternal age • Multiple pregnancies • Amniotic fluid issues • Preeclampsia
32-36 Weeks
Ultrasonography (if indicated) Chlamydia, gonorrhea (if indicated) Mental Health Screening (if indicated)
35-37 Weeks
CBC Group B Strep If group B strep positive, resistance testing if penicillin allergic

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Table 2: Ultrasounds

1. Limited
   A. 1st trimester for dating
   B. 2nd or 3rd trimester if needed for checking amniotic fluid index, placenta location, viability or position
2. Basic Anatomy survey
   A. Ideally performed between 18-22 weeks
   B. Patients with low risk of having baby with a birth defect
3. Detailed Anatomy survey
   A. Ideally performed between 18-22 weeks
   B. Patients with higher risk of having baby with a birth defect
   C. Examples of conditions in which this study is recommended:
      i. Advanced Maternal Age (age 35 or older)
      ii. Abnormal aneuploidy screening test (quad screen, first trimester screen)
      iii. Previous child with chromosomal abnormality or birth defect
      iv. Medication exposure or illicit drug exposure
      v. Thyroid disorder
      vi. Family history of hereditary disorder
      vii. Pre-gestational diabetes

I. Definitions

A. Gestation: time period between conception and birth
   1. Gestational age: measured in weeks, from the first day of last menstrual cycle to present day. Normal pregnancy ranges from 37 weeks to 42 weeks.
B. Prenatal/Antenatal: before child-birth
   1. Prenatal care: refers to care provided during pregnancy to both mother and baby
C. Ante-partum: time period before child-birth
D. Postpartum: time period after child-birth
   1. Post-partum care: care provided to mother after child—birth
E. Postnatal care: care provided to child after birth

II. Classification

A. Unit of Assignment
   1. All pregnant patients regardless of risk category or gestational age should be assigned to Carole Young upon intake.
B. Housing Assignment
   1. Bottom bunk
   2. Ground floor
C. Work Restrictions
   1. Limited standing, no walking over 100 yards, no lifting over 15 lbs, no bending at waist, no repetitive squatting, no climbing
   2. Sedentary work only or medically unassigned if clinically indicated
D. Transportation
   1. Pregnant offenders who are less than 36 weeks gestation and without acute medical issues, may travel by regular offender transportation. All other pregnant offenders will be transferred by alternate transportation.

Table 3: Formulary Drugs to Avoid During Pregnancy**
Atorvastatin
Divalproex
Efavirenz
Estrogens
Ethynediol Diacetate/Ethinyl Estradiol
Fluconazole- **avoid prior to 14 weeks of pregnancy**
Hydroxyzine – **avoid in 1st trimester**
Lisinopril
Losartan
Medroxyprogesterone
Metronidazole - **avoid prior to 14 weeks of pregnancy**
Norethindrone/Estinyl Estradiol
Norgestrel/Estradiol
Pravastatin
Ribavirin
Ulipristal
Warfarin
NSAIDs (Ibuprofen, meloxicam, naproxen) – **avoid in 3rd trimester**

Table 4: Formulary Drugs to *Consider* Avoiding During Pregnancy (assess risk versus benefit)**
Amiodarone
Aspirin (NSAIDs)
Azathioprine
Carbamazepine
Carvedilol – **avoid in 2nd and 3rd trimester**
Phenytoin
Lithium
Primidone
Mycophenolate
Prednisone
Sulfasalazine
Minocycline
Topiramate

****This list is not all inclusive. If uncertain, please check a drug reference or contact Pharmacy prior to prescribing.**

Table 5: ANTEPARTUM MANAGEMENT OF COMMON CONDITIONS		
Condition	**Recommendation**	
Alcohol use/abuse	Counsel all women to avoid alcohol use during pregnancy	
Anemia	Hgb ≤ 11 g/dL in the first and third trimester, or lower than 10.5 g/dL in the second trimester	
	Consult specialist when hgb ≤ 8g/dL and there is proven compliance with iron supplementation and no improvement in anemia	
	Prevention: prenatal vitamins	
	Treatment	Nutritional assessment
		Ferrous sulfate (Feosol®) 325 mg tablet BID or TID
		Vitamin C (ascorbic acid) 500 mg tablet PO TID (Note: nonformulary approval required) with iron supplementation
		If no improvement in 4 weeks and patient is compliant, refer to specialist
Antepartum Fetal Surveillance	The primary indication for antepartum testing is a pregnancy at increased risk for fetal demise. Some conditions in which testing may be helpful include: - **Maternal conditions**: antiphospholipid syndrome, thyroid abnormalities, hemoglobinopathies, congenital heart disease, lupus, chronic kidney disease, diabetes, hypertension - **Pregnancy-related conditions**: Previous fetal demise (unexplained or recurrent risk), placental abnormalities, pregnancy induced hypertension (PIH), decreased fetal movement, oligohydramnios, fetal growth restriction, post term pregnancy (41 weeks and beyond), isoimmunization (at risk for fetal anemia), multiple gestation (with significant growth discrepancy)	
Bacterial Vaginosis	Treatment	Metronidazole (Flagyl®) 500 mg tablet PO BID x 7 days or 250 mg tablet PO TID x 7 days (**Please note: Oral metronidazole should not be prescribed prior to 14 weeks gestation**)
		Clindamycin (Cleocin®) 150 mg capsule – 2 capsules (300 mg) PO BID x 7 days
Breast Mass or Bloody Nipple Discharge	Document personal and family history Document size, location, mobility, tenderness, etc. Teach self-breast exam Re-evaluation must occur within 4 weeks. If not resolved, refer for breast imaging. Refer for breast imaging as appropriate Repeat referral for any changes in size, shape or consistency	
Candida Vaginitis	Counseling on personal hygiene, clothing, etc.	
	Treatment	Miconazole (Monistat-7®) 100 mg vaginal suppository QD x 7 days
		Fluconazole (Diflucan®) 150 mg tablet x 1 dose **(Oral fluconazole should not be prescribed prior to 14 weeks gestation. Note: prior authorization criteria must be typed in special instructions field: vaginal candidiasis)**
	Recurrent (>3 during pregnancy) consider HIV, diabetes rescreening, and consult specialist	
Cardiac Abnormality	Refer to cardiology	

Table 5 (continued)		
Condition	Recommendation	
Chlamydia	Evaluate patient for risk of concomitant coexisting sexually transmitted disease-culture, counsel, and/or test for as indicated	
	Pregnant women diagnosed with chlamydial infection during the first trimester should receive a test to document chlamydial eradication and be retested 3 months after treatment	
	Repeat testing to document chlamydial eradication 3 weeks after completion of therapy. Women aged <25 years and those at increased risk for chlamydia (i.e., women who have a new or more than 1 sex partner) also should be retested during the third trimester to prevent maternal postnatal complications and chlamydial infection in the infant.	
	Report to the Office of Public Health (OPH) or Health Department per Infection Control Policy B-14.19	
	Treatment	Azithromycin (Zithromax®) 600 mg tablet – 2 tablets (1200 mg) PO x 1 (Preferred treatment. Note: include prior authorization criteria in special instructions field: Pregnancy)
		Amoxicillin (Amoxil®) 500 mg capsule PO TID x 7 days
Cystic Fibrosis	Refer to specialist	
Diabetes	Treatment	Lifestyle modifications
		Insulin is 1st line for management of type I and type 2 diabetes in pregnancy
		Metformin and glyburide should not be used as 1st line in type 2 diabetes because oral agents cross the placenta and lack long-term safety data
	Diagnosis	Goal A1c is 6%. If patient cannot tolerate, may increase A1c goal to 7%. For screening/diagnosis using OGTT (*See Table 6 on Page 10*)
Drug Abuse	• Refer to specialist for appropriate antenatal surveillance recommendations • Continue methadone during pregnancy (see Opioid Discontinuation DMG)	
Edema	Generalized edema: evaluate for preeclampsia Unilateral edema: consider deep vein thrombosis (DVT) Dependent edema: resolution of edema with rest and elevation of dependent part overnight. Dependent edema may be treated by: • Resting on left or right side • Diet counseling: increased protein, increased fluids, and avoidance of excessive sodium • Elevation of dependent part when possible • Removal of restrictive clothing • TED hose • Shower shoe pass	
Fetal Arrhythmias	Refer to specialist	
Genetic Counseling	Refer to telehealth genetics counseling	
Gonorrhea	Treatment	Ceftriaxone 500 mg IM x 1 dose; add treatment for chlamydia if infection has not been excluded. Refer to specialist if cephalosporin allergy.
		Rectal and pharyngeal cultures as indicated
	Retest for gonorrhea in 3 months – not a test for cure but for re-infection. If patient continues high risk behaviors, rescreen at 36 weeks.	
	Counsel patient regarding safe sex	
	Report to the OPH or Health Department per Infection Control Policy B-14.19	

Table 5 (continued)		
Condition	Recommendation	
Group B Beta Hemolytic Streptococcus (GBBS)	Routine testing at 35-37 weeks for asymptomatic GBBS bacteriuria	
	Positive urine GBBS (**Any positive GBBS during pregnancy – consider as GBBS positive for duration of current pregnancy**)	
	Treatment	Amoxicillin (Amoxil®) 500 mg capsule PO TID x 3-7 days
		If penicillin allergy and low risk for anaphylaxis: Cephalexin (Keflex®) 500 mg capsule PO BID x 5-7 days
		Penicillin allergy with severe IgE-mediated hypersensitivity to penicillin and cephalosporin: Clindamycin (Cleocin®) 150 mg capsule – 2 capsules (300 mg) Q6H
		If resistant to clindamycin, desensitization to penicillin may be warranted
Hepatitis/Herpes/HIV	Refer to specialist	
Chronic Hypertension (cHTN)	Refer to specialist if uncontrolled Pass for blood pressure checks Monday, Wednesday, and Friday	
Immunizations	The American College of Obstetricians and Gynecologists recommends the use of a single dose of the RSV vaccine (Abrysvo) for those who are currently pregnant if they are between 32 and 36 weeks of gestation (using seasonal administration), who do not have a planned delivery within two weeks, and who did not receive the maternal RSV vaccine during a previous pregnancy. Nonformulary approval is required for Abrysvo. Refer to Infection Control Policy B-14.07 for additional immunizations	
Multiple Gestation	Refer to specialist	
Nausea and Vomiting	Check ketones, if trace to +1→ encourage oral fluids and small, frequent, low fat, high protein meals	
	If ketones are large and patient cannot retain PO fluids→ Consider IV D5LR at 500 mL per hour, then decrease to 250 mL/hr. When patient can void, recheck ketones. When ketones have decreased to 1+ may discontinue IV. (may give a max of 2L of IV fluids)	
	Treatment: Promethazine 25 mg tablets PO or suppository TID PRN	
	If does not resolve by 14 weeks gestation, consult specialist	
Pre-eclampsia/eclampsia	Refer to specialist	
Preterm Labor /Prevention of Preterm Birth	Refer to specialist	
Psychiatric disorder, current or recent mental health treatment	Refer to Mental Health department	
Recurrent Pregnancy Loss	3 or more pregnancy losses – regardless of gestational age→ refer to specialist	
Rh Negative	Rh determination and antibody→ refer to specialist for screening	
	Refer to specialist regarding administration of Rho(D) immune globulin(generally administered at 26 to 30 weeks' gestation) if antibody screen is negative initially (Note: Non-formulary approval is required. Floor stock is allowed at Carole Young.)	

Table 5 (continued)	
Condition	Recommendation
Syphilis Positive	Refer to specialist
Thalassemia, Thrombocytopenia, Thrombocytosis, Thyroid abnormalities, Toxoplasmosis	Refer to specialist
Trichomoniasis	Treat if identified on pap smear or do wet mount for confirmation
	Treatment: Metronidazole (Flagyl®) 500 mg tablet – 4 tablets (2000 mg) PO x 1 dose or 500 mg PO BID x 7 days (**Please note: Oral metronidazole should not be prescribed prior to 14 weeks gestation**)
Tuberculosis	Refer to specialist
Urinary Tract Infections (UTIs)	Order culture and susceptibility (C&S) • Initially on all patients • Every trimester for patients with Hgb SS, SC, S Thalassemia • For patients with symptoms of UTI

	Asymptomatic bacteriuria: clean catch – isolation of bacteria in concentration >100,000 CFU/ml
	• Treat according to C&S, or with:
	  • Nitrofurantoin (Macrobid®) 100 mg capsule PO BID x 5-10 days (<37 weeks gestation)
	  • Amoxicillin (Amoxil®) 500 mg capsule PO TID X 5-10 days

	Symptomatic UTI
	• Supportive measure: fluids, rest, good hygiene
	• Treat according to C&S, or with:
	  • Nitrofurantoin (Macrobid®) 100 mg capsule PO BID x 7-10 days (<37 weeks gestation)
	  • Cephalexin (Keflex®) 250-500 mg capsule PO QID x 10 days
	  • SMZ/TMP (Bactrim DS®) 1 tablet PO BID X 5 days (before 32 weeks gestation)

Vaginal Bleeding	**First trimester:**
	• Obtain a thorough history including last menstrual period (LMP) and past bleeding episodes
	• Assess for cervicitis, vaginitis, and hemorrhoids; treat as appropriate
	• If unstable, refer to closest ER as appropriate
	• Rhogam if RH negative as appropriate
	• Patients seen in local ER and diagnosed as complete spontaneous abortion need a urine pregnancy test (UPT) in 4 weeks
	  • If negative→ no further follow-up is indicated
	  • If positive→ draw serum beta hCG and refer to specialist without waiting for result

	Second/Third trimester: • Rule out hemorrhoids, cervicitis and vaginitis • Rhogam for Rh negative when appropriate • If no apparent treatable cause, consult specialist • If not significant amount of bleeding refer for ultrasound if appropriate. Patients with significant bleeding which is suspected to be uterine should be sent out 911

Table 6: Diabetes Screening During Pregnancy

History of diabetes prior to pregnancy: consult with specialist
- Genetic counseling for patients with abnormal A1c in the first trimester
- Interval growth ultrasound every 4 weeks and estimated fetal weight (EFW) sonogram at 37-38 weeks

Gestational Diabetes (GDM)
- Test for undiagnosed diabetes at the first prenatal visit in those with risk factors:
    - Family history of diabetes, first degree relative (parent, sibling, or child)
    - Previous history of gestational diabetes
    - Previous unexplained stillbirth history of polyhydramnios
    - History of infant born with fetal abnormalities
    - Overweight/Obese: pre-pregnant body mass index > 25
    - Previous infant > 4 kg
    - Maternal age > 25 years
    - Recurrent glycosuria (2 occasions of 1+ or greater)
    - >28-week gestation at first visit
- A normal screen prior to 24 weeks should be repeated when the high-risk patient is 24-28 weeks gestation
- All patients, except those with known diabetes, should be screened for diabetes at 24-28 weeks
- **Screening method:**
    - **One-step strategy:** Perform a 75g OGTT (oral glucose tolerance test), with plasma glucose measurement when patient is fasting and at 1 and 2 h
        - The OGTT should be performed in the morning after an overnight fast of at least 8 h.
        - The diagnosis of GDM is made when any of the following plasma glucose values are met or exceeded:
            - Fasting: 92 mg/dL
            - 1 h: 180 mg/dL
            - 2 h: 153 mg/dL
    - **Two-step strategy**
        - Step 1: Perform a 50g OGTT (non-fasting), with plasma glucose measurement at 1 h
            - If the plasma glucose level measured 1 h after the load is ≥135 mg/dL, proceed to a 100g OGTT.
        - Step 2: The 100g OGTT should be performed when the patient is fasting.
            - The diagnosis of GDM is made if at least two (or one elevated value per ACOG guidelines) of the following four plasma glucose levels (measured fasting and 1 h, 2 h, 3 h during OGTT) are met or exceeded: **see Table 7**
- If patient cannot tolerate OGTT, draw A1c. If A1c is > 6.5%, start diabetic diet, blood glucose diary, and consult specialist.

Postpartum: Test women with gestational diabetes for prediabetes or diabetes at 4-12 weeks post-partum
- If poorly controlled, do fasting finger stick before receiving Glucola. If glucose level is >120 mg/dL do not give Glucola
- One-step strategy and non-pregnancy diagnostic criteria (see Diabetes DMG)

Table 7: Criteria for Diagnosis of GDM using Two-step Criteria

	Carpenter-Coustan	NDDG (National Diabetes Data Group)
Fasting	≥95 mg/dL	≥105 mg/dL
1h	≥180 mg/dL	≥190 mg/dL
2h	≥155 mg/dL	≥165 mg/dL
3h	≥140 mg/dL	≥145 mg/dL

EDINBURGH POSTNATAL DEPRESSION SCALE (EPDS)

The EPDS was developed for screening postpartum women in outpatient, home visiting settings, or at the 6 –8 week postpartum examination. The EPDS consists of 10 questions and can usually be completed in less than 5 minutes. Responses are scored 0, 1, 2, or 3 according to increased severity of the symptom. Items marked with an asterisk (*) are reverse scored (i.e., 3, 2, 1, and 0). The total score is determined by adding together the scores for each of the 10 items. The EPDS is only a screening tool. It does not diagnose depression – that is done by appropriately licensed healthcare personnel

Instructions for Users

1. The mother is asked to underline 1 of 4 possible responses that comes the closest to how she has been feeling the previous 7 days
2. All 10 items must be completed
3. Care should be taken to avoid the possibility of the mother discussing her answers with others
4. The mother should complete the scale herself, unless she has limited English or has difficulty with reading

Name:
Date:
UOA:
Baby's Age:

As you have recently had a baby, we would like to know how you are feeling. Please CIRCLE the answer which comes closest to how you have felt IN THE PAST 7 DAYS, not just how you feel today.

1. I have been able to laugh and see the funny side of things:
As much as I always could ____ (0)
Not quite so much now ____ (1)
Definitely not so much now ____ (2)
Not at all ____ (3)

2. I have looked forward with enjoyment to things:
As much as I ever did ____ (0)
Rather less than I used to ____ (1)
Definitely less than I used to ____ (2)
Hardly at all ____ (3)

3. I have blamed myself unnecessarily when things went wrong:*
Yes, most of the time ____ (3)
Yes, some of the time ____ (2)
Not very often ____ (1)
No, never ____ (0)

4. I have been anxious or worried for no good reason:
No, not at all ____ (0)
Hardly ever ____ (1)
Yes, sometimes ____ (2)
Yes, very often ____ (3)

5. I have felt scared or panicky for no good reason:*
Yes, quite a lot ____ (3)
Yes, sometimes ____ (2)
No, not much ____ (1)
No, not at all ____ (0)

6. Things have been getting to me:*
Yes, most of the time I haven't been able to cope at all __ (3)
Yes, sometimes I haven't been coping as well as usual __ (2)
No, most of the time I have coped quite well ___(1)
No, I have been coping as well as ever ___(0)

7. I have been so unhappy that I have had difficulty sleeping:*
Yes, most of the time ____ (3)
Yes, sometimes ____ (2)
No, not very often ____ (1)
No, not at all ____ (0)

8. I have felt sad or miserable:*
Yes, most of the time ____ (3)
Yes, quite often ____ (2)
Not very often ____ (1)
No, not at all ____ (0)

9. I have been so unhappy that I have been crying:*
Yes, most of the time ____ (3)
Yes, quite often ____ (2)
Only occasionally ____ (1)
No, never ____ (0)

10. The thought of harming myself has occurred to me:*
Yes, quite often ____ (3)
Sometimes ____ (2)
Hardly ever ____ (1)
Never ____ (0)

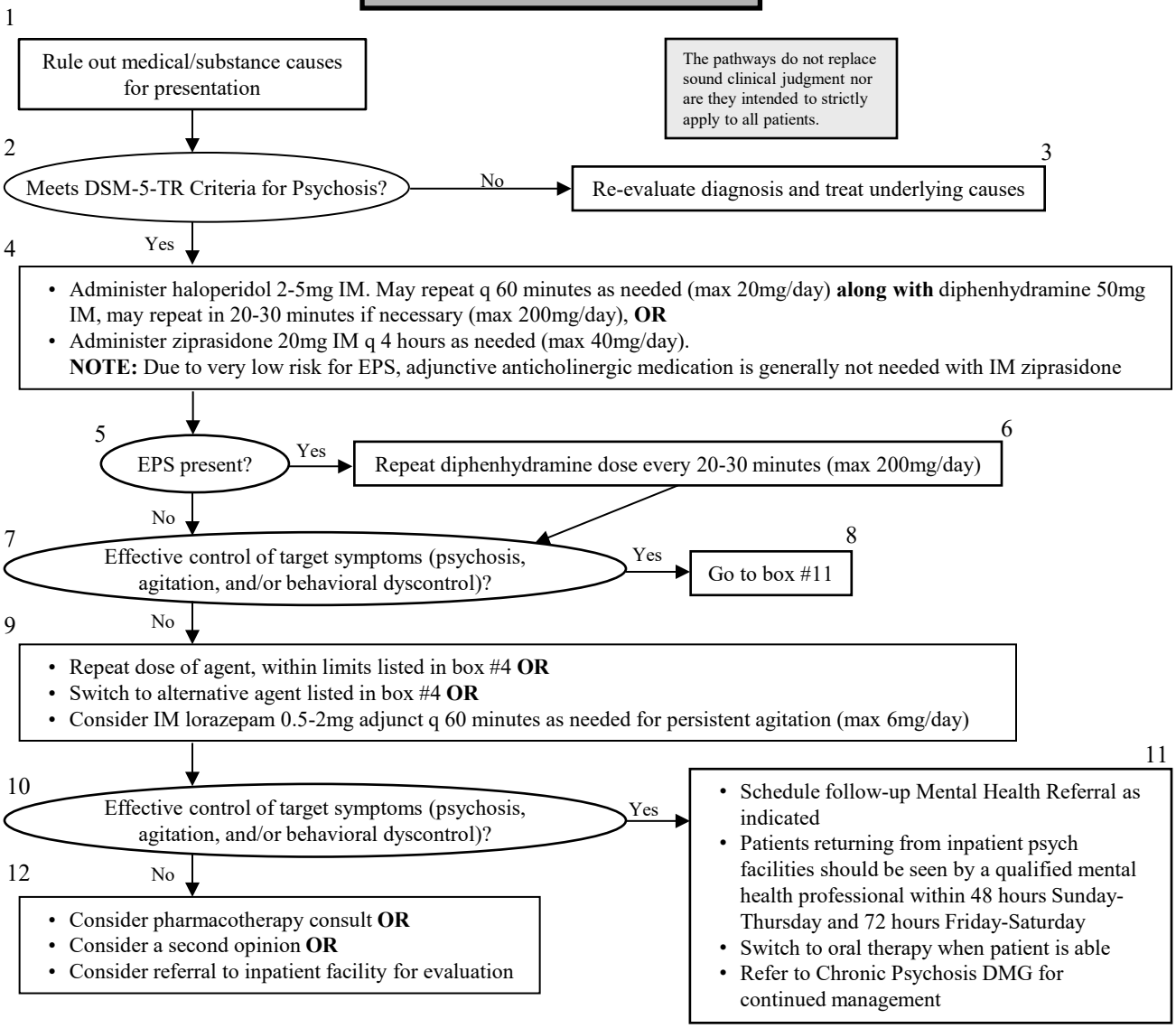
Administered/Reviewed by _____ Date _____

1 Source: Cox, J.L., Holden, J.M., and Sagovsky, R. 1987. Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry* 150:782-786.
2 Source: K. L. Wisner, B. L. Parry, C. M. Piontek, Postpartum Depression N Engl J Med vol. 347, No 3, July 18, 2002, 194-199.

SCORING
Questions 1, 2, and 4 (without an *) Are scored 0, 1, 2, or 3, with top box scored as 0 and the bottom box scored as 3
Questions 3, 5-10 (marked with an *) Are reversed scored, with the top box scored as 3 and the bottom box scored as 0

Max score: 30
Possible depression: 10 or greater
Always look at item 10 (suicidal thoughts)

ACUTE PSYCHOSIS



Monitoring Parameters: Check patient at least once in first 15 minutes, then every 30 minutes at least twice in the next hour if patient remains on the unit.

- Mental Status: Alert and oriented, motor activity, speech, excess sedation
- Extrapyramidal Symptoms (EPS): Dystonia, parkinsonism, akathisia, tremor, dyskinesia
- Behavior: Psychosis (ie. hallucinations, delusions, disorganized speech/behavior), assaultive, agitated
- Neuroleptic Malignant Syndrome (NMS): Dehydration, vital signs, muscle rigidity, diaphoresis, alteration in consciousness, autonomic dysfunction (orthostatic hypotension, drooling, urinary incontinence, unusually rapid breathing)
- Vital Signs: Blood pressure, pulse, temperature, respiration (as clinically indicated)

Management of Adverse Effects

- Neuroleptic Malignant Syndrome
  - Medical emergency; evaluate through medical department for possible referral to hospital ER
- Acute Dystonic Reaction
  - Diphenhydramine 50mg IM (max 200 mg/day)
- Worsening Mental Status
  - Immediately contact psychiatric provider for evaluation
  - Reconsider possible medical etiology for presentation

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.

Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee. Approved 12/02; reviewed 4/03, 3/11, 5/16; revised 11/05, 1/09, 7/10, 5/13,3/21,1/26

Psychosis, Chronic

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

1 Rule out medical/substance causes for presentation.

2 Meets DSM-5-TR Criteria for Psychosis?

No → 3 Re-evaluate diagnosis and treat underlying causes.

Yes

4 Obtain baseline information including BPRS, AIMS, and labs in Table 1

*Antipsychotic trial of adequate dose/duration is 4-6 weeks at FDA approved maximum dosage or maximum tolerated dose with a minimum of 80% adherence.

5 Initiate monotherapy with formulary antipsychotic

- First Generation Antipsychotic (FGA) – titrate up to a maximum of 1,000 mg CPZ equivalents and treat for at least 6 weeks (Table 5)
- Second Generation Antipsychotic (SGA) – risperidone up to a maximum of 6 mg/day, lurasidone up to 160 mg/day, aripiprazole up to 30 mg/day or ziprasidone up to 160 mg/day and treat for at least 6 weeks
  - Consider formulary SGA if:
    - AIMS positive for tardive dyskinesia
    - First break psychosis
    - History of positive response

Note: If at any time compliance is poor despite adequate education and/or compelled antipsychotic medications are necessary, consider use of long-acting injectable antipsychotic preparation. Refer to long-acting injectable antipsychotic guidance- page 2.

6 Signs of Adverse Effects?

Yes → 7 If at any time adverse effects are noted, go to Adverse Effect Management page 8

No

8 Adequate response per BPRS?

Yes → 9

- Continue treatment and taper to lowest effective dose
- Monitor per recommendations in Tables 1& 4

No Assess compliance

10*

- Provide compliance counseling as indicated, and re-evaluate diagnosis
- Change drug therapy
  - Increase dose of current agent to maximal tolerated dose (Table 5) **or**
  - Switch to another formulary agent from a different class **or** within the same class.

11 Adequate response per BPRS?

Yes → 12

- Continue treatment and taper to lowest effective dose
- Monitor per recommendations in Tables 1& 4

No Assess compliance

13

- Provide compliance counseling as indicated, and re-evaluate diagnosis
- Change drug therapy
  - If patient has received trial of 2 SGAs and has no contraindications, consider trial of an FGA
  - If patient has not received a trial of a SGA, consider trial of risperidone, lurasidone, aripiprazole or ziprasidone
  - Consider non-formulary SGA

14 Adequate response per BPRS?

Yes → 15

- Continue treatment and taper to lowest effective dose
- Monitor per recommendations in Tables 1& 4

No Assess compliance

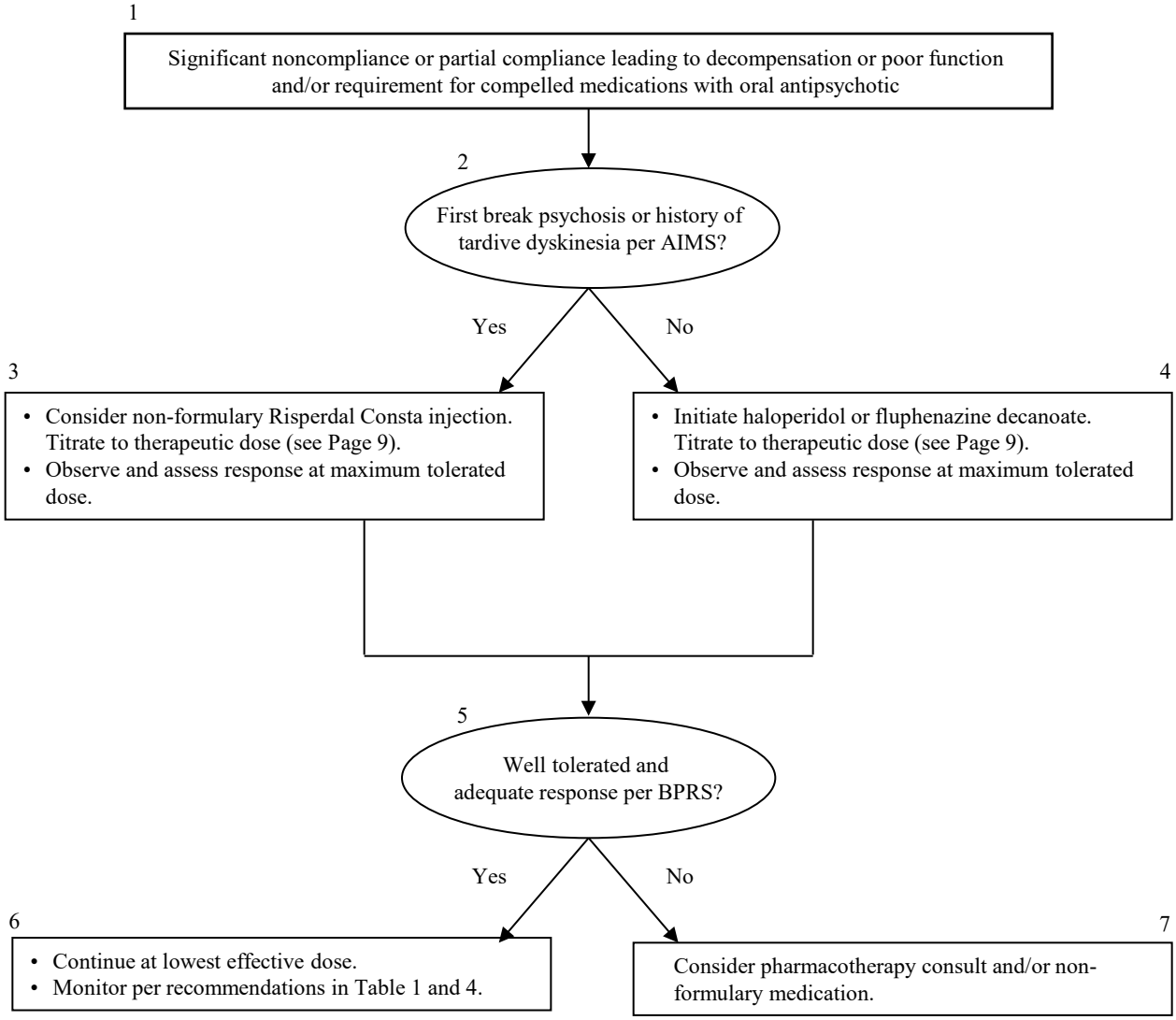
16

- Provide compliance counseling as indicated, and re-evaluate diagnosis
- Change drug therapy
  - Refer patient to inpatient facility for possible clozapine therapy
  - Consider augmentation with formulary mood stabilizer lithium or divalproex sodium
  - Consider pharmacotherapy consult and/or non-formulary medication

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.

Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee, 1/99; revised 4/00, 9/01, 5/02, 7/05, 9/07, 9/10, 5/13, 7/14, 5/16;7/21; 1/25,1/26 reviewed 4/03

Guidelines for Use of Long-Acting Injectable Antipsychotic Agents



Antipsychotic Monitoring Parameters

Table 1: Monitoring Guidelines[1]

Parameter	Baseline	Follow-Up
Weight, Height, BMI	X	BMI every visit for 6 months and quarterly thereafter
Blood Pressure, Pulse, Temperature	X	As clinically indicated
Fasting Blood Glucose[4]	X	At 4 months after initiating new antipsychotic, then annually
Fasting Lipid Profile[4]	X	At 4 months after initiating new antipsychotic, then annually
Complete Metabolic Panel	X	As clinically indicated
CBC	X	As clinically indicated
TSH	X	As clinically indicated
EKG[2]	As clinically indicated	
Prolactin[3]	As clinically indicated	

Providers should consider obtaining any of the laboratories listed above more frequently if clinically indicated.

1. Additional assessments may be necessary based on patient's history, preexisting conditions and clinical circumstances.
2. Providers should consider obtaining an EKG at baseline and periodically when there is a personal or family history of cardiovascular disease or the patient is > 40 years old. Also, consider obtaining EKG prior to treatment with chlorpromazine, iloperidone, pimozide, thioridazine, clozapine or ziprasidone or with addition of other medications that can affect QTc interval in patients with cardiac risk factors or elevated QTc intervals.
3. Providers should consider obtaining a prolactin level if the patient is complaining of gynecomastia, galactorrhea, irregular or absent menses, or sexual dysfunction. Consider screening for symptoms at each visit until stable and annually if treated with an antipsychotic known to increase prolactin.
   - Routine prolactin levels are **not** recommended unless symptoms are present
   - The normal range of prolactin is 10-20 mcg/L in males and 10-25 mcg/L in females
   - Symptoms typically do not appear until levels reach 60-100 mcg/L
   - Patients should be referred to medical to rule-out other etiologies of hyperprolactinemia
4. Providers should consider determining if metabolic syndrome criteria are met at 4 months after initiating a new antipsychotic and annually thereafter. Metabolic syndrome is defined by the presence of at least 3 of the following risk factors: elevated waist circumference(>40.2 inches for males and >34.6 inches for females), elevated triglycerides (≥150 mg/dL)or drug treatment for elevated triglycerides, reduced HDL (<40 mg/dL in men or <50 mg/dL in women) or treatment of low HDL, elevated BP (≥130/85)or antihypertensive treatment and elevated fasting glucose or drug treatment for high glucose.

Additional Monitoring Parameters for Specific Agents

- Ziprasidone (Geodon®) - EKG at baseline then annually or as clinically indicated
- Quetiapine (Seroquel®) - Ophthalmic exam checking for cataracts every 6 months
- Clozapine (Clozaril®) - Refer to Tables 2 & 3 for monitoring. Additional monitoring, discontinuation and restarting clozapine can be found of page 6.

Notable Drug Interactions

- Latuda® (lurasidone) - Common lurasidone contraindications: carbamazepine, protease inhibitors (lopinavir, ritonavir, darunavir) phenytoin and rifampin.

*Note: This is not a complete list of drug interaction. Dose adjustments may also be required.

Clozapine Monitoring

Table 2: Recommended Clozapine Monitoring

ANC Level	Dose Modification	Recommended Frequency of ANC Testing During Treatment
Within Normal Range ≥1500/ul	No dose modification; continue treatment	• Day 1 to Month 6 : Weekly • Month 7 to Month 12: Every 2 weeks • 13 Months: Every month If clozapine treatment is reinitiated after a dosage interruption (ex: patient develops neutropenia which lead to interruption and now has normal ANC) for: • <30 days, continue the previous ANC testing frequency • ≥ 30 days, obtain ANC tests according to the frequency for the patient who initiate treatment
Mild Neutropenia (ANC 1000 to 1499/ul)	No dosage modification; continue treatment	• Three time weekly • Once ANC ≥ 1500, recommend returning to the patient's last normal range ANC testing frequency
Moderate Neutropenia (ANC between 500 to 999/ul)	• Interrupt treatment and recommend hematologic consultation • Resume treatment once ANC≥ 1000/ul	• Daily • Once ANC ≥ 1000/ul, three times weekly • Once ANC ≥ 1500, test weekly for 4 weeks. If ANC ≥ 1500/ul after monitoring weekly for 4 weeks, return to the patient's last normal range ANC testing frequency.
Severe Neutropenia (ANC less than 500/ul)	• Discontinue treatment and recommend hematology consultation	• Daily • Once ANC ≥ 1000/ul, three times weekly • Once ANC ≥ 1500, if the benefits outweigh the risks of restarting treatment, resume treatment and obtain ANC tests according to the frequency for patients who initiate treatment.

*Confirm all initial reports of ANC less than 1500/ul with repeat ANC measurement within 24 hours

Clozapine Monitoring

Table 3: Recommended Clozapine Monitoring in Patients with Benign Ethnic Neutropenia (BEN)

ANC Level	Dose Modification	Recommended Frequency of ANC Testing During Treatment
Within Normal Range ≥1000/ul *obtain 2 baseline ANC levels	No dose modification; continue treatment	• Day 1 to Month 6 : Weekly • Month 7 to Month 12: Every 2 weeks • 13 Months: Every month If clozapine treatment is reinitiated after a dosage interruption (ex: patient develops neutropenia which lead to interruption and now their ANC > 1000/ul and ≥ the patient's ANC baseline prior to treatment) for: • <30 days, continue the previous ANC testing frequency • ≥30 days, obtain ANC tests according to the frequency for the patient with BEN who initiate treatment
Mild Neutropenia (ANC 500 to 999/ul)	• Recommend hematology consultation • No dosage medication; continue treatment	• Three time weekly • Once ANC ≥ 1000/ul and ≥ the patient's ANC baseline, obtain ANC tests weekly for 4 weeks • If ANC ≥1000/ul and ≥ the patient's ANC baseline after monitoring for 4 weeks, return to the patient's last normal ANC range testing frequency for patients with BEN
Severe Neutropenia (ANC less than 500/ul)	• Discontinue treatment and recommend hematology consultation	• Daily • Once ANC ≥ 500/ul, three times weekly • Once ANC ≥ 1000 and ≥ the patient's ANC baseline, if the benefits outweigh the risks of restarting treatment, resume treatment and obtain ANC tests according to the frequency for patients with BEN who initiate treatment.

*Benign Ethnic Neutropenia (BEN) is also known as Duffy-null associated neutrophil count.
**Confirm all initial reports of ANC less than 1500/ul with repeat ANC measurement within 24 hours

Clozapine Monitoring

Other Clozapine Warnings and Precautions:

1. Myocarditis, pericarditis, cardiomyopathy, and mitral valve have occurred with clozapine treatment. Discontinue clozapine and obtain cardiac evaluation upon suspicion of these reactions. Generally, patients with clozapine-related myocarditis or cardiomyopathy should not be rechallenged. Consider the possibility of myocarditis, pericarditis, or cardiomyopathy if chest pain, tachycardia, palpitations, dyspnea, fever, flu-like symptoms, hypotension or ECG changes occur.
2. Orthostatic hypotension, bradycardia, syncope, and cardiac arrest have occurred with clozapine treatment. The risk is highest during the initial titration period, particularly with rapid dose escalation. Titrate slowly and use divided dosages to minimize risk. Risk is dose-related.
3. Seizure risk is dose related. Titrate gradually and use divided doses. Use caution in patients with a history of seizure or other predisposing risk factors for seizure.
4. Eosinophilia (defined as a blood eosinophil count of greater than 700 per μL) has been associated with clozapine treatment and may be associated with myocarditis, pancreatitis, hepatitis, colitis, and nephritis. Such organ involvement could be consistent with drug reaction with eosinophilia and systemic symptoms syndrome (DRESS), also known as drug induced hypersensitivity syndrome (DIHS). If eosinophilia develops during treatment, evaluate promptly for the signs and symptoms of systemic reactions such as rash or other allergic symptoms, myocarditis, or other organ-specific disease associated with eosinophilia. If suspected, discontinue clozapine immediately.
5. Gastrointestinal hypomotility such as constipation or paralytic ileus may occur. Screening and reassessment of bowel function and symptoms of complications of hypomotility (nausea, vomiting, abdominal distention or pain) is recommended.
6. QT Prolongation and Torsade de Pointes may occur. Risk factors for QT prolongation should be considered. Additionally, baseline ECG and serum chemistry panel should be considered.

Discontinuing Clozapine

- Refer to Table 2 & 3
- For normal or mild neutropenia, reduce the dosage gradually over a period of 1 to 2 weeks and continue monitoring ANC levels until ANC is $\geq$ 1500/ul

Restarting Clozapine

- If one day is missed: resume clozapine treatment at 40% to 50% of the previous dose.
- If two days are missed: resume clozapine treatment at approximately 25% of the previous dose.
- For longer interruptions, restart clozapine treatment with a dosage of 25 mg daily. If well tolerated, may increase the dose to previous dosage more quickly than recommended for initial treatment.

Table 4: Outcome and Adverse Effect Monitoring

Assessment	Baseline	Follow-up
AIMS (Abnormal Involuntary Movement Scale) •Acute EPS – Akathisia, dystonia, parkinsonism •Tardive Dyskinesia	X	Annually *every 6 months in high-risk patients
Mental Status Exam	X	Baseline and at least every 6 months
BPRS (Brief Psychiatric Rating Scale)	X	Baseline and at least every 6 months Medication is started, changed or discontinued

Table 5: Antipsychotic Dosages and Adverse Effects

Agent	Formulary Status	Potency	CPZ Equivalents (approx.mg)	Dose Range (mg/day)	Adverse Effects				
					Weight Gain	EPS	Sedation	Anticholinergic	Orthostasis
First Generation Antipsychotics									
Chlorpromazine (Thorazine®)	NF	Low	100	300-800	++	++	+++	+++	+++
Fluphenazine (Prolixin®)	F	High	2	1-40	++	+++	+	+	+
Haloperidol (Haldol®)	F	High	2	1-100	++	+++	+	+	+
Perphenazine (Trilafon®)	F	Mid	8	12-64	++	++	++	++	++
Thioridazine* (Mellaril®)	NF	Low	100	20-800	++	+	+++	+++	+++
Thiothixene (Navane®)	F	High	4	6-60	+	+++	+	+	+
Trifluoperazine (Stelazine®)	F	High	5	2-40	++	+++	+	++	+
Second Generation Antipsychotics		**5HT2$_a$/D2**							
Aripiprazole (Abilify®)	F	++++/++++#	7.5	10 – 30	+	++	+	+	+
Asenapine (Saphris ®)	NF	++++/+++	?	5-20	++	++	++	+	++
Brexpiprazole (Rexulti)	NF	++++/+++#	?	2-4	+	++	++	+	+
Cariprazine (Vraylar®)	NF	++/+++#	?	1.5-6	++	++	++	++	+
Clozapine (Clozaril®)	NF	++++/+	50	25 – 900	+++	+	+++	+++	+++
Iloperidone (Fanapt ®)	NF	+++++/++++	?	12-24	++	+	++	+	+++
Lurasidone (Latuda®)	~~NF~~	++++/+++	?	40-80	+	++	+	+	+
Olanzapine (Zyprexa®)	NF	++++/++	5	5 – 20	+++	++	+++	++	++
Paliperidone (Invega®)	NF	+++++/++++	3	3 – 12	++	+++	+	+	++
Quetiapine (Seroquel®)	NF	+/+	125	300 – 800	++	+	+++	++	++
Risperidone (Risperdal®)	F	+++++/++++	2	0.5-6	++	+++	++	+	++
Ziprasidone (Geodon®)	F	+++++/++++	60	120 -160	+	++	++	+	++

*Should only be used in treatment refractory illness. Contraindicated for use with agents that are known to prolong QTc and agents that inhibit metabolism of thioridazine (such as: fluoxetine, paroxetine, fluvoxamine, propranolol).

partial D2 agonist

Table 6 : Adverse Effect Management

Side Effect	Recommended Management Strategies

EPS	• Lower the dose of the antipsychotic agent to the lowest effective dose **or**
	• Review table 5 and consider selecting an agent with a lower incidence of EPS **or**
	• Switch to an SGA **or**
	• Treat EPS with one of the following agents
	  • Benztropine 1 – 6 mg/day
	  • Diphenhydramine 25 – 100 mg/day
	  • Amantadine 100 – 300 mg/day
	  • Propranolol 20 – 120 mg/day
	  • Short term use of benzodiazepines may be considered in severe cases in an inpatient setting
	  • Increase dose of agent or switch to alternate anti-EPS agent if ineffective

Akathisia	• Lower the dose of the antipsychotic agent to the lowest effective dose **or** • Switch to an SGA **or** • Treat with propranolol 20 – 120 mg/day. Titrate dose as tolerated and as needed.
Tardive dyskinesia	• Diagnosis supported by AIMS? • Switch to an SGA • Consider pharmacotherapy consult for treatment options
Neuroleptic Malignant Syndrome	• Medical emergency • Evaluate through medical department for possible referral to emergency room • Consider STAT CPK • Discontinue antipsychotic

Appropriate use of Anticholinergic Medications

Benztropine and diphenhydramine are associated with significant side effects and may potentially increase the risk of developing tardive dyskinesia, cognitive impairment, anticholinergic side effects, and delirium. Current treatment guidelines recommend **against** the use of anticholinergics for prevention of EPS unless the patient has a history of severe EPS.

- Anticholinergic medications use should be limited to the treatment of confirmed EPS and scheduled prophylactic use should be minimized.
- Lower starting doses of FGA with reasonable titration rates could potentially reduce the risk of treatment-emergent EPS.
- When treating EPS, use of anticholinergic medications should be evaluated every 3 months for possible discontinuation, as most cases of EPS are self-limiting and do not require long-term treatment.

Quick Reference Guide for Initiating Long-Acting Injectable Antipsychotics

Haloperidol Decanoate (Haldol-D®)

General information

- Formulary strength available: 100 mg/mL solution for injection
- The first dose should be no more than 100 mg
  - If > 100 mg is needed, administer the remainder 3-7 days later
  - All future injections can be administered in doses up to 300 mg at a time
- Inject in the gluteal muscle by z-track administration
- Dosing interval: 4 weeks
- Maximum approved dose = 450 mg q 4weeks

Loading dose method (preferred)

- Month 1: Initiate haloperidol decanoate at 20 times the oral haloperidol dose
  - Discontinue oral haloperidol at time of first injection
- Month 2: Haloperidol decanoate 15 times the oral haloperidol dose
- Month 3 and thereafter: Haloperidol decanoate 10 times the oral haloperidol dose

Traditional dosing method

- Initiate haloperidol decanoate at 10-15 times the oral haloperidol dose
- Continue oral haloperidol for 1 month, then discontinue

Fluphenazine Decanoate (Prolixin D®)

General information

- Formulary strength available: 25 mg/mL solution for injection
- Inject in the gluteal muscle by z-track administration
- Dosing interval: 2-3 weeks
- Maximum approved dose = 100 mg q 2weeks
- Accumulation may occur over time; consider dose reduction after 6 months of treatment

Dosing method

- Initiate fluphenazine decanoate at 1.2-1.6 times the oral fluphenazine dose
  - Round to the nearest 12.5 mg
- Continue oral fluphenazine for 1-4 weeks, then discontinue

Risperdal Consta®

General information

- Requires nonformulary approval
- Oral test dose is required if the patient has no documented history of risperidone use
  - Administer 1-2 mg oral risperidone for 2 days prior to injection
- Inject in the deltoid or gluteal muscle
- Dosing interval: 2 weeks
- Maximum approved dose = 50 mg q 2 weeks

Dosing method

- Initiate Risperdal Consta 25 mg q 2 weeks
- Continue oral antipsychotic for 3 weeks, then discontinue
- Adjust dose no sooner than q 4 weeks, as needed

ABNORMAL INVOLUNTARY MOVEMENT SCALE

Complete examination procedure outlined in the instructions before making rating. Rate highest severity observed. Movements occurring upon activation rate one less than those occurring spontaneously.
0 = None 1 = Minimal 2 = Mild 3 = Moderate 4 = Severe

Date of Evaluation									
1	**Muscles of facial expression** e.g., movements of forehead, eyebrows, preorbital area, cheeks, include frowning, blinding, smiling, grimacing								
2	**Lips and perioral area** e.g., puckering, pouting, smacking								
3	**Jaw** e.g., biting, clenching, chewing, mouth opening, lateral movement								
4	**Tongue** Rate only increase in movement both in and out of mouth, not inability to sustain movement								
5	**Upper (arms, wrists, hands, fingers)** Include chronic movements (i.e., rapid objectively purposeless, irregular, spontaneous); athetoid movements (i.e., slow, irregular, complex, serpentine). DO NOT include tremor (i.e., repetitive, regular, rhythmic).								
6	**Lower (legs, knees, ankles, toes)** e.g., lateral knee movement, foot tapping, heel dropping, foot squirming, inversion, and eversion of foot								
7	**Neck shoulders, hips** e.g., rocking, twisting, squirming, pelvic gyrations								
8	**Severity of abnormal movements**								
9	**Incapacitation due to abnormal movements**								
10	**Patient's awareness of abnormal movements** Rate only patient's report: No awareness=0 Aware, no distress=1 Aware, mild distress=2 Aware, moderate distress=3 Aware, severe distress=4								
11	**Current problems with teeth &/or dentures?** No=0 Yes=1								
12	**Does patient usually wear dentures?** No=0 Yes=1								
13	**COMMENTS:**								

BRIEF PSYCHIATRIC RATING SCALE (BPRS) - Instructions for the Clinician

Background:
The Brief Psychiatric Rating Scale (BPRS) is a widely used instrument for assessing psychopathology at baseline and longitudinally as an outcome measurement when treatment is introduced. The BPRS is a scale measuring positive symptoms, general psychopathology and affective symptoms. It has proven particularly valuable for documenting the efficacy of treatment in patients who have moderate to severe psychopathology. The BPRS has been well validated in the clinical literature and is reportedly the most studied psychometric instrument currently in use.

The BPRS should be administered by a clinician who is knowledgeable concerning psychiatric disorders and is able to interpret the constructs used in the assessment. The individual's behavior over the previous 2-3 days should also be considered and can be reported by the patient's caregivers or teachers. It should be utilized at baseline and then at each visit if the patient is prescribed an antipsychotic.

The BPRS utilized in the electronic medical record (EHR) consists of a range of 23 symptom constructs covering a broad array of potential psychopathology. The assessment typically takes 10-20 minutes or less for the interview and scoring.

Instructions for Use and Scoring:
Each item is rated on a seven-point scale (1=not present to 7=extremely severe). Zero (0) is entered if the item is not assessed. The scores of the 23 items should be summed and recorded. The total score should be compared to the total score from one evaluation to the next as a measure of response to treatment. In addition, a single subscale (symptom) or cluster of subscales (e.g., grandiosity, elevated mood, excitement, distractibility) can be followed over time.

Brief Psychiatric Rating Scale (BPRS)

Patient Name _____ Patient Number _____ Date_____

Facility _____ Practitioner _____

Enter the score for the term that best describes the patient's condition.

0 = Not assessed, 1 = Not present, 2 = Very mild, 3 = Mild, 4 = Moderate, 5 = Moderately severe, 6 = Severe, 7 = Extremely severe

Score		
____	1.	SOMATIC CONCERN - Preoccupation with physical health, fear of physical illness, hypochondriasis.
____	2.	ANXIETY - Worry, fear, over-concern for present or future, uneasiness
____	3.	EMOTIONAL WITHDRAWAL - Lack of spontaneous interaction, isolation deficiency in relating to others.
____	4.	CONCEPTUAL DISORGANIZATION - Thought processes confused, disconnected, disorganized, disrupted.
____	5.	IMPULSIVENESS
____	6.	MOTOR HYPERACTIVITY - Increase in energy level evidenced in more frequent movement and/or rapid speech. Do not rate if restlessness is due to akathisia.
____	7.	MANNERISMS AND POSTURING - Peculiar, bizarre, unnatural motor behavior (not including tic).
____	8.	GRANDIOSITY - Exaggerated self-opinion, arrogance, conviction of unusual power or abilities.
____	9.	DEPRESSIVE MOOD - Sorrow, sadness, despondency, pessimism.
____	10	HOSTILITY - Animosity, contempt, belligerence, disdain for others.
____	11.	SUSPICIOUSNESS - Mistrust, belief others harbor malicious or discriminatory intent.
____	12.	HALLUCINATORY BEHAVIOR - Perceptions without normal external stimulus correspondence.
____	13.	MOTOR RETARDATION - Slowed, weakened movements or speech, reduced body tone.
____	14.	UNCOOPERATIVENESS - Resistance, guardedness, rejection of authority.
____	15.	UNUSUAL THOUGHT CONTENT - Unusual, odd, strange, bizarre thought content.
____	16.	BLUNTED AFFECT - Reduced emotional tone, reduction in formal intensity of feelings, flatness.
____	17.	EXCITEMENT - Heightened emotional tone, agitation, increased reactivity.
____	18.	DISORIENTATION - Confusion or lack of proper association for person, place or time.
____	19.	ELEVATED MOOD - A pervasive, sustained and exaggerated feeling of well-being, cheerfulness, or euphoria implying a pathological mood. Optimism that is out of proportion to the circumstances.
____	20.	SUICIDALITY - Expressed desire, intent, or actions to harm or kill self.
____	21.	BIZARRE BEHAVIOR - Reports of behaviors which are odd, unusual, or psychotically criminal. Not limited to interview period. Include inappropriate sexual behavior and inappropriate affect.
____	22.	SELF-NEGLECT - Hygiene, appearance, or eating behavior below usual expectations, below socially acceptable standards or life threatening.
____	23.	DISTRACTIBILITY - Degree to which observed sequences of speech and actions are interrupted by stimuli unrelated to the interview. Distractibility is rated when the individual shows a change in the focus of attention as characterized by a pause in speech or a marked shift in gaze. Individual's attention may be drawn to noise in adjoining room, books on a shelf, interviewer's clothing, etc.

This dosing tool does not replace sound clinical judgment, nor is it intended to strictly apply to all patients.

Psychotropic Agents: Dosing, Approximate Equivalent Doses, & Recommendations for Switching Agents

Patients should be evaluated for use of formulary psychotropics when possible. Clinicians should consider history of response, contraindications, co-morbidities, compliance, potential adverse effects, and drug interactions when making treatment decisions. When medications are changed, patients should be monitored closely for worsening symptoms and adverse effects. The recommendations listed below are not intended to replace sound clinical judgment. When treating elderly patients with psychotropic agents, lower starting doses and slower titration may be required.

***Note**: All inmates arriving in TDCJ with a current prescription for psychoactive medications will be continued on agency approved medications (unless clinically contraindicated) until they are assessed by a psychiatrist or psychiatric physician assistant/nurse practitioner. Inmates referred for initial psychiatric assessment must be seen within 30 days of referral.*

Caution: Approximate equivalent doses are only applicable within each antidepressant class, not between antidepressant classes.

ANTIDEPRESSANTS

Table 1: Antidepressants

Generic Name (Brand Name)	Formulary Agent	Usual Dose (mg/day)	Approximate Equivalent Dose (mg) †
Tricyclic Antidepressants (TCAs)			
Amitriptyline (Elavil®)	N	100-300	100
Amoxapine (Asendin®)	N	100-400	100
Clomipramine (Anafranil®)	N	100-250	100
Desipramine (Norpramin®)	N	100-300	100
Doxepin (Sinequan®)	N	100-300	100
Imipramine (Tofranil®)	Y (TJJD only)	100-300	100
Maprotiline (Ludiomil®)	N	100-225	100
Nortriptyline (Pamelor®)	N	50-150	50
Protriptyline (Vivactil®)	N	15-60	20
Trimipramine (Surmontil®)	N	100-300	100
Selective Serotonin Reuptake Inhibitors (SSRIs)			
Citalopram (Celexa®)	Y	20-40	20
Escitalopram (Lexapro®)	Y (TJJD only)	10-20	10
Fluoxetine (Prozac®)	Y	20-80	20
Fluoxetine Delayed Release (Prozac Weekly®)	N	Administered weekly (usual dose = 90 mg/week)	90
Fluvoxamine (Luvox®)	N	100-300	100
Paroxetine (Paxil®)	N	IR = 20-50 CR = 25-75	IR = 20 CR = 25
Sertraline (Zoloft®)	Y	50-200	50
Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)			
Venlafaxine (Effexor®)	Y (ER only)	IR = 75-375 ER = 75-225	IR = 150 ER = 150
Duloxetine (Cymbalta®)	Y	40-60	60
Levomilnacipran (Fetzima®)	N	40-120	N/A
Desvenlafaxine (Pristiq®, Khedezla®)	N	50	N/A

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.

ANTIDEPRESSANTS

Table 1: Antidepressants, Continued

GENERIC NAME (BRAND NAME)	FORMULARY AGENT	USUAL DOSE (MG/DAY)	APPROXIMATE EQUIVALENT DOSE (MG) †
Norepinephrine Dopamine Reuptake Inhibitors (NDRIs)			
Bupropion HCl (Wellbutrin®)	N	IR = 300-450 SR = 150-400 XL = 150-450	IR = 150 SR = 150 XL = 150
Bupropion HBr (Aplenzin®)	N	174-522	174
Monoamine Oxidase Inhibitors (MAOIs) *(the following are inexact estimates for approximate equivalent dosing)*			
Isocarboxazid (Marplan®)	N	10-40	10
Phenelzine (Nardil®)	N	15-90	15
Tranylcypromine (Parnate®)	N	10-60	10
Selegiline (Emsam®)	N	6-12 (transdermal)	6
Serotonin Receptor Modulators and Tetracyclic Antidepressants *(the following are inexact estimates for approximate equivalent dosing)*			
Mirtazapine (Remeron®)	N	15-45	15
Trazodone (Desyrel®)	Y	150-600	150
Nefazodone (Serzone®)	N	300-600	200
Vilazodone (Viibryd®)*	N	20-40	30
Vortioxetine (Brintellix®)*	N	5-20	N/A

†Doses are approximate equivalencies only within the specified drug class
*No data currently available on equivalent dosing

Switching Antidepressant Agents

TCA to SSRI/SNRI
Discontinue the TCA and immediately start SSRI or SNRI. Providers may consider a short –term order for diphenhydramine (e.g., 3 days) for patients on an antidepressant dose of TCA or longer duration of therapy (> 8 weeks).

SSRI to SSRI or SNRI
If switching from one SSRI to another, or to an SNRI, a cross-taper is generally not necessary. Fluoxetine in particular may be stopped abruptly due to its long half-life. If switching from fluoxetine, start new SSRI at ½ normal starting dose 4-7 days later.

SSRI to non-SSRI/SNRI antidepressant
Discontinue the SSRI and start Drug #2 the next day OR discontinue the SSRI by taper and start Drug #2 gradually.

MAOI to MAOI or other antidepressant
Discontinue MAOI. After a 2-week washout, start MAOI, SSRI, or other antidepressant.

Other antidepressant to MAOI
Start MAOI after 5-week washout for fluoxetine or 2-week washout for other antidepressants.

Discontinuing Antidepressant Agents
Antidepressants may be associated with adverse effects associated with discontinuation, particularly when the discontinuation is in an abrupt manner. A gradual dose reduction is recommended when possible.

ANTIPSYCHOTICS

Table 2: Oral Antipsychotics

Generic Name (Brand Name)	Formulary Agent	Usual Dose (mg/day)	Approximate Equivalent Dose (mg)
High-Potency First Generation Agents			
Pimozide (Orap®)	N	1-10	2
Fluphenazine (Prolixin®)	Y	2.5-20	2
Haloperidol (Haldol®)	Y	1-20	2
Mid-Potency First Generation Agents			
Loxapine (Loxitane®)	N	60-100	10
Perphenazine (Trilafon®)	Y	16-64	10
Thiothixene (Navane®)	Y	15-30	4
Trifluoperazine (Stelazine®)	Y	15-20	5
Low-Potency First Generation Agents			
Chlorpromazine (Thorazine®)	N	200-1000	100
Thioridazine (Mellaril®)	N	200-800	100
Second Generation Agents			
Aripiprazole (Abilify®)	Y	10-30	5
Brexpiprazole (Rexulti®)	N	4	1
Cariprazine (Vraylar®)*	N	1.5-6	N/A
Clozapine (Clozaril®)	N	300-450	125**
Olanzapine (Zyprexa®)	N	5-20	4
Quetiapine (Seroquel®)	N	Regular Release = 400-800 ER = 400-800	Regular Release = 100 ER = 100
Risperidone (Risperdal®)	Y	2-8	1.5
Ziprasidone (Geodon®)	Y	40-160	30
Paliperidone (Invega®)	N	3-12	2
Asenapine (Saphris®)*	N	10-20	5
Iloperidone (Fanapt®)*	N	12-24	5**
Lurasidone (Latuda®)*	N	40-80	20
Lumateperone (Caplyta®)*	N	42	N/A

*No data currently available on equivalent dosing
**Caution: clozapine and iloperidone require slow titration at initiation to decrease risk of orthostasis, regardless of approximate equivalent doses calculated

Switching Antipsychotic Agents

Studies of abrupt discontinuation versus cross-tapering from other antipsychotics to ziprasidone, olanzapine, aripiprazole, and iloperidone found no difference in outcomes.[13,18-22] Methods should be individualized, and antipsychotic overlap periods should be minimized if cross-tapering is selected. Cross-tapering may be considered for patients who are clinically unstable or only recently stabilized, are on high doses, have had a recent relapse, are outpatient, or are having a partial response to their current agent and may require slow titration of the new agent to improve tolerability. Cross-tapering may also be preferred when switching to an alternative antipsychotic with a vastly different receptor profile (table 4) to prevent discontinuation reactions and rebound effects (table 5). Unless intolerance is present, switching antipsychotics is not advised until a trial of adequate dose and duration (4-6 weeks) is completed.

Switching from Clozapine to other Antipsychotics
A cross-taper of at least 4 weeks in duration is preferred when switching from clozapine to other antipsychotics, when possible. This decreases risk of cholinergic rebound and rebound psychosis.

Table 3: Basic Switch Strategies for Antipsychotics

STRATEGY	DEFINITION	ADVANTAGES	DISADVANTAGES	RECOMMENDED FOR:
Abrupt Switching	Simultaneous cessation of the prior antipsychotic and initiation of the new antipsychotic.	Low risk of drug interactions	Potential for discontinuation reactions	Patients with serious adverse event(s)
Gradual Switching	Tapering the current antipsychotic off, and initiating and titrating the new antipsychotic thereafter	Low risk of discontinuation reactions, few drug interactions	Risk of symptom exacerbation	Patients with low risk of relapse
Cross-Tapering	Gradually tapering the existing antipsychotic, while at the same time initiating and titrating the new antipsychotic.	Low risk of relapse	Increased risk of drug interactions	Recently stabilized patients
Plateau Cross-Titration	Gradually titrating the new antipsychotic to a full dose, then tapering and discontinuing the initial antipsychotic	Low risk of relapse	Increased risk of drug interactions	Initiation of agents w/ long half-lives that may not build up as quickly (i.e., aripiprazole)

Table 4. Activity of Atypical Antipsychotics at Select Receptors†

Antipsychotic	Receptor Binding Affinity							
	5-HT$_{1A}$	**5-HT$_{2A}$**	**5-HT$_{2C}$**	**D$_2$**	**α_1**	**α_2**	**H$_1$**	**M$_{1-5*}$**
Ziprasidone	++	++++	++	+++	++	++	++	+
Risperidone	+	++++	++	+++	+++	+++	++	+/-
Paliperidone	+	++++	++	+++	+++	+++	++	+/-
Lurasidone	+++	+++	+	+++	++	++	+/-	+/-
Iloperidone	++	+++	+	+++	++++	++	++	+/-
Olanzapine	+	+++	++	++	++	+	+++	++
Clozapine	+	++	++	+	+++	++	+++	+++
Asenapine	++	++++	++++	+++	+++	+++	+++	+
Quetiapine	+	++	+	+	+++	+	+++	++
Aripiprazole	+++	++	+	+++	++	++	++	+/-
Brexpiprazole	++++	++++	++	++++	+++	++	++	+
Cariprazine	+++	++	+	++++	+	+	++	+
Lumateperone	+	+++	+	++	++	+	+	+

+/- negligible affinity, + low affinity, ++ moderate affinity, +++ high affinity, ++++ very high affinity
† Antipsychotic receptor activity may differ slightly by source.
*Activity at individual muscarinic receptors may vary.

First generation antipsychotics (FGAs): High potency FGAs have a high affinity for the D_2 receptor and a low affinity for alpha-adrenergic, histaminergic, and muscarinic receptors vs. low-potency FGAs, which have a low affinity for the D_2 receptor and a high affinity for alpha-adrenergic, histaminergic, and muscarinic receptors.

Table 5. Effects of Receptor Blockade and Associated Discontinuation/Rebound Effects

Receptor	Relevant Effects of Receptor Blockade	Expected Rebound/ Discontinuation Effect
D_2	Antipsychotic, anti-manic, and anti-aggressive effects, extrapyramidal symptoms	Psychosis, mania, agitation/aggression, withdrawal dyskinesias
α_1	Orthostasis	Tachycardia, hypertension
α_2	Increased blood pressure	Hypotension
H_1	Sedation, anxiolysis, weight gain	Insomnia, restlessness, anxiety, agitation
$M_{1\text{-}5}$	Impaired cognition, sedation, dry mouth, constipation, tachycardia, hypertension, urinary retention, blurred vision, mitigation of extrapyramidal symptoms	Agitation, confusion, anxiety, insomnia, sialorrhea, diarrhea, nausea, vomiting, sweating, bradycardia, hypotension, syncope, extrapyramidal symptoms
5-HT_{1A} (partial agonism)	Anxiolysis, antidepressant effects, mitigation of extrapyramidal symptoms	Anxiety, extrapyramidal symptoms
5-HT_{2A}	Sedation, mitigation of extrapyramidal symptoms	Insomnia, extrapyramidal symptoms
5-HT_{2C}	Carbohydrate craving, increased appetite, weight gain	Decreased appetite

Long-Acting Injectable (LAI) Antipsychotics

Use of a long-acting injectable antipsychotic should be considered for patients with significant noncompliance or partial compliance leading to decompensation, poor function, and/or requirement for compelled medications. A brief trial of the corresponding oral antipsychotic formulation should be provided, when possible, to establish tolerability before starting the LAI formulation. A longer (14 day) trial of oral aripiprazole may be necessary due to the long half-life of this medication. After 6 months of LAI treatment, it is recommended that a transition back to oral therapy be considered if the patient's symptoms have stabilized and compliance with oral medications is >80%.

Table 6: Long-Acting Injectable Antipsychotics

GENERIC NAME (BRAND NAME)	FORMULARY AGENT	USUAL DOSAGE	MAXIMUM DOSAGE
Haloperidol decanoate (Haldol-D®)	Y	50-200 mg Q 4 wks	450 mg Q 4 wks
Fluphenazine decanoate (Prolixin-D®)	Y	25-50 mg Q 2-3 wks	100 mg Q 2 wks
Risperidone long acting (Risperdal Consta®)	N	25-50 mg Q 2 wks	50 mg Q 2 wks
Paliperidone palmitate (Invega Sustenna®)	N	39-234 mg Q 4 wks	234 mg Q 4 wks
Paliperidone palmitate (Invega Trinza®)	N	273-819 mg Q 3 mos	819 mg Q 3 mos
Paliperidone palmitate (Invega Hafyera®)	N	1,092-1,560 mg Q 6 mos	1,560 mg Q 6 mos
Aripiprazole long acting (Abilify Maintena®)	N	400 mg Q 4 wks	400 mg Q 4 wks
Aripiprazole lauroxil (Aristada)®	N	441-882 mg Q 4 wks	882 mg Q 4 wks

Initiating Long-Acting Injectable Antipsychotics

Haloperidol Decanoate (Haldol-D®)*

Loading dose method (preferred)
- Month 1: Initiate haloperidol decanoate at 20 times the oral haloperidol dose; discontinue oral haloperidol at time of first injection
- Month 2: Haloperidol decanoate 15 times the oral haloperidol dose
- Month 3 and thereafter: Haloperidol decanoate 10 times the oral haloperidol dose

Traditional dosing method
Initiate haloperidol decanoate at 10-15 times the oral haloperidol dose. Provide oral overlap for 1 month.

*Note: Initial doses > 100 mg should be administered as 2 separate injections spread out by 3-7 days.

Fluphenazine Decanoate (Prolixin D®)

Initiate fluphenazine decanoate at 1.2-1.6 times the oral fluphenazine dose; continue oral fluphenazine for 1-4 weeks, then discontinue

Risperidone Long-Acting Injection (Risperdal Consta®)

Initiate Risperdal Consta at 25mg IM q 2weeks; continue oral risperidone for 3 weeks, then discontinue. A 12.5 mg starting dosage may be considered for patients with poor psychotropic tolerability or those on CYP2D6 inhibitors.

Paliperidone palmitate (Invega Sustenna®)

Initiate 234 mg IM, then give 156 mg IM in 1 week. A monthly maintenance dose of 117 mg IM may be initiated 4 weeks later and adjusted as necessary thereafter. Oral overlap is not recommended. Dosage adjustment is necessary in renal dysfunction and considered for patients on strong CYP3A4 or P-gp inducers.

Paliperidone palmitate (Invega Trinza®)

May initiate after 4 monthly injections of Invega Sustenna, as long as the last two doses have been stable. Dosing is determined based on dosage equivalencies in table below.

Paliperidone palmitate (Invega Hafyera®)

May initiate after treatment with either once- a month paliperidone palmitate extended-release injection for at least 4 months or an every-3-month paliperidone palmitate extended-release injection for at least one 3-month cycle.

Aripiprazole long acting (Abilify Maintena®)

Initiate 400 mg IM once monthly with 14 days of oral overlap. Dosage adjustment is recommended if adverse effects develop, in CYP2D6 poor metabolizers, and in patients prescribed a concomitant CYP2D6 and/or 3A4 inhibitor for >14 days.

Aripiprazole lauroxil (Aristada®)

Dosing is determined based on previous oral dosage (table 8). Provide oral overlap for 21 days. Dosage adjustment may be required for patients prescribed a CYP2D6 or 3A4 inhibitor for >14 days, or a CYP3A4 inducer.

Converting from one LAI Antipsychotic to an Alternative LAI Antipsychotic*

Table 7. Conversion to and from Risperidone and Paliperidone Long-Acting Injections

RISPERIDONE LONG-ACTING (RISPERDAL CONSTA®) DOSAGE	APPROXIMATE EQUIVALENT PALIPERIDONE PALMITATE (INVEGA SUSTENNA®) DOSAGE	APPROXIMATE EQUIVALENT PALIPERIDONE PALMITATE (INVEGA TRINZA®) DOSAGE
25 mg IM every 2 weeks	78 mg IM every 4 weeks	273 mg IM every 3 months
37.5 mg IM every 2 weeks	117 mg IM every 4 weeks	410 mg IM every 3 months
50 mg IM every 2 weeks	156 mg IM every 4 weeks	546 mg IM every 3 months
----------	234 mg IM every 4 weeks	819 mg IM every 3 months

*There is currently insufficient data on dose conversion to and from long-acting injections other than the paliperidone palmitate and risperidone LAIs.

Transitioning from Long-Acting Injectable Antipsychotics back to Oral Therapy

Table 8. Oral Antipsychotic Dosage Equivalents for Long-Acting Injectable Antipsychotics

LONG-ACTING INJECTION	DOSAGE (MG)	APPROXIMATE EQUIVALENT ORAL DOSAGE (MG/DAY)
Haloperidol decanoate (Haldol-D®)	10 times the daily oral dose given once monthly	1/10 of the monthly LAI dose given daily
Fluphenazine decanoate (Prolixin-D®)	12.5 mg IM every 3 weeks	10 mg/day
Risperidone long acting (Risperdal Consta®)	25 mg IM every 2 weeks	≤ 3 mg/day
	37.5 mg IM every 2 weeks	3-5 mg/day
	50 mg IM every 2 weeks	>5 mg/day
Paliperidone palmitate (Invega Sustenna®)	39-78 mg IM every 4 weeks	3 mg/day
	117 mg IM every 4 weeks	6 mg/day
	156 mg IM every 4 weeks	9 mg/day
	234 mg IM every 4 weeks	12 mg/day
Paliperidone palmitate (Invega Trinza®)	273 mg IM every 3 months	3 mg/day
	410 mg IM every 3 months	6 mg/day
	546 mg IM every 3 months	9 mg/day
	819 mg IM every 3 months	12 mg/day
Paliperidone palmitate (Invega Hafyera®)	1,092 mg IM every 6 months	9 mg/day
	1,560 mg IM every 6 months	12 mg/day
Aripiprazole long acting (Abilify Maintena®)*	400 mg IM every 4 weeks	N/A
Aripiprazole lauroxil (Aristada®)	441 mg IM every 4 weeks	10 mg/day
	662 mg IM every 4 weeks 882 mg IM every 6 weeks 1064 mg IM every 2 months	15 mg/day
	882 mg IM every 4 weeks	≥ 20 mg/day

*No data available on equivalent dosing

Additional Guidance: Switching from an LAI to an oral antipsychotic may be accomplished by initiating an equivalent oral dosage on the date that the next LAI is due. Alternatively, a 4 week overlap period may be considered to allow for observation of oral adherence prior to discontinuation of the LAI. The LAI may then be abruptly discontinued, as its long half-life should limit the risk of discontinuation reactions. A brief cross-taper is another alternative that may be considered.

AGENTS USED IN THE TREATMENT OF BIPOLAR DISORDER

Table 9: Agents Used to Treat Bipolar Disorder

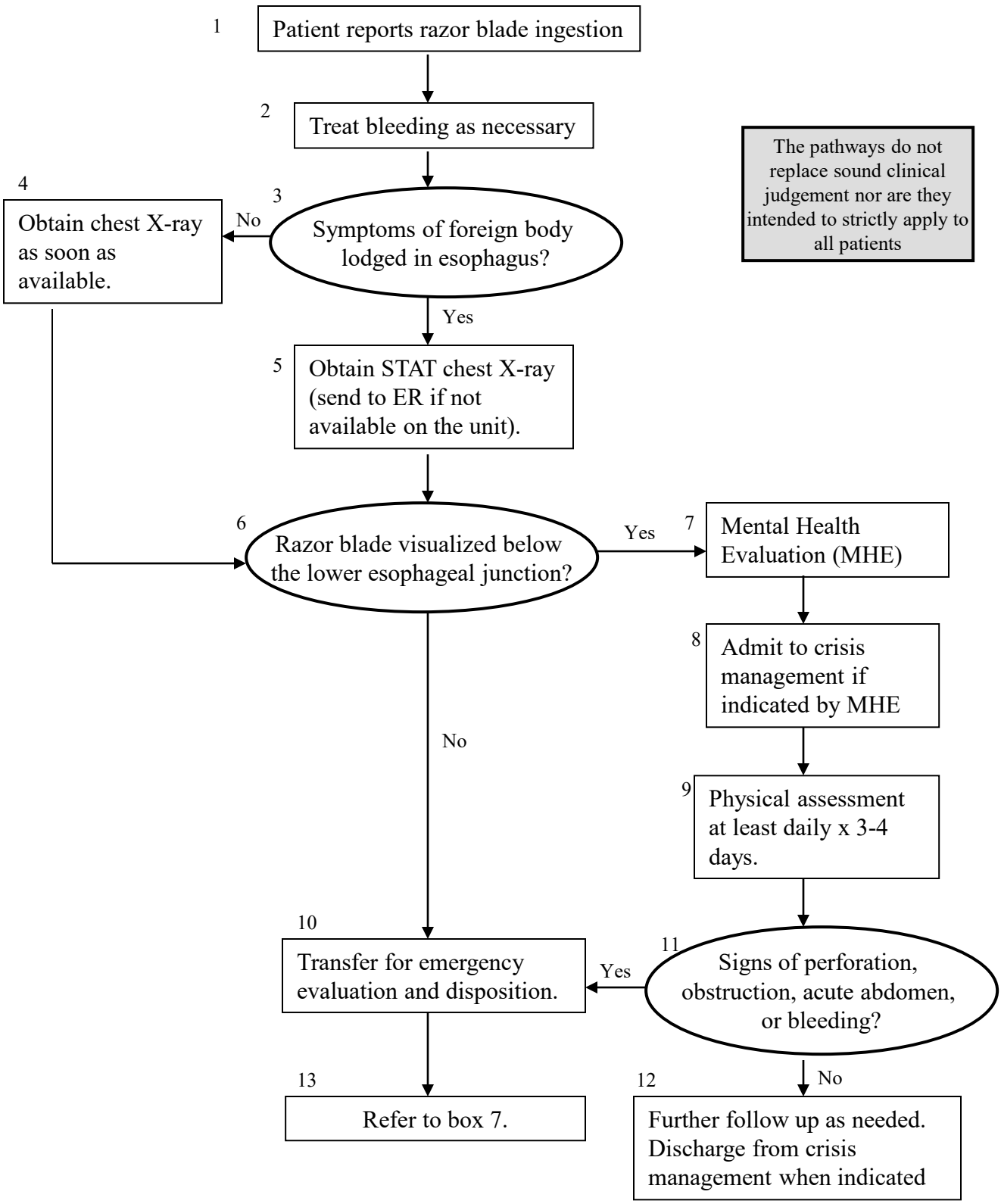
GENERIC NAME (BRAND NAME)	FORMULARY AGENT	USUAL DOSE (MG/DAY)	TARGET DRUG CONCENTRATION
Lithium	Y	900-1800	0.6 – 1.2 mmol/L
Olanzapine and Fluoxetine (Symbyax®)	N	6/25-12/50	N/A
Anticonvulsant Agents			
Oxcarbazepine (Trileptal®)	N	1200-2400	N/A
Carbamazepine (Tegretol®)	Y	IR= 400-1600 ER= 400-1600	4-12 mcg/mL*
Lamotrigine (Lamictal®)	N	100-400	N/A
Valproic Acid (Depakene®)	N	1000-2800 (20 mg/kg/d)	50-125 mcg/mL
Divalproex Sodium (Depakote®)	Y (DR only)	1000-2800 (DR= 20 mg/kg/d) (ER = 25 mg/kg/d)	50-125 mcg/mL
Second Generation Antipsychotics			
Olanzapine (Zyprexa®)	N	5-20	N/A
Quetiapine (Seroquel®)	N	Regular Release = 300-800 ER = 300-800	N/A
Risperidone (Risperdal®)	Y	2-6	N/A
Ziprasidone (Geodon®)	Y	80-160	N/A
Aripiprazole (Abilify®)	Y	10-30	N/A
Asenapine (Saphris®)	N	10-20	N/A
Lurasidone (Latuda®)	N	20-60	N/A
Cariprazine (Vraylar®)	N	3-6	N/A
Lumateperone (Caplyta®)	N	42	N/A

**Serum concentrations established for treatment of seizure disorders are generally applied*

Switching Agents for the Treatment of Bipolar Disorder

If intolerance is not present, the new agent should be started and titrated to an effective dose before the current agent is tapered and discontinued. The old agent may then be decreased gradually over the next month. The goal is to avoid abrupt discontinuation of the old medication until the new agent is established.

Management of Razor Blade Ingestion



The pathways do not replace sound clinical judgement nor are they intended to strictly apply to all patients

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider**.

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Approved 7/2006. Reviewed 3/09, 3/12. Revised 3/19, 11/23

Management of Razor Blade Ingestion

While razor blade ingestion has the potential for severe outcomes, it generally is not as serious as many would think. Once the razor blade reaches the stomach, gastric acid quickly dulls the edge and erodes the body of the razor blade. The most dangerous potential complication of razor blade ingestion is esophageal perforation. Once the blade has passed into the stomach the risk of serious complications is much lower.

When a foreign body is ingested, the most clinically significant locations for it to be come lodged are the level of the cricopharyngeus muscle and the ileocecal valve. However, most foreign bodies that have passed through the esophagus will continue to pass through the body uneventfully.

When a patient gives a history of razor blade ingestion, treat clinically significant bleeding if present. A chest x-ray should be obtained and should be adequate to visualize the entire esophagus. This may require 2 films.

If x-ray is not immediately available on the unit, it may be acceptable to observe the patient closely while awaiting the x-ray, if the patient is asymptomatic. Mental health evaluation may be done during this period if indicated. However, if the patient is symptomatic of a foreign body lodged in the esophagus, the CXR should be done as soon as possible and may require transfer to a local medical center.

If the x-ray shows the razor blade above the level of the lower esophageal junction, or if the patient has signs or symptoms of esophageal perforation (swelling, erythema, tenderness or crepitus in the neck region, or fever or chest pain), they should be referred immediately to an appropriate medical center for removal of the foreign body.

If the razor blade has already passed into the stomach, off site referral is rarely needed. Mental health evaluation should be done if indicated. The patient should be examined daily for 3-4 days with particular attention to the RLQ location of the ileocecal valve. The patient should be instructed to return immediately if they experience localized abdominal pain, vomiting, abdominal distension, melena or rectal bleeding, fever or dizziness.

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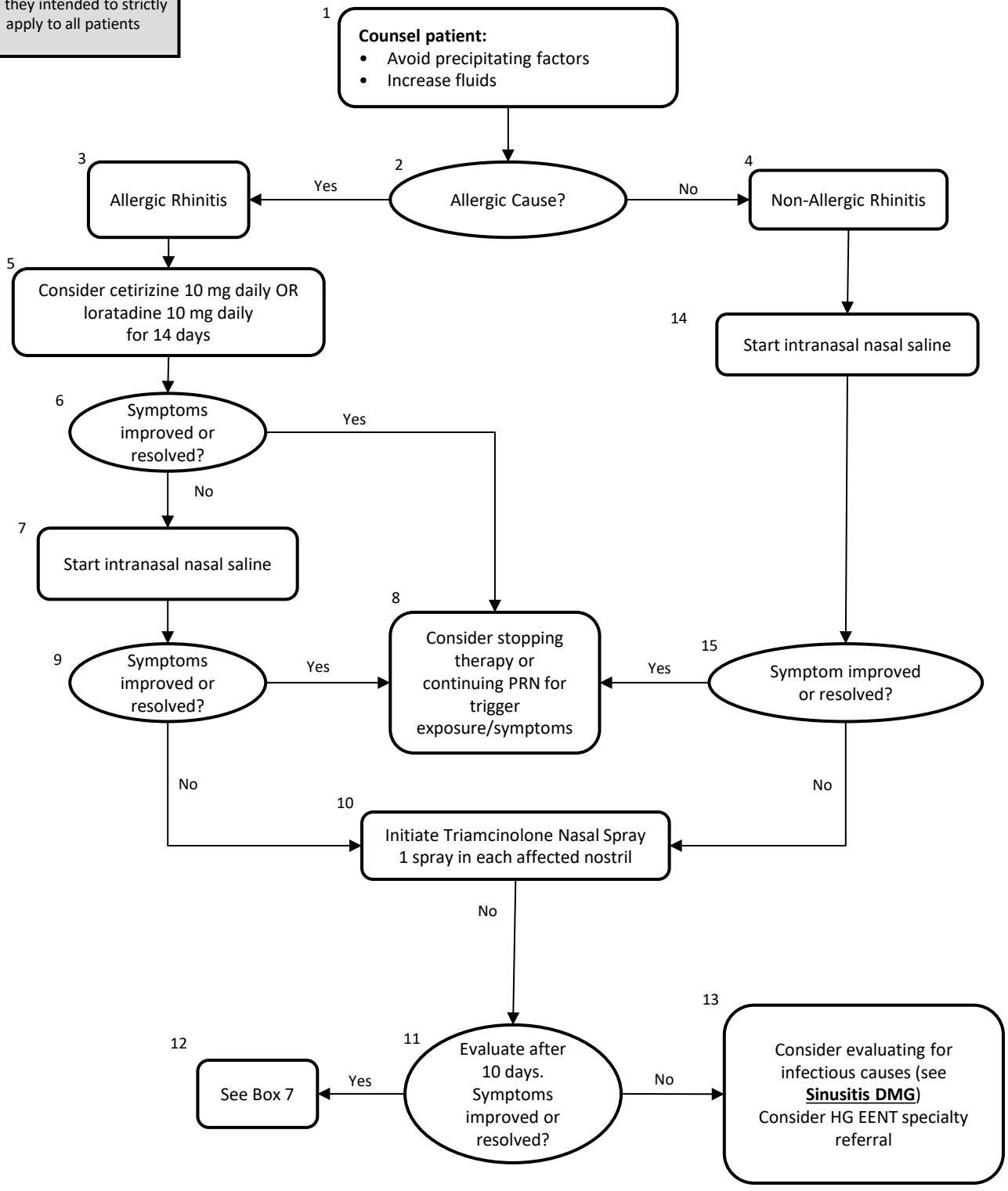
RHINITIS



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Reviewed 5/11, 11/14, 7/18; Revised 8/98, 12/98, 3/01, 4/03, 3/07, 5/07, 1/10, 5/23, 3/25.

Table 1. Common Symptoms of Allergic Rhinitis and Non-Allergic Rhinitis
(Differentiating Symptoms are **Bolded**)

Allergic Rhinitis (AR)	Non-Allergic Rhinitis (NAR)
- Rhinorrhea and sniffing (most common symptom in AR, clear and watery) - Sneezing (Very common) - Nasal congestion - **Ocular pruritis** - **Nasal/palate/ear itching** - Chronic cough - Sleep disturbance/sleep apnea	- May or may not have rhinorrhea (les common in NAR) - Sneezing (less common in NAR) - Nasal congestion, mouth breathing - **Post-nasal drip** (Very common) - **Constant clearing of throat** - **Facial or sinus pain/pressure** - Snoring - Sleep disturbances/sleep apnea - Headache as part of symptomology

Table 2. Clinical Pearls on Formulary Agents for Rhinitis

Medication Class	Common Dosing	Caution Regarding Prescribing
Oral Second-Generation Antihistamines • Cetirizine 10 mg • Loratadine 10 mg	1 tablet per day	- May need to be dose reduced in significant kidney/liver injury
Intranasal Saline	2 to 3 sprays in each nostril as needed	- Minimal risk for all populations when administered appropriately
Intranasal Steroids • Triamcinolone 55 mcg Nasal Spray	1 spray in each nostril per day (maximum: 2 sprays in each nostril twice daily, maximum of two refills)	- Consistent use can assist with response to symptoms but consider prioritizing use with allergen exposure. Can be used PRN. - Although the risk is minimal, long-term use of nasal steroids may contribute to increased ocular pressure. Monitor intraocular pressure in patients with pre-existing glaucoma or those at significant risk. - Although risk has been demonstrated to be minimal, long-term use can also contribute to adrenal suppression, osteoporosis, and growth suppression. Do not exceed maximum dose and consider minimal duration or PRN use when used with other steroid agents. - Assess technique when prescribing. Ensure patient does not aim for septum when administering.

Acute Seizures

1

Seizure Activity for 0-5 Minutes

- Confirm clinical findings by observing continuous seizure activity or one additional seizure.
- Rule out suspected symptom amplification.
- Rule out underlying medical issue.

2

Suspect seizure activity?

No → 3

Observe x 2 hours; if no activity, discharge from medical department.

Yes

4

- Administer oxygen by nasal cannula or mask, position head for unobstructed airway, consider intubation if respiratory assistance is needed.
- Obtain and record vital signs, initiate ECG monitoring.
- Establish an IV (normal saline).
- Obtain glucose finger stick. If glucose is < 60mg/dl or if blood glucose is not available, consider administering 50 mL IV D50W. If alcohol abuse is suspected, consider administering 100 mg IV thiamine prior to glucose administration.
- Draw venous samples for glucose, chemistries, hematology parameters, toxicology screens, and antiepileptic drug (AED) levels (if available).
- Determine oxygenation with oximetry or arterial blood gases (if available).

5

Seizure activity continuing for 5-20 minutes?

No → 6

- New onset seizures: refer to Seizure Disorder DMG for care.
- Consider administering extra dose of currently ordered oral AED if receiving treatment.
- Observe for a minimum of 2 hours and discharge from medical after full recovery.
- Follow up with medical provider in 48-72 hours.
- Follow up in Chronic Care Clinic per ITP.
- Confirm medication adherence.
- Modify therapy if indicated per Seizure Disorder DMG.

Yes

7

- AED therapy should be initiated if seizure lasts >5 minutes.
- Administer lorazepam 4 mg at 2 mg/minute by slow IVP
- May repeat after 10 minutes (usual maximum total dose 8 mg) if seizures do not stop or another begins.
- Monitor BP and watch for signs of respiratory depression.
- If IV access is unavailable, transport to a higher level of care.

8

Seizure activity continuing for 20-40 minutes?

No → 9

- New onset seizures: refer to Seizure Disorder DMG for care.
- Consider administering extra dose of currently ordered oral AED.
- Observe for a minimum of 2 hours and discharge from medical after full recovery.
- Follow up next day and obtain AED serum levels.
- Follow up in Chronic Care Clinic per ITP.
- Confirm medication adherence.
- Modify therapy if indicated per Seizure Disorder DMG.

Yes

10

- If the patient does not respond to 2 doses of lorazepam, transport to a higher level of care- transfer to the nearest emergency room.
- Follow current unit protocol.
- Follow up within 1 week upon return from the emergency room or hospital.
- Confirm medication adherence and reinforce education.
- Obtain AED serum levels and adjust treatment plan if indicated.
- Follow up in chronic care clinic per ITP.
- New onset seizures: refer to Seizure Disorder DMG for care.

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Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee, March 1998, Reviewed 3/01, 4/03, 1/07, 1/13, 1/23. Revised 7/07, 10/08, 9/10, 11/18, 9/20.

Seizure Disorder

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**One seizure event is not necessarily diagnostic for a seizure disorder and may not require long-term AED therapy*

1 Seizure activity and seizure classification documented?*

No → 2 Attempt accurate diagnosis if new onset. Rule out underlying medical etiology. Consult Neurology if necessary.

Yes → 11 Confirm diagnosis of seizure disorder.

2 → 3 Is patient on AED therapy?

Yes → 5 Is antiepileptic drug (AED) therapy appropriate for diagnosis?

12 Is patient on AED therapy? → Yes → 5

3 Is patient on AED therapy? → No → 4

4 If seizure disorder is confirmed, initiate AED therapy based on seizure classification (App. A and B). Go to box 7

OR

If seizure activity is ruled out, discontinue from Chronic Care Clinic

OR

If no seizure activity for ≥ 2 years, may consider discontinuing from Chronic Care Clinic and any associated restrictions.

12 Is patient on AED therapy? → No → 13

13
- Initiate AED based on seizure classification (App. A and B).
- Go to box #7.
- If patient has been seizure free for > 2 years, may consider discontinuing from Chronic Care Clinic and any associated restrictions.

5 Is antiepileptic drug (AED) therapy appropriate for diagnosis?

No → 6

6 Initiate AED regimen (App. A and B). Once new AED is at therapeutic dose, taper the old agent slowly and discontinue. Go to box 7.

OR

Discontinue AED if chronic seizure diagnosis is ruled out.

Successful discontinuation of AED may be possible if:
- Seizure free for ≥ 2 years
- Single type of partial or generalized seizure
- Normal neurological exam
- EEG normalized with AED treatment

Yes → 7

7
- Check medication compliance.
- Obtain AED level if indicated.
- Obtain baseline labs appropriate for AED (App. C).

7 → 8 Is AED therapy effective and tolerated?

No → 9
- Monitor & obtain laboratories appropriate for AED utilized (App. C).
- Counsel on importance of compliance.
- Adjust dose.

OR

- Change to alternate AED. Once new AED is at therapeutic dose, taper the old agent slowly and discontinue.

OR

- Add additional AED if patient has failed 2 monotherapy regimens.
- Consider referral if patient remains poorly controlled.

Yes → 10
- Follow up in Chronic Care Clinic as clinically indicated.
- Monitor & obtain laboratories appropriate for AED utilized. (App. C).
- Consider discontinuation of AED if patient has a normal EEG and has been seizure free for > 2 years. Slowly taper AED over 3-6 months and then discontinue.

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I. Definitions:

- **Seizure -** isolated clinical event consisting of paroxysmal discharges occurring synchronously in a large population of cortical neurons, characterized on the electroencephalogram (EEG) as a sharp wave or "spike."
- **Epilepsy -** a chronic disorder of the nervous system characterized by recurrent and unprovoked seizures. Term may be applied after two unprovoked seizures occurring greater than 24 hours apart or one unprovoked seizure with the probability of further seizure events > 60% over the next 10 years.
- **Status epilepticus** - continuous seizure activity or 2 or more seizures without full recovery of consciousness between seizures lasting longer than 30 minutes.

II. Initial Assessment

A. Medical history:

1. Verify any existing seizure diagnoses
2. Identify exact seizure type by obtaining a detailed seizure history
    a. Age at onset and frequency of seizure
    b. Symptoms during ictal and post-ictal phase (patient and observer)
    c. Seizure triggers (e.g., sleep deprivation, alcohol, stress)
3. Identify all comorbidities
4. Identify possible causes including family history of epilepsy, history of head trauma, birth complications, febrile convulsions, alcohol or drug abuse, cancer, or vascular abnormalities (stroke).

B. Medication history:

1. Identify all current and prior medication regimens including response and adverse events.
2. Rule out alcohol or other drug withdrawal seizures as these do not generally require AED therapy.
3. Rule out drugs which may cause or exacerbate seizures (e.g., psychotropics, antimicrobials, stimulants, narcotics, lidocaine, metoclopramide, theophylline, antiarrhythmics, antiepileptics, baclofen).

C. Physical examination:

1. Identify disorders associated with seizures, including head trauma, infections of the ears or sinuses (which may spread to the brain), congenital abnormalities, neurological disorders, alcohol or drug abuse, metabolic disorders, or cancer.
2. A complete neurologic and mental status exam should be performed.

D. Electroencephalographic (EEG) studies:

1. The purpose of the EEG is to confirm the presence of abnormal electrical activity, provide information about the type of seizure disorder, and locate the seizure focus. An EEG should be used to support the diagnosis of epilepsy and cannot rule out seizure disorder.
2. Approximately 50% of epileptic patients show no abnormality on a single EEG, and 10% of persons with true seizures show no abnormalities on multiple EEG studies.

E. Lab tests and neuroimaging: The following tests may be useful in determining the underlying cause of seizure activity.

1. Electrolytes
2. Blood glucose
3. Liver and kidney function
4. Toxicology screening
5. MRI (CT if unavailable or contraindicated)
6. 12 lead ECG
7. Lumbar puncture if infection suspected
8. Prolactin levels if pseudoseizure is suspected

F. Treatment plan:

1. Treatment with AED therapy is generally recommended after a second epileptic seizure. Selection of an appropriate AED should be based on the following:
    a. Age and child-bearing potential
    b. Seizure type and syndrome
    c. Comedications
    d. Comorbidities
    e. AED adverse effect profile
2. AED initiation after the first seizure may be warranted in patients with a high risk of recurrence (e.g., unequivocal epileptic activity on EEG, structural abnormality, or family history of seizures).

G. Principles of Treatment

1. Goals of therapy
    a. Seizure free with minimal adverse effects
    b. Maintain normal lifestyle
    c. Use lowest effective AED dose
2. Assessment of disease control
    a. Good control – seizure free since last visit or last 6 months
    b. Fair control – 1 seizure since last visit or in last 6 months
    c. Poor control – $\geq$ 2 seizures since last visit or last 6 months
3. Potential reasons for treatment failure
    a. Incorrect diagnosis
    b. Incorrect AED for seizure type/syndrome
    c. Subtherapeutic level (inadequate dosing, drug interactions, poor adherence- most common reason for treatment failure)
    d. Refractory seizures

4. Step therapy
    a. Monotherapy is preferred. Generally, consider at least 2 monotherapy trials before using combination therapy. Two-thirds of patients become seizure free with the first or second drug prescribed. When switching agents, the old agent should be continued until a therapeutic level of the new drug is achieved. The old agent is then tapered slowly and discontinued.
    b. Polytherapy with 2 agents - if indicated, add an AED with a different mechanism of action. Start low and titrate slowly. Confirm medication adherence prior to the addition of a second agent.
    c. Polytherapy with $\geq$ 3 agents – rarely needed. Consider only after 2 or more adequate trials of dual AEDs have failed, adherence is confirmed, and a combination of AEDs is tolerated and significantly reduces seizure frequency or severity. Consider referral prior to triple AED therapy.
    d. Consider patient co-morbidities and possible drug interactions upon initiation of therapy, during therapy, and upon drug discontinuation. Many of the AEDs may increase or decrease metabolism of other medications.
5. Use of newer AEDs
    a. Recommended for those who have failed traditional or first-generation AEDs or when traditional AEDs are unsuitable (contraindications, drug interactions, intolerance, pregnancy, etc.).
    b. Traditional AEDs have the advantage of broad familiarity, lower cost, known efficacy and long-term experience.
6. Pregnancy considerations
    a. Benefits versus risks must be weighed during pregnancy. The fewest number of antiepileptic agents (and lowest dose) that control seizures should be used.
    b. Fetal risk cannot be ruled out - gabapentin, lamotrigine, levetiracetam, oxcarbazepine, phenobarbital, phenytoin, primidone, tiagabine, vigabatrin
    c. Fetal harm has been demonstrated - carbamazepine
    d. Contraindicated – valproic acid
    e. If possible, avoid carbamazepine and valproic acid

H. Pseudoseizures

1. Definition- episodes involving affective, autonomic, or sensorimotor manifestations that are precipitated by emotional distress. Also known as nonepileptic seizures, hysterical seizures, pseudoseizures, and nonepileptic attack disorder.
2. Epidemiology- pseudoseizures account for 15-20% of admissions to epilepsy units. Women are affected more frequently than men by a factor of 3.5:1. Peak incidence is in the third to fourth decades.

Table 1. Clinical characteristics of pseuodseizures

Strongly Suggestive of Pseudoseizure	Strongly Against Pseudoseizure
• Prolonged duration of event (10-30 minutes) • Preservation of consciousness despite whole body jerking • Bizarre and asynchronous motor movements • Pelvic thrusting movements • Not stereotypical	• Injuries sustained during spells • Tongue laceration, especially sides of tongue • Incontinence

3. The diagnosis of pseudoseizure should not be solely based on clinical information. Video EEG monitoring is recommended if pseudoseizure is suspected.
4. Elevated prolactin may be predictive of tonic clonic or partial seizures (more reliable in tonic clonic seizures). Blood sample should optimally be drawn within 30 minutes of seizure. A normal prolactin level does not confirm pseudoseizures.
5. Management- Anticonvulsant therapy is not indicated in pseudoseizures; a mental health referral should be considered. Psychotherapy and drug therapy for underlying psychiatric disorder is indicated in most cases. Psychogenic seizures occur in patients with conversion disorders, anxiety and panic disorder, depression, post-traumatic stress disorder, schizophrenia, and personality disorders.

III. Withdrawal of Anticonvulsants.

A. Risk of Seizure Relapse:

1. Relapse rates are highest in the first 12 months (especially in the first 6 months) after AED withdrawal.
2. Risk of relapse continues to decrease with time.

B. Considerations for AED Discontinuation:

1. Seizure-free for a minimum of two years on AED treatment
2. Single type of focal seizure or a single type of generalized tonic-clonic seizure
3. Normal neurological examination and normal intelligence quotient IQ
4. EEG normalized with treatment

C. Drug Discontinuation:

1. Risks and consequences of seizure recurrence versus continued treatment should be weighed.
2. If discontinuation of AED is warranted, the tapering schedule should be slow (most clinical trials suggest dose should be tapered over 6 months) and tailored to the specific drug, dosage, and serum concentrations for each patient.

Table 2. Factors to consider when discontinuing AEDs

Factors Against Drug Withdrawal	Factors in Favor of Drug Withdrawal
• Adolescent-onset epilepsy • Adult-onset epilepsy • Focal epilepsy • Juvenile myoclonic epilepsy • Presence of underlying neurological condition • Abnormal EEG (children)	• Childhood-onset epilepsy • Elderly-onset epilepsy • Idiopathic generalized epilepsy • Benign epilepsy with centrotemporal spikes • Normal EEG (children) • Childbearing potential and planning pregnancy • Co-morbidity with concurrent treatments

D. Phenobarbital Tapering

1. Phenobarbital monotherapy – if AED needs to be continued, the new agent should be started, and therapeutic levels achieved prior to initiating phenobarbital taper (Table 3).
2. Phenobarbital polypharmacy – please note that monotherapy is preferred
    a. If patient is a good candidate for monotherapy (based on type of seizure, history of past treatments, compliance), initiate phenobarbital taper (Table 3) without the addition of another agent.
    b. If patient needs to be continued on polytherapy, a new agent should be started, and therapeutic levels achieved prior to initiating the phenobarbital taper (Table 3).

Table 3: Phenobarbital taper

Tapering schedule: Decrease phenobarbital dose by 30 mg a month over 1–6-month period. Example: Patient is receiving 120 mg/day 1st month, patient receives 90 mg/day 2nd month, patient receives 60 mg/day 3rd month, patient receives 30 mg/day 4th month, patient receives 0 mg/day
Labs: If patient has undetectable phenobarbital levels (< 2 mg/L) and a history of noncompliance, a taper may not be necessary
Monitor: Provider must monitor patient for any new seizure activity. Determine if the underlying disorder has returned or if the seizures were the result of withdrawing the phenobarbital too quickly. Phenobarbital should be tapered more slowly if the latter is true.

A. Focal seizures - Begin in one hemisphere of the brain and, unless they become focal to bilateral tonic-clonic, result in an asymmetric clinical manifestation. Focal epilepsy may begin in infancy and may be difficult to recognize in the elderly population.

1. Focal aware seizure - no loss of consciousness
    a. Motor function symptoms
    b. Sensory or somatosensory symptoms
    c. Automatisms
2. Focal impaired awareness seizure - alteration/loss of consciousness
    a. Focal aware onset followed by impairment of consciousness, with or without automatisms
    b. Impaired consciousness at onset, with or without automatisms
    c. Other symptoms may include memory loss or aberrations of behavior
    d. May be misdiagnosed as psychotic episodes
    e. Generally amnestic to these events
3. Focal to bilateral tonic-clonic - focal onset evolving to generalized tonic-clonic seizures
4. Treatment Options:
    a. Formulary: carbamazepine, divalproex sodium, levetiracetam*, phenytoin, primidone
    b. Nonformulary: eslicarbazepine, gabapentin*, lacosamide*, lamotrigine, oxcarbazepine, perampanel, phenobarbital, tiagabine*, topiramate, vigabatrin±, zonisamide*

B. Generalized Seizures - Involves both brain hemispheres with bilateral motor manifestations and loss of consciousness

1. Generalized Absence Seizure - sudden onset, brief (seconds), blank stare, possibly a brief upward rotation of the eyes, and lip-smacking (confused for daydreaming)
    a. Generally, occurs in young children through adolescence
    b. Can be precipitated by hyperventilation
    c. EEG during the seizure has a characteristic 2-to-4 cycle/s spike and slow-wave complex
    d. Important to differentiate from focal impaired awareness seizures
    e. Formulary treatment options: divalproex sodium
    f. Nonformulary treatment options: clonazepam, ethosuximide, lamotrigine
2. Generalized Tonic-Clonic Seizure (formerly called grand mal seizure) - includes both an atonic and clonic phase
    a. Tonic phase: rigid, violent, sudden muscular contractions (stiff or rigid); cry or moan; deviation of the eyes and head to one side; rotation of the whole body and distortion of features; suppression of respiration; falls; loss of consciousness; tongue biting; involuntary urination
    b. Clonic phase: repetitive jerks; cyanosis continues; foam at the mouth; small grunting respirations between seizures; deep respirations as all muscles relax at the end of the seizure
    c. Formulary treatment options: carbamazepine, divalproex sodium, levetiracetam*, phenytoin, primidone
    d. Nonformulary treatment options: gabapentin*, lamotrigine, oxcarbazepine, phenobarbital, topiramate
3. Myoclonic Seizure - Brief shock-like muscular contractions of the face, trunk, and extremities. May be isolated or rapidly repetitive.
4. Atonic Seizure - sudden loss of muscle tone lasting 1-2 seconds
    a. May be described as a head-drop, the dropping of the limb, or a slumping to the ground
    b. These patients often wear protective head-ware to prevent trauma
    c. Formulary treatment options: divalproex sodium, levetiracetam*, primidone
    d. Nonformulary treatment options: phenobarbital, oxcarbazepine, topiramate
5. Juvenile Myoclonic Epilepsy (JME) - Myoclonic seizures precede generalized tonic-clonic seizure
    a. Generally, occur upon awakening
    b. Sleep deprivation and alcohol commonly precipitate an episode
    c. Formulary treatment options: divalproex sodium
    d. Nonformulary treatment options: lamotrigine

C. Other Seizure Types

1. Catamenial Epilepsy - Associated with hormonal changes during menstruation; may be treated with acetazolamide (Diamox®)
2. Post-traumatic Epilepsy - Seizures that occur after head trauma; patients may be started on phenytoin for a period of 7 days; if no seizures occur, it should be discontinued. The utility of this therapy is controversial.

*Adjunctive therapy

±Only available through a restricted distribution program called the Vigabatrin REMS Program.

Appendix B: Antiepileptic Drugs For Specific Seizures

Begin treatment with single AED using recommended initial daily dosing. Up to 80% of patients can be managed with monotherapy. Ensure proper medication adherence prior to modifying regimen.

Type of Seizure	Formulary Medications			Nonformulary Medications		
Focal Aware	Carbamazepine Divalproex	Levetiracetam* Phenytoin	Primidone	Brivaracetam Eslicarbazepine Felbamate Gabapentin* Lacosamide*	Lamotrigine Oxcarbazepine Perampanel± Phenobarbital± Pregabalin*±	Tiagabine* Topiramate Zonisamide*
Focal Impaired Awareness	Carbamazepine Divalproex	Levetiracetam* Phenytoin	Primidone	Brivaracetam Eslicarbazepine Felbamate Gabapentin* Lacosamide*	Lamotrigine Oxcarbazepine Perampanel± Phenobarbital± Pregabalin*±	Tiagabine* Topiramate Vigabatrin§* Zonisamide*
Generalized Tonic-Clonic	Carbamazepine Divalproex	Levetiracetam* Phenytoin	Primidone	Gabapentin* Lamotrigine	Oxcarbazepine Phenobarbital±	Topiramate
Absence	Divalproex			Clonazepam*	Ethosuximide	Lamotrigine
Preferred with Clinical Evidence of Cirrhosis	Levetiracetam			Gabapentin		

*Adjunctive therapy. ±Schedule III – V controlled substances. §Only available through a restricted distribution program called the Vigabatrin REMS Program. Indicated for refractory complex partial seizures as adjunct therapy in patients that have failed several alternative treatments. Black box warning for possible permanent vision loss.

Appendix C. Monitoring Parameters for Formulary AEDs

Medication	Dosage and Monitoring Parameter & Frequency
Carbamazepine	• Prior to initiation of therapy, screen patients with ancestry in genetically at-risk populations (i.e., Asians, including South Asian Indians) for the presence of the HLA-B*1502 allele. The risk of developing Steven- Johnson syndrome and toxic epidermal necrolysis is higher in this patient population. • CBC with platelets (emphasis ANC) – baseline, monthly for the first 2 months, then every 6 months and as clinically indicated. • Chemistry (emphasis hepatic & renal function & electrolytes) – baseline, at 3 months, then annually and as clinically indicated • EKG at baseline if > 40 years old or as clinically indicated • Perform baseline and periodic eye examinations. Use with caution in patients with increased intraocular pressure. • Levels at 2 weeks, one month, and then annually or when clinically indicated. Auto-induction occurs ~ 3 days from first dose, with maximum effect at ~30 days. Dose adjustments should be made no sooner than 4 weeks after initiation. • Therapeutic level – 4 to 12 mcg/mL, toxic concentration > 15 mcg/mL
Levetiracetam	• Chemistry – renal function in patients with preexisting renal impairment • Therapeutic level – not established
Phenytoin	• CBC – baseline and when clinically indicated • Chemistry (emphasis hepatic & renal function) – baseline, then annually and as clinically indicated • EKG at baseline if > 40 years old or as clinically indicated • Levels – one week, one month, and then annually and as clinically indicated • Therapeutic level – 10 to 20 mcg/mL, toxic dose > 20 mg/kg
Primidone	• CBC – baseline and annually or when clinically indicated • Chemistry (emphasis hepatic function) – baseline, then annually and as clinically indicated • Levels – primidone and phenobarbital levels annually and as clinically indicated • Therapeutic level – 5 to 12 mcg/mL, toxic concentration > 12 mcg/mL
Valproic Acid	• CBC with platelets – baseline and when clinically indicated • Chemistry (emphasis hepatic function) – baseline, one month, then annually and as clinically indicated • Protime, INR, PTT at baseline, annually, and prior to surgery • Perform baseline and periodic fundoscopic examinations as clinically indicated • Levels – weekly for 2 weeks, then annually and as clinically indicated • Therapeutic level – 50 to 100 mcg/mL, toxic concentration >150 mcg/mL

Appendix D: Antiepileptic Drugs (AEDs)

Generic Name	Usual Dose	Adverse Effects
Formulary Agents		
Carbamazepine Tegretol®	• Initial: 200 mg twice daily. Titrate at weekly intervals as indicated. • Maintenance: 800-1200 mg/day divided in 3 or 4 doses	• Somnolence, dizziness, fatigue, ataxia, GI upset • **Serious**: agranulocytosis, aplastic anemia, hepatitis & hepatic failure, hypersensitivity, rash including Stevens Johnson & toxic epidermal necrolysis, hyponatremia
Levetiracetam Keppra®	• Initial: 500 mg once daily. Titrate every 2 weeks as indicated. • Maintenance: 1000-3000 mg/day divided in 2 doses	• Irritability, behavioral changes, somnolence, asthenia, uncoordination
Phenytoin Dilantin®	• Initial: 100 mg three times daily. • Maintenance: 300 mg/day divided in 3 doses (range of 200-1200 mg/day)	• Nystagmus, blurred vision, diplopia, ataxia, dizziness, drowsiness, headache, GI upset, gingival hyperplasia, hirsutism, acne, osteomalacia • **Serious**: rash including Stevens Johnson, blood dyscrasias, hepatotoxicity, systemic lupus erythematosus
Primidone Mysoline®	• Initial: 100-125 mg daily x 3 days. Increase by 100-125 mg daily every 3 days. • Maintenance: 750 – 1500 mg/day divided in 3 to 4 doses.	• Ataxia, dizziness, somnolence • **Serious**: megaloblastic anemia, thrombocytopenia
Valproic Acid Depakote®	• Initial: 10-15 mg/kg/day. Titrate weekly as indicated. • Maintenance: 1000-2500 mg/day in 2 to 4 divided doses (15-60 mg/kg/day).	• GI upset somnolence, ataxia, dizziness, rash • **Serious**: pancreatitis, thrombocytopenia, hepatotoxicity • Patients at increased risk for hepatotoxicity include children • Female adolescents have an increased risk for development of Polycystic Ovary Syndrome
Non-formulary Agents		
Brivaracetam Briviact® C-V	• Initial: 50 mg twice daily. • Maintenance: 25-100 mg twice daily.	• Nausea, vomiting, dizziness, sedation, fatigue • **Serious**: hypersensitivity, cerebellar ataxia, psychiatric symptoms
Eslicarbazepine Aptiom®	• Initial: 400 mg once daily. Titrate once weekly as indicated. • Maintenance: 800-1600 mg daily.	• GI upset, ataxia, dizziness, headache, somnolence, tremor, vertigo, fatigue, blurred vision, dilpopia • **Serious**: Stevens-Johnson syndrome, toxic epidermal necrolysis, hyponatremia, anaphylaxis
Ethosuximide Zarontin®	• Initial: 500 mg/day. Titrate every 4-7 days as indicated. • Maintenance: 20-40 mg/kg/day divided in 2 doses.	• Behavioral changes, anorexia, GI upset, ataxia, dizziness, headache, somnolence, hiccups • **Serious**: rash including Stevens Johnson, agranulocytosis, aplastic anemia, leukopenia, pancytopenia, systemic lupus erythematosus
Felbamate Felbatol®	• Initial: 1200 mg/day divided in 3-4 doses. Titrate every 2 weeks as indicated. • Maintenance: 3600 mg/day divided in 3-4 doses.	• GI upset, dizziness, headache, insomnia, somnolence • **Serious:** aplastic anemia, hepatic failure
Gabapentin Neurontin®	• Initial: 300 mg three times daily. • Maintenance: 900-1800 mg/day divided in 3 doses.	• Somnolence, dizziness, ataxia, fatigue, weight gain, peripheral edema, behavioral changes in children
Lacosamide Vimpat® C-V	• Initial: 100 mg twice daily. Titrate weekly as indicated. • Maintenance: 200-400 mg/day divided in 2 doses.	• Dizziness, nausea, vertigo, abnormal coordination and ataxia are the most frequently reported side effects • **Serious:** atrial fibrillation and flutter, first degree atrioventricular block, drug hypersensitivity syndrome
Lamotrigine Lamictal®	• Initial: o Monotherapy: 25 mg/day x 2 wk, 50 mg/day x 2 wk. Titrate by 50 mg/day every 1-2 weeks as indicated. o With VPA: 25 mg every other day x 2 wk, 25 mg daily x 2 wk. Titrate by 25-50 mg/day every 1-2 weeks as indicated. o With enzyme inducers*: 50 mg/day x 2 wk, 50 mg bid x 2 wk. Titrate by 100 mg/day every 1-2 weeks as indicated. • Maintenance: o Monotherapy: 225-375 mg/day divided in 2 doses. o With VPA: 100-200 mg/day. o With enzyme inducers*: 300-500 mg/day divided in 2 doses.	• Tics in children, insomnia, dizziness, headache, diplopia, ataxia, nausea, vomiting, somnolence • **Serious**: Rash including Stevens Johnson & toxic epidermal necrolysis. Usually occurs in first 2-8 weeks. Increased risk in children, rapid dose titration, and concomitant use of valproic acid. Risk reduced with slow titration. Hypersensitivity reactions including risk of hepatic and renal failure, disseminated intravascular coagulation, arthritis.

*Examples of enzyme inducers include but are not limited to carbamazepine, lopinavir, phenytoin, and rifampin.

Appendix D. (Continued)

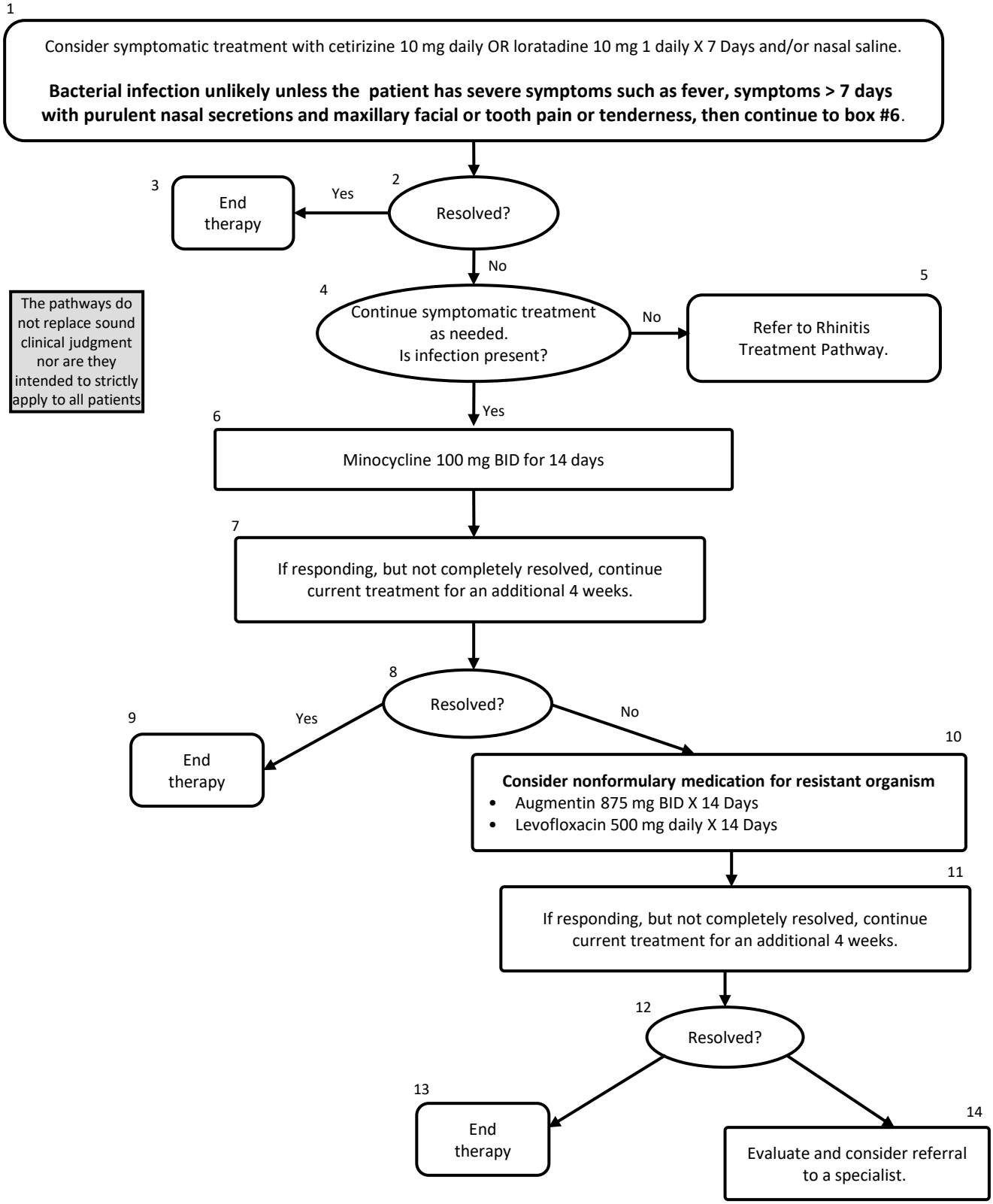
Generic Name	Usual Children, Adolescent and Adult Dose	Adverse Effects
Oxcarbazepine Trileptal®	• Initial: 300 mg twice daily. Titrate weekly as indicated. • Maintenance: 600 mg twice daily.	• Somnolence, dizziness, drowsiness, diplopia, nausea, ataxia • **Serious**: Hyponatremia, skin rash.
Perampanel Fycompa® C-III	• Initial: 2 mg once daily. Titrate weekly as indicated. • Maintenance: 4-12 mg daily.	• Dizziness, somnolence, headache, fatigue, irritability, gait disturbance, falls, nausea and weight gain • **Serious:** neuropsychiatric effects including alteration of mood and aggression
Phenobarbital Luminal® C-IV	• Initial: 50-100 mg 2 or 3 times daily. • Maintenance: 50-100 mg 2 or 3 times daily.	• Drowsiness, somnolence, headache, dizziness, ataxia, cognitive effects, GI upset • **Serious**: rash including Stevens Johnson, agranulocytosis
Pregabalin Lyrica® C-V	• Initial: 150 mg/day divided in 2 or 3 doses. Titrate weekly as indicated. • Maintenance: up to 600 mg/day divided in 2 doses.	• Somnolence, dizziness, headache, ataxia, asthenia, xerostomia, peripheral edema • **Serious**: jaundice, angioedema
Tiagabine Gabitril®	• Initial: 4 mg once daily. Titrate weekly as indicated. • Maintenance: 4-56 mg/day divided in 2 to 4 doses.	• Somnolence, dizziness, tremor, headache, weakness, difficulty concentrating • **Serious**: Stupor or spike wave stupor
Topiramate Topamax®	• Initial: 25-50 mg daily. Titrate weekly as indicated. • Maintenance: 200-400 mg/day divided in 2 doses.	• Behavioral changes especially in children, anorexia, weight loss, sleep disorders, fatigue, dizziness, headache, paresthesia • **Serious**: Nephrolithiasis, open angle glaucoma, and hypohidrosis especially in children
Vigabatrin Sabril®	• Initial: 500 mg twice daily. Titrate weekly as indicated. • Maintenance: 1500 mg twice daily.	• Drowsiness, fatigue, headache, and dizziness • **Serious:** Black box warning regarding possible permanent vision loss, severe hypersensitivity reactions and angioedema have been reported • Reserved for refractory cases that have failed several alternative treatments. Limited number of specialty pharmacies in the US dispense this drug as part of the Vigabatrin REMS Program. Physicians must be registered to prescribe.
Zonisamide Zonegran®	• Initial: 100 mg daily. Titrate every 2 weeks as indicated. • Maintenance: 100-400 mg/day in 1 divided doses.	• Drowsiness, ataxia, anorexia, GI upset, headache, pruritus • **Serious**: Rash, renal calculi, and hypohidrosis especially in children • Do not take if history of sulfa allergy.

Note: *In 2008, the FDA issued a warning for a possible increased risk of suicidal ideation and behavior associated with antiepileptic drugs. This was based on an FDA review of 199 trials including 11 different antiepileptic drugs. Patients should be monitored for the emergence of suicidal thoughts or changes in behavior. Referral to mental health may be considered if appropriate.*

Appendix E: Formulary AED Drug Interactions

Medication	Drug Interactions and Comments
Carbamazepine (CBZ)	• DI: levels increased by VPA, phenytoin, vigabatrin, erythromycin, fluoxetine, isoniazid, propoxyphene, & verapamil; levels decreased by phenobarbital & primidone
Levetiracetam	• DI: probenecid- clinical significance unknown; not metabolized thru CYP450. • Renal elimination- dose adjust in renal insufficiency • No dose adjustment for hepatic impairment.
Phenytoin	• DI: levels increased by VPA, topiramate, oxcarbazepine, allopurinol, diltiazem, fluconazole, fluoxetine, ibuprofen, isoniazid, methylphenidate, metronidazole, omeprazole, propoxyphene, ritonavir, Bactrim; levels decreased by CBZ, vigabatrin, antacids, rifampin, methotrexate
Primidone	• Potent and broad-spectrum inducer of CYP • Dose adjustment is needed in renal impairment. Use with caution in patients with hepatic insufficiency.
Valproic Acid (VPA)	• DI: levels increased by aspirin & isoniazid; levels decreased by CBZ, phenobarbital, & phenytoin • Contraindicated hepatic disease/significant hepatic dysfunction; known urea cycle disorder

SINUSITIS

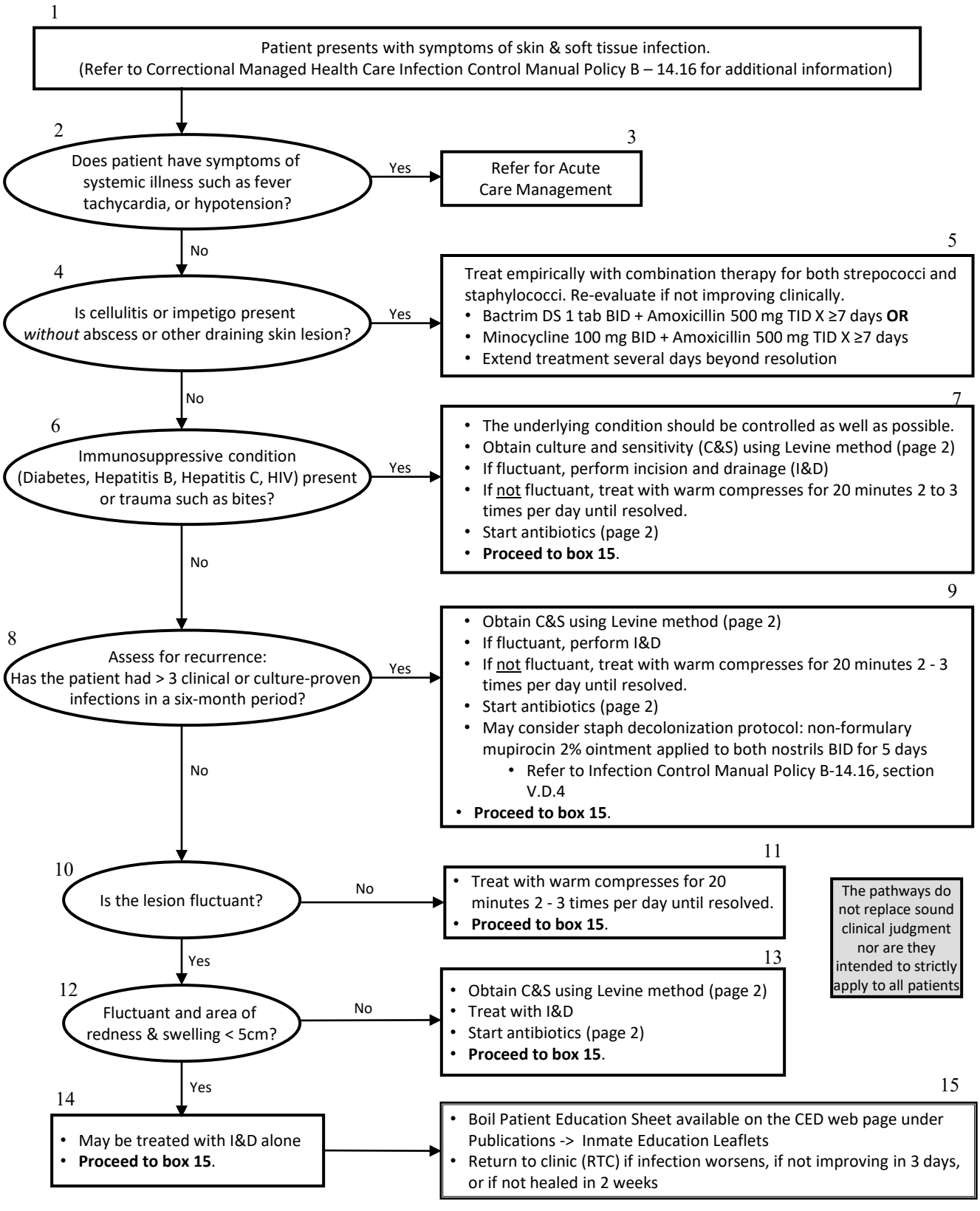


The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients

Nurses: DMGs are to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.**

Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee. Approved August 1995; Reviewed 3/05, 5/11, 5/18; Revised 8/98, 4/02, 4/03, 5/04, 5/08, 11/14, 5/23

SKIN AND SOFT TISSUE INFECTION



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Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee. Approved 09/12; Revised 11/14, 07/17, 9/19, 1/22.

Culture Using the Levine Method

- Cleanse the wound with sterile water or normal saline to wash away any slough, necrotic tissue or dried exudate.
- Moisten the culture tip. If the wound is moist, a sterile swab can be used straight from the packaging. If the wound is dry, then the swab tip should be moistened with sterile water to increase the chances of recovering organisms from the site.
- Collect in a zig-zag motion – the swab should be moved across the wound surface in a zig-zag motion, at the same time, being rotated between the fingers.
- Send to lab – immediately following the collection, the swab should be returned to its container (placed into the transport medium) and accurately labeled.

Antibiotic Selection

- If possible, begin after C&S results available. May treat with soaks or dressing changes pending results.
- If empiric therapy must be started, begin empiric therapy with Bactrim DS.
- If allergic or failure on treatment, consider referral to higher level of care for recommendations.
- Antibiotic therapy **should be guided by C&S** results once available. All cases of methicillin sensitive Staphylococcus aureus (MSSA) and methicillin resistant Staphylococcus aureus (MRSA) must be reported to the Office of Public Health by the facility Infection Control Nurse (ICN). Refer to the Infection Control Policy Manual (B-14.16 Attachment B).
- Duration generally at least 7 days and should extend several days past clinical resolution.
- Empiric therapy to avoid: rifampin alone, flouroquinolone, cephalosporin, clindamycin, or erythromycin.

THYROID DISORDERS

1

Screen for thyroid abnormalities upon intake in patients age 50 and older and every 5 years thereafter.
Screen for thyroid abnormalities if patient is enrolled in Hypertension, Diabetes Mellitus, Hyperlipidemia, or Depression Chronic Care Clinics as part of baseline work-up.
Screen for thyroid abnormalities if patient is symptomatic of hypothyroidism or hyperthyroidism (Table 1), has risk factors for thyroid disease (Table 2), or if patient is taking amiodarone, lithium, or on antineoplastic agents (Table 3).

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients

2

Draw Thyroid Stimulating Hormone (TSH).
Is TSH level normal?
(0.4-5 mIU/L)

Yes →

3

- Rescreen when clinically indicated.
- If patient is symptomatic of hypo-or hyperthyroidism and TSH is normal, check Free T4. Consider referral to specialist

No ↓

4

Is TSH high?

No → *(Low TSH)*

5

Hyperthyroidism Assessment
Repeat TSH and draw Free T4 and T3.
Diagnosis is primarily based off of lab values.
See Table 4.

6

In the absence of contraindications, start a beta-blocker (See Page 4) in all patients symptomatic of thyrotoxicosis, especially elderly patients and patients with resting heart rate > 90 bpm and/or coexistent cardiovascular disease

7

Determine underlying etiology by referring to specialist. Consider ordering a thyroid scan while awaiting appointment for specialist. If medical management is warranted pending referral, see Box 8.

Yes →

9

Hypothyroidism Assessment
Repeat TSH and draw Free T4 in 4-8 weeks.
Diagnosis is primarily based off of lab values.
See Table 4.

10

Is TSH > 10 mIU/L?

Yes →

11

Treat with Levothyroxine.
See Box 13

No ↓

12

Consider treatment with levothyroxine in
- Patients with symptoms of hypothyroidism
- Patients with subclinical hypothyroidism and risk factors of cardiovascular disease
- Do not initiate treatment in patients over the age of 70 yrs or refer to endocrine for recommendation. Can increase risk of arrythmias, angina, and myocardial infarction.

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider**.

8

Initial Methimazole Dosing:*
- **Mild Hyperthyroidism** (free T4 levels 1-1.5 times x Upper Limit Normal (ULN))**:** 5-10 mg/day
- **Moderately Severe Hyperthyroidism** (free T4 levels 1.5-2x ULN): 10-20 mg/day
- **Severe Hyperthyroidism** (free T4 2-3x ULN): 20-40 mg/day in 2 or 3 divided doses to minimize GI upset

Maintenance Methimazole Dose: 5-10 mg/day

Monitoring Recommendations:
- After initiation of therapy, free T4 *and T3 levels* should be monitored every 4-8 weeks. Adjust methimazole dose by 5 mg until free T4 is within normal range.

**First trimester Pregnancy: Propylthiouracil is recommended in place of Methimazole*

13

Levothyroxine Dosing:
- Initial: 25 -100 mcg once daily. Consider starting at the lowest dose if pt is > 50 yo or has coronary heart disease.
- Subclinical Hypothyroidism (High TSH, Normal Free T4): 25-50 mcg once daily as starting dose

Monitoring Recommendations:
- Monitor TSH in 6-8 weeks after initiation and after any dosage change. If dose change is needed, titrate by 50 mcg or by 25 mcg if pt is >50 yo or has coronary heart disease.

I. Assessment

A. Screening

1. Upon intake in patients age 50 and older and every 5 years thereafter
2. In patients enrolled in Chronic Care Clinics for hypertension, hyperlipidemia, diabetes and depression
3. If patient is exhibiting signs and symptoms of hypothyroidism or hyperthyroidism (see Table 1).
4. If patient has risk factors for thyroid disease (see Table 2)
5. If patient is taking amiodarone, lithium, or on antineoplastic agent. (see Table 3)

Table 1. Signs and Symptoms of Hypothyroidism and Hyperthyroidism

Hypothyroidism Symptoms	Hyperthyroidism Symptoms
• Constipation • Cold sensitivity • Dry skin • Hair loss or change in texture • Fatigue • Myalgia/arthralgia • Hoarseness • Weight gain despite poor appetite • Bradycardia • Cognitive deficits/depression • Thyroid enlargement/nodules • Carpal tunnel syndrome • Sleep apnea • Menorrhagia, amenorrhea, and galactorrhea in females	• Anxiety • Weakness • Tremors • Palpitations • Heat intolerance • Increased perspiration • Weight loss

Table 2.

Risk Factors for Thyroid Disease
• Autoimmune disease • Pernicious anemia • First-degree relative with autoimmune thyroid disease • History of neck radiation to the thyroid gland, including radioactive iodine therapy and radiotherapy • History of thyroid surgery or dysfunction • Abnormal thyroid upon examination • Pituitary and/or hypothalamic disorders

Table 3. Medications Associated with Thyroid Dysfunction

Amiodarone	Lithium
Can cause hypothyroidism and hyperthyroidism. Before initiating amiodarone: • Order thyroid function tests Monitoring: • Check thyroid function tests every 3 months while on amiodarone. • Continue checking thyroid function tests for at least one year after amiodarone is discontinued.	Can cause goiter and hypothyroidism and has been associated with thyroid immunity and hyperthyroidism. Before initiating lithium: • Perform thyroid physical exam • Order thyroid function tests Treat thyroid dysfunction if present. Lithium can still be given while thyroid is being treated. Monitoring: • Hypothyroid – See page 3 Monitoring Recommendations • Hyperthyroid – See page 5 Monitoring Recommendations

Table 3. *Medications Associated with Thyroid Dysfunction (continued)*

<table>
<tr><td colspan="3">Immune Checkpoint Inhibitors</td></tr>
<tr><td colspan="3">Can cause hypothyroidism or asymptomatic thyrotoxicosis (lasting 4-6 weeks), followed by hypothyroidism. Consider referral to specialist.

Before initiating immune checkpoint inhibitor:
• Order thyroid function tests

Monitoring:
• Check thyroid function tests at least every 4-8 weeks and as clinically indicated, or as recommended by specialist.

Immune checkpoint inhibitors include but are not limited to PD-1 and PD-L1 inhibitors: pembrolizumab (Keytruda), nivolumab (Opdivo), cemiplimab (Libtayo), atezolizumab (Tecentriq), avelumab (Bavencio), durvalumab (Imfinzi); CTLA-4 inhibitors: ipilimumab (Yervoy), tremelimumab (Imjuno); LAG-3 inhibitors/PD-1 inhibitor combo: relatlimab/nivolumab (Opdualag)

PD-1, programmed death receptor 1; PD-L1, programmed death receptor ligand 1; CTLA-4, cytotoxic T lymphocyte-associated antigen 4; LAG-3, lymphocyte activation gene-3</td></tr>
<tr><td>Tyrosine kinase inhibitors</td><td>Interferon-alpha</td><td>Immuno-therapies</td></tr>
<tr><td>Can cause hypothyroidism and thyrotoxicosis.

Before initiating tyrosine kinase inhibitors:
• Order thyroid function tests

Monitoring:
• If previously on levothyroxine therapy, monitor thyroid function every month until stable, then monitor every 2 months
• If previously euthyroid, check thyroid function tests every month for 4 months, then every 2-3 months
• Or as recommended by specialist

Tyrosine kinase inhibitors include but are not limited to imatinib (Gleevec), sunitinib (Sutent), sorefanib (Nevaxar), dasatinib (Sprycel), nilotinib (Tasigna), and axitinib (Inlyta)</td><td>Can cause hyperthyroidism.

Before initiating interferon-alpha:
• Order thyroid function tests

Monitoring:
• Check for clinical symptoms and thyroid function tests at least every 6 months
• Or as recommended by specialist</td><td>Can cause hypothyroidism and hyperthyroidism.

Before initiating immuno-therapy:
• Order thyroid function tests

Monitoring:
• Check thyroid function tests every month for first 4 months, then every 2-3 months while on agent
• Or as recommended by specialist

Immunomodulary agents include angiogenesis inhibitors like thalidomide (Thalomid) and lenalidomide (Revlimid) as well as interleukin-2 human recombinant product (IL-2), aldesleukin (Proleukin)</td></tr>
</table>

II. Diagnosis
   A. TSH is the primary screening test for thyroid dysfunction.
   B. If hypothyroidism is suspected, repeat TSH four to eight weeks later as TSH levels can temporarily be elevated. Order Free T4 with the repeat TSH. Free T4 differentiates between primary hypothyroidism and subclinical hypothyroidism (See Table 4). Note: TSH levels in hospitalized, recently ill, or patients on glucocorticoid therapy may be inaccurate.
   C. If hyperthyroidism is suspected, repeat TSH and order Free T4 and T3 levels.
   D. Lab Evaluation – see pathway for frequency
      1. TSH
      2. Free T4
      3. T3
   E. Physical Exam (Intake and CCC)
      1. Vitals
      2. HEENT (thyroid palpation)
      3. Cardiovascular (ECG and auscultation)
      4. Skin, nails, hair examination
      5. Neurologic (ankle reflex relaxation time)
   F. Psychiatric and cognitive evaluation

Table 4.

Thyroid Disorder Diagnosis			
	TSH	Free T4	T3
Subclinical Hypothyroidism	High TSH	Normal Free T4	n/a
Primary Hypothyroidism	High TSH	Low Free T4	n/a
Subclinical Hyperthyroidism	Low TSH	Normal Free T4	Normal T3
Primary Hyperthyroidism	Low TSH	High Free T4	High T3
T3-Toxicosis	Low TSH	Normal Free T4	High T3
T4-Toxicosis	Low TSH	High Free T4	Normal T3

III. Plan/Treatment
   A. Hypothyroidism – Treatment is recommended in those diagnosed with primary hypothyroidism (>10 mIU/L TSH). Treatment is considered in patients with subclinical hypothyroidism if the patient is symptomatic of hypothyroidism or has cardiovascular risk factors (e.g., elevated LDL).
      1. Pharmacological Therapy: Levothyroxine (Synthroid®, Levoxyl®) is drug of choice.

Table 5. Levothyroxine Dosing

	Primary Hypothyroidism	Patients with Primary Hypothyroidism with CHD	Patients with Primary Hypothyroidism >50 yo	Subclinical Hypothyroidism
Starting dose	25 mcg to 100 mcg once daily	25 mcg once a day	25 mcg once a day	25 mcg to 50 mcg once a day
CMC Formulary Levothyroxine Strengths: 25 mcg, 50 mcg, 100 mcg, 150 mcg				

2. Treatment goals include:
   a. Symptom relief
   b. Target TSH within normal value range (0.4-5 mIU/L)
   c. Free T4 within normal value range based on lab assay
   d. Avoid overtreatment (iatrogenic thyrotoxicosis), especially in the elderly
3. Monitoring Recommendations: TSH should be measured every 6-8 weeks post-initiation of levothyroxine or after change in dose. Upon adequate replacement, TSH should be monitored at 6 months and then every 12 months thereafter.
   a. If TSH is suppressed (<0.35mIU/L) - consider dose reduction by 25 – 50 mcg. Excess replacement increases the risk of osteoporosis and arrhythmias, especially in the elderly.
   b. If TSH is normal- dose has been established. Monitor TSH at 6 months and then every 12 months thereafter.
   c. If TSH is elevated (>5.5 mIU/L) – consider dose increase by 25- 50 mcg.
4. Clinical pearls on levothyroxine
   a. Levothyroxine is best absorbed on an empty stomach, at least 60 minutes before breakfast. If taken in the evening, patient should wait at least 4 hours from last meal before taking levothyroxine.
   b. Patients should take levothyroxine 4 hours apart from antacids, iron and calcium supplements.
   c. Patients should take levothyroxine with a full glass (8oz) of water ONLY.

Table 6.

Agents Impacting Levothyroxine Therapy or the Hypothalamic-Pituitary Axis (HPA)		
Interferes with absorption of levothyroxine	Increases clearance of levothyroxine	Direct and indirect effects on the HPA
• Bile acid sequestrants • Sucralfate • Kayexalate • Oral bisphosphonates • Proton pump inhibitors • Multivitamins (containing ferrous sulfate or calcium carbonate) • Ferrous sulfate • Phosphate binders • Calcium salts • Ciprofloxacin • H2 receptor antagonists Diet: • Ingestion with a meal • Grapefruit juice • Espresso coffee • High fiber diet • Soy	• Phenobarbital • Primidone • Phenytoin • Carbamazepine • Rifampin • Sertaline • Quetiapine • Stavudine • Nevirapine	Decreases TSH secretion • Dopamine • Dopaminergic agonists (bromocriptine, cabergoline) • Glucocorticoids • Thyroid hormone analogues • Metformin • Opiates Increases TSH secretion • Dopamine receptor blockers (metoclopramide) • Hypoadrenalism • Amphetamines • Ritonavir • St. John's Wort

5. Hypothyroidism during pregnancy
   a. TSH goals vary depending on the trimester

Table 7. TSH Goal During Pregnancy Based on Trimester

	First Trimester	Second Trimester	Third Trimester
TSH Goal	0.1-2.5 mIU/L	0.2-3.0 mIU/L	0.3-3.0 mIU/L

   b. Treatment for pregnant women with hypothyroidism is oral levothyroxine.
   c. At 4-6 weeks pregnant, a dose increase will be needed if the patient is taking levothyroxine, potentially as much as 50%, due to the increase in size of the thyroid gland. Refer to OBGYN for recommendations.
   d. Monitor TSH and Free T4 every 4 weeks until 16-20 weeks of gestation, and at least once between 26 weeks and 32 weeks.
   e. TSH levels decline in the first trimester when HCG levels are high and rise after 10-12 weeks gestation.
   f. Please consider consulting with OBGYN for recommendations on management.

B. Hyperthyroidism – treatment should be managed by the Specialist. While waiting for appointment, the primary care provider may initiate medical management.

1. Pharmacological Therapy:

a. Start a beta blocker in all patients symptomatic of thyrotoxicosis, especially in elderly patients and patients with resting heart rate of >90 bpm and/or coexistent cardiovascular disease.

i. Atenolol 25 mg to 100 mg, 1-2 times per day (Avoid during pregnancy)

ii. Metoprolol succinate 25 mg to 100-200 mg per day

iii. Propranolol 10 mg to 40 mg, 3-4 times per day (Preferred agent during pregnancy)

b. Methimazole (MMI) is the drug of choice for hyperthyroidism for its longer duration of action, more rapid efficacy, and lower incidence of side effects.

c. Propylthiouracil (PTU) is recommended in the first trimester of pregnancy. Pregnant women who are in need of continuing anti-thyroid therapy during pregnancy should be converted from MMI to PTU at a dose ratio of 1:20 (e.g., MMI 5 mg/d = PTU 100 mg/day). Current guidelines provide no recommendation for converting back to MMI after the first trimester due to insufficient evidence. Hyperthyroidic pregnant patients should be under the care of a specialist.

Table 8. Hyperthyroidism Medication Dosing

	Initial Dose	Maintenance
Drug of Choice: Methimazole Formulary strength: 5 mg	• Mild Hyperthyroidism (free T4 levels 1-1.5x ULN): 5-10 mg/day • Moderately Severe Hyperthyroidism (free T4 levels 1.5-2x ULN): 10-20 mg/day • Severe Hyperthyroidism (free T4 2-3x ULN): 20-40 mg/day in 2 or 3 divided doses to minimize GI upset	• Minimum maintenance dose to maintain euthyroidism, typically 5-10 mg/day
In pregnancy, first trimester: Propylthiouracil Non-formulary	• 50 -100 mg two to three times a day (depending on severity of hyperthyroidism)	• Minimum maintenance dose to maintain euthyroidism, typically 50 mg twice daily.

Table 9.

Side Effects of Methimazole	Side Effects of Propylthiouracil
• Agranulocytosis • Leukopenia • Thrombocytopenia • Aplastic Anemia • Hepatitis	**<u>Black Box Warning-Severe liver injury and acute liver failure have been reported</u>** • Agranulocytosis • Leukopenia • Thrombocytopenia • Aplastic anemia • Hepatitis • Acute renal failure, glomerulonephritis

Table 10.

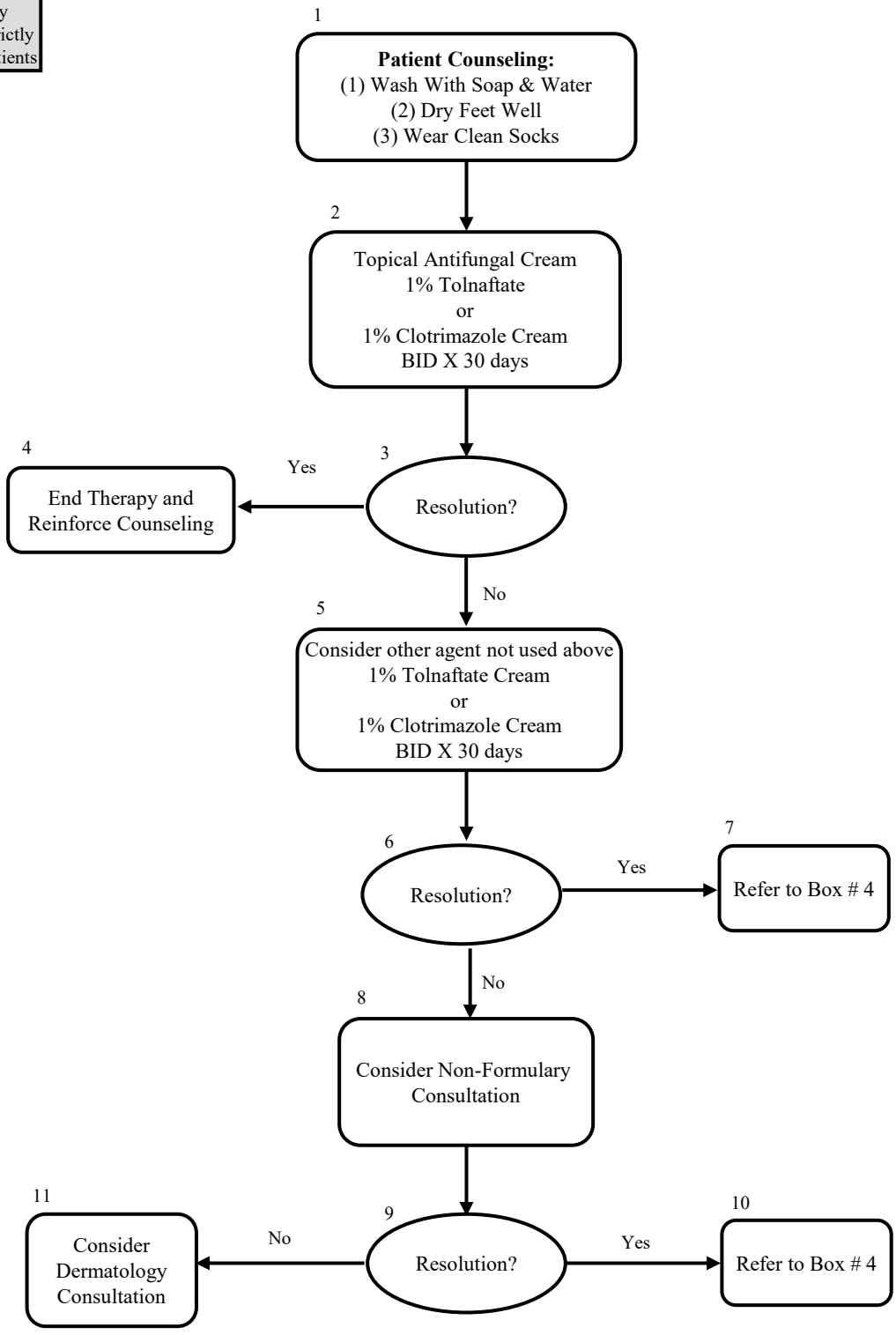
Drug Interactions			
Methimazole may increase the levels of the following agents	Methimazole may decrease the levels of the following agents	Propylthiouracil* may increase the levels of the following agents	Propylthiouracil may decrease the levels of the following agents
• Aripiprazole • Cardiac glycosides • Clozapine • Lomitapide • Pimozide • Theophylline derivatives	•Sodium Iodide •Vitamin K antagonists	•Cardiac glycosides •Clozapine •Theophylline derivatives	•Sodium Iodide •Vitamin K antagonists

**Propylthiouracil levels may be altered if taken with food. Either always take with food or always take without food.*

2. Treatment goals include:
   a. Symptom relief
   b. TSH within normal value range (0.4 to 5 mU/L)
   c. Free T4 and T3 within normal value range based on lab assay
3. Monitoring Recommendations
   a. Baseline tests: prothrombin, CBC, and liver function enzymes.
   b. Free T4 and T3 level should be drawn 4-8 weeks after initiating MMI. Adjust MMI dose accordingly. Recheck Free T4 and T3 levels every 4-8 weeks and continue to adjust MMI dose by 5mg until patient is euthyroidic with the minimal dose of medication.
   c. Once patient is euthyroidic and stabilized on maintenance dose, monitoring intervals can increase to every 2-3 months.
   d. TSH should be monitored at 6 months and then every 6 months until 18 months of therapy are complete. TSH may remain suppressed for several months after starting therapy and is therefore not a good parameter to guide medication adjustment.
   e. Patients should report signs/symptoms of liver injury when using MMI or PTU including: pruritic rash, jaundice, light-colored stool or dark urine, joint pain, abdominal pain or bloating, anorexia, nausea, or fatigue. Patients who experience these symptoms, should have their LFTs monitored.
   f. Continue to monitor for presence of nodules or goiters in hyperthyroid patients and refer to specialist if needed.
4. Hyperthyroidism during pregnancy
   a. Refer to OBGYN for management of hyperthyroidism in pregnant patients

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients

TINEA PEDIS



Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider**.

Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee, September 1996, Revised 8/98, 12/98, 3/01, 7/04, 03/19. Reviewed 4/03,1/07, 5/10, 1/13, 07/2024.

Anticoagulation Using Warfarin

The pathways do not replace sound clinical judgment, nor are they intended to strictly apply to all patients.

1 Does patient have 1 or more documented indications for anticoagulation therapy? See Table 5 for indications.

No → 2 Re-evaluate need for continued therapy. Discontinue if not indicated.

Multiple indications → 3 Compare the goal INR ranges and therapy durations for each indication. If the INRs differ, choose the higher goal. Continue therapy for the longest duration suggested. Document date of therapy completion if applicable.

One indication → 4 Determine the goal INR range and therapy duration for the patient's indication. Document date of therapy completion, if applicable.

5 Does the patient have signs/symptoms of thromboembolism (DVT, PE, or stroke) or moderate to severe bleeding? See Tables 6, 7, & 8.

Yes → 6 Consider transport to higher level of care.

No

7 Does patient have a contraindication to warfarin? See Table 9.

Yes → 8 Refer to Specialty Clinic

No

9 Is patient initiating anticoagulation or continuing therapy?

Initiating → 10 Refer to Tables 10 – 12.

Continuing

11 Duration of therapy completed?

Yes → 12 Discontinue warfarin and document therapy completion.

No

13 Was PT/INR measured > 4 weeks ago?

Yes → 14 Order PT/INR* to be drawn as soon as possible. Schedule follow-up in 7 days. Continue to Box 5.

No

15 Is patient's INR within the goal range?

Yes → 16 Continue current regimen. Order PT/INR* (Mon-Fri) within 1 week before next visit.

No

17
- Assess compliance in the 7 days before INR was drawn
- Assess any changes that could have modified warfarin's effect. Refer to Tables 16-18.

18 **If INR < goal INR range:**
- Counsel patient on warfarin compliance
- Counsel patient on the effects of medication / food / conditions on INR.
- If the patient has no missed doses within the 7 days before INR was drawn, adjust the warfarin dose if needed (especially if factors that modify warfarin's effect are expected to stay consistent). Refer to Tables 13 & 14.
- Repeat INR prior to follow-up visit
- Schedule follow-up in 1-2 weeks
- Return to box 1

19 **If INR > goal INR range:**
- Counsel patient on the effects of medication / food / conditions on INR.
- Adjust the warfarin dose if needed (especially if factors that modify warfarin's effect are expected to stay consistent). Refer to Table 15.
- Repeat INR prior to follow-up visit
- Schedule follow-up in 1-2 weeks, unless recommended sooner in Table 15.
- Return to box 1

Nurses: DMGs are guidelines to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider**.

*PT/INR – should be drawn during weekday (Mon-Fri), at least every 28 days. Visit frequency may be extended to every 12 weeks if INR is consistently stable. A stable patient is considered having at least 3 months of consistent INR within goal with no need to adjust warfarin dosing.

Prepared By The Correctional Managed Care Pharmacy & Therapeutics Committee. Approved May 2007. Revised 5/10, 05/16, 07/21. Reviewed 1/13.

I. Treatment Principles

A. Possible adverse outcomes of NOT providing venous thromboembolism (VTE) prophylaxis:
1. Symptomatic deep venous thrombosis (DVT) or pulmonary embolism (PE), which can be fatal
2. Development of post-thrombotic syndrome

B. Possible adverse outcomes of NOT providing anticoagulation prophylaxis in atrial fibrillation (AF) patients:
1. Cardiac thrombus
2. Stroke

C. Risk Factors Associated With VTE (Table 1)

Table 1 Risk Factors Associated with Deep Vein Thrombosis and Pulmonary Embolism

- Cancer: currently on treatment, treatment within past 6 months, or not receiving curative treatment
- Prolonged immobility
- Major surgery (esp. orthopedic) in the last 12 weeks
- Heparin-Induced Thrombocytopenia (HIT)
- Pharmacotherapy
  - Estrogenic oral contraceptive agents
  - Post-menopausal hormone therapy
  - Cancer treatments (Hormonal, Radiotherapy, chemotherapy
- History of VTE
- Age > 60 years
- Fracture of hip / pelvis / leg(s)
- Indwelling central venous catheter
- Resting heart rate consistently > 100 beats/minute
- Major medical illness (e.g., heart failure (HF), myocardial infarction(MI), transient ischemic attack (TIA), ischemic stroke)

- Hypercoagulable States
  - Cancer
  - Activated Protein C Resistance Factor / Factor V Leiden mutation
  - Prothrombin 20210A mutation
  - Protein C or S deficiency
  - Antithrombin deficiency
  - Factor VIII or XI excess (> 90th percentile)
  - Antiphospholipid Antibody Syndrome
  - Dysfibrinogenemia
  - Hyperhomocysteinemia
  - Excess of Inhibitor of Plasminogen Activator
  - Inflammatory Bowel Disease
    - Ulcerative Colitis
    - Crohn's Disease
  - Nephrotic Syndrome
  - Pregnancy and post-partum period

D. Assessment of Ischemic Stroke Risk Associated with Atrial Fibrillation (annual assessment is recommended)

Table 2. $CHADS_2$-VAS_2C

Condition	Points
Recent decompensated HF or moderate-severe left ventricular (LV) dysfunction	1
Hypertension (HTN) (BP > 140/90 at least on 2 occasions or currently on antihypertensive treatment)	1
Age ≥ 75 years	2
Diabetes mellitus (DM)	1
Stroke or TIA	2
Vascular Disease (coronary artery disease (CAD), peripheral vascular disease, aortic plaque)	1
Age 65 – 74 years	1
Female Sex	1
Maximum Score of 10. Refer to Table 5 for treatment recommendations.	

E. Bleeding Risk (Tables 3 and 4) - Modifiable risk factors should be reduced when possible (e.g., controlling blood pressure, removing concomitant antiplatelet or NSAID drugs, and counseling patients on risk factors such as alcohol use, etc.). Patients with a higher risk of bleeding should be followed more closely. A high bleeding risk score should not be the only reason to avoid anticoagulation.

1. Risk Factors Associated with Developing a Severe Bleed While on Warfarin Therapy for AF patients (annual assessment is recommended).

Table 3. Assessing Bleeding Risk in AF Patients using HAS-BLED Score

Condition	Points
Hypertension (Uncontrolled, systolic blood pressure (SBP) >160 mmHg)	1
Abnormal renal function (Dialysis, transplant, or serum creatinine (SCr) > 2.26 mg/dL)	1
Abnormal liver function (Cirrhosis or bilirubin > 2x normal with AST/ALT/Alkaline Phosphatase > 3x normal)	1
Stroke history	1
Prior major bleeding or predisposition to bleeding	1
Labile INR (Unstable/high INRs, time in therapeutic range < 60%)	1
Elderly, Age > 65	1
Drugs (aspirin, NSAIDS, clopidogrel)	1
Alcohol use (> 8 drinks/week)	1
A score of ≥ 3 warrants a high bleed risk and patient should be followed more closely. Maximum score of 9	

2. Risk Factors Associated with Developing a Severe Bleed While On Warfarin Therapy for VTE Patients (annual assessment is recommended).

Table 4: Assessing Bleeding Risk in VTE Patients

- Age > 65 years
(add 1 extra point if age >75 years)
- Previous bleeding
- Cancer
(add 1 extra point if metastatic cancer)
- Renal Failure
- Liver Failure
- Thrombocytopenia
- Previous Stroke
- Anemia
- Antiplatelet therapy
- Poor anticoagulant control
- Comorbidity and reduced functional capacity
- Recent surgery
- Frequent falls
- Alcohol abuse
- NSAID use
- Diabetes

0 risk factors = Low risk (0.8% risk) 1 risk factor = Moderate risk (1.6% risk) ≥2 risk factors = High risk (≥6.5% risk)

F. Determining the target INR (International Normalized Ratio) and INR Range for Warfarin

1. The target, or goal INR is indication specific (Table 5) and represents the intensity of warfarin therapy.
2. A subtherapeutic INR increases the risk of developing a thromboembolic event, while a supratherapeutic INR increases the risk of developing a bleed.
3. A patient's INR can be affected by multiple variables (Tables 16-18) such as:
   - Age
   - Drug interactions
   - Food interactions
   - Medical condition
   - Laboratory error
   - Poor medication adherence
   - Genetic and environmental factors
   - Drug interactions

G. Determining Treatment Duration

1. Studies have consistently shown that a longer duration of treatment with warfarin is associated with both a decrease in the incidence of VTE and an increase in the risk of experiencing a bleeding event.
2. Duration is determined by indication

ACRONYMS: **AF** = Atrial Fibrillation, **CTPH** = Chronic Thromboembolic Pulmonary Hypertension, **DM** = Diabetes Mellitus, **DVT** = Deep Venous Thrombosis, **HF** = Heart Failure, **HTN** = Hypertension, **INR** = International Normalized Ratio, **LMWH** = Low Molecular Weight Heparin, **PAF** = Paroxysmal (*intermittent*) Atrial Fibrillation, **PE** = Pulmonary Embolism, **TEE** = Transesophageal Echocardiography, TIA = Transient Ischemic Attack, **UFH** = Unfractionated Heparin, **NSR** = Normal Sinus Rhythm, **STEMI** = ST-segment Elevation Myocardial Infarction, **MI** = Myocardial Infarction, **VKA** = Vitamin K Antagonist (i.e., warfarin), **ASA** = Aspirin, **PMBV** = Percutaneous mitral balloon valvotomy, **NA** = Not applicable

Medical Condition	Specific Indication	Target INR	INR Range	Duration of Therapy	Comments
Atrial Fibrillation or Atrial Flutter	$CHADS_2$-VAS_2C = 0 for males, 1 for females (Refer to Table 2)	NA	NA	NA	Aspirin 81 – 325 mg daily
	$CHADS_2$-VAS_2C = 1 for males, 2 for females (Refer to Table 2)	2.5	2 – 3	Indefinite	May start therapy based on clinical judgement
	$CHADS_2$-VAS_2C ≥ 2 for males, ≥ 3 for females (Refer to Table 2)	2.5	2 – 3	Indefinite	
	Planned conversion to sinus rhythm	2.5	2 – 3	Start 3 weeks before elective cardioversion and continue for 4 weeks after successful cardioversion	
	AF with mechanical heart valve	3	2.5 – 3.5	Indefinite	
Antiphospholipid Antibody Syndrome or Prescence of Lupus Inhibitor	Primary prevention of thrombosis	NA	NA	NA	
	Secondary prevention of thrombosis	2.5	2 – 3	Indefinite	
Cerebral Venous Sinus Thrombosis	Provoked	2.5	2 – 3	3 – 6 months	
	Unprovoked	2.5	2 – 3	6 – 12 months	
CTPH		2.5	2.0 – 3.0	Indefinite	Consider specialist referral
DVT or PE	1st episode, secondary to reversible risk factor or 1st isolated distal DVT	2.5	2 – 3	3 months	
	1st episode, idiopathic	2.5	2 – 3	At least 3 months; consider long-term therapy	Depending on bleeding risk (Refer to Table 4)
	Recurrent	2.5	2 – 3	Indefinite	
	Cancer	2.5	2 – 3	Until cancer resolves or Indefinitely	LMWH for the first 3 – 6 months.
Mitral Annular Calcification	Complicated by systemic embolism, ischemic stroke, or TIA without AF	NA	NA	NA	Aspirin 81 mg/day
	Recurrent episodes despite aspirin therapy or with AF	2.5	2 – 3	Indefinite	

Medical Condition	Specific Indication	Target INR	INR Range	Duration of Therapy	Comments
Mitral Valve Stenosis undergoing PMBV	With pre-procedure TEE showing left atrial thrombus	3	2.5 – 3.5	Until thrombus resolution (on repeat TEE)	PMBV performed if no thrombus present on TEE
Mitral Valve Prolapse	With TIA or ischemic stroke	NA	NA	NA	Aspirin 81 mg/day
	With: AF, documented systemic embolism, or recurrent TIA with aspirin therapy	2.5	2 – 3	Indefinite	
MI	Post-MI, high risk with intracardiac thrombus	2.5	2 – 3	At least 3 months post-MI	Combine with aspirin 81 mg/day
Rheumatic Mitral Valve Disease	• AF • Systemic embolism • Left atrial thrombus • NSR with atrial diameter > 55 mm	2.5	2 – 3	Indefinite	
	AF with systemic embolism and/or left atrial thrombus while at therapeutic INR	3	2.5 – 3.5	Indefinite	
Valves, Heart, Mechanical	AORTIC Position in NSR w/o left atrial enlargement: Bileaflet or Tilting disk	2.5	2 – 3	Indefinite	On-X bileaflet aortic valve: INR 2-3 for 3 months, then 1.5-2.0 afterwards
	AF with mechanical heart valve	3	2.5 – 3.5	Indefinite	
	MITRAL Position: Bileaflet or Tilting disk	3	2.5 – 3.5	Indefinite	
	ANY Position • Caged ball or caged disk • Anterior-apical STEMI • Left atrial enlargement • Hypercoagulable state • Low ejection fraction	3	2.5 – 3.5	Indefinite	Combine with ASA 81 mg/day if multiple risk factors for thromboembolism and atherosclerotic disease.
	Systemic embolism despite previously therapeutic INR: • Target 2.5 (2.0 – 3.0) • Target 3.0 (2.5 – 3.5)	 3 3.5	 2.5 – 3.5 3 – 4	Indefinite	Combine with aspirin 81 mg/day **or** upward titrate warfarin dose and INR.
Valves, Heart, Bioprosthetic	AORTIC Position with NSR or no other VKA indication	NA	NA	NA	Aspirin 81 mg/day.
	MITRAL Position	2.5	2 – 3	First 3 months following valve insertion	ASA 81 mg/day **afterwards** in patients with NSR and no other indications for warfarin.
	ANY Position with history of systemic embolism	2.5	2 – 3	First 3 months following valve insertion	ASA 81 mg/day **afterwards** in patients with NSR and no other indications for warfarin.
	ANY Position with: • AF • Hypercoagulable state • Low ejection fraction • Any additional thromboembolic risk	2.5	2 – 3	Indefinite	Consider addition of aspirin 81 mg/day in patients with atherosclerotic disease.

II. Patient Evaluation

A. Medical History: Obtain the following information to use with recent INR value to evaluate / develop treatment plan:
   1. Indication(s) for treatment
   2. Treatment duration*:* determined by indication and patient's risk factors. See Table 5.
   3. Medical History
      a. Thrombophilia
      b. Comorbidities (CAD, HF, HTN, or DM)
      c. History of past VTE or stroke
   4. Family history
   5. Review
      a. Adherence
      b. Recent illness / hospitalization
      c. Most current medication profile
      d. Diet
      e. Commissary purchases
      f. Drug use

B. Baseline Monitoring
   1. CBC
   2. Creatinine
   3. PT/INR
   4. Albumin and liver enzymes (AST/ALT)

C. At each visit, assess the patient for signs and symptoms of possible acute, severe bleed and for signs and symptoms of thromboembolism.

Table 6: Signs and Symptoms of Possible Acute, Severe Bleed

• Severe headache that fails to resolve
• Decrease ≥ 10 mmHg in systolic BP or an ↑ ≥ 10 beats per minute or more in pulse rate when rising from a lying down position to a standing position
• Dyspnea
• Decrease in supine blood pressure
• Hematemesis
• Hemoptysis
• Fainting upon rising from a lying position or from a sitting position
• Hypovolemic shock
	• Tachycardia at rest or with mild exertion (skin may be cool and clammy)
	• Hematuria
	• Melena
	• Menorrhagia
	• Hematochezia as indicated by ≥ 1 of the following:
	  ○ Bright red colored stool
	  ○ Mahogany colored stool
	  ○ Pure blood
	  ○ Blood mixed with formed stool
	  ○ Bloody diarrhea

Table 7: Signs and Symptoms of VTE

Deep Vein Thrombosis	Pulmonary Embolism
• Tenderness localized to deep venous system (e.g., calf) • Difference in calf circumference > 3 cm when compared to asymptomatic leg (measure 10 cm (4 in) below the tibial tuberosity) • Pitting edema present on symptomatic leg only • Collateral superficial veins, non-varicose • Elevated D-dimer reading	• Hemoptysis • Chest pain • Recent onset and/or worsening dyspnea • Any clinical signs or symptoms of VTE • Elevated D-dimer reading (> 500 micrograms / L)

Table 8: Signs and Symptoms of Stroke in AF patients

- Sudden numbness or weakness in face, arm, or leg, especially on one side of the body
- Sudden confusion, trouble speaking, slurred speech
- Sudden trouble seeing in one or both eyes
- Sudden trouble walking, loss of balance, lack of coordination
- Sudden severe headache with no known cause

III. Initiation of warfarin therapy:

A. Ensure there are no contraindications for warfarin therapy. See Table 9.

Table 9. Warfarin Contraindications	
• Hypersensitivity to warfarin • Active/severe bleeding • Hemorrhagic or bleeding tendencies • Blood dyscrasias • Intracranial bleeding • Major Trauma	• Recent or planned emergent/high risk surgery • Recent neurosurgery or ocular surgery • Spinal puncture or other procedures with potential for uncontrollable bleeding • Malignant hypertension • Pregnancy

B. Warfarin Initiation Dose

1. Start at 5 mg daily.

   Consider patient's age, weight, comorbidities to determine if the patient should be started on a lower dose of 2.5mg daily. See Table 10.

Table 10. Considerations for Lower Initiation Dose
Consider initiating at lower dose of 2.5 mg daily
• Advanced age • Weight < 50 kg • Asian ancestry • Multiple comorbidities: CHF, renal/liver disease, or cancer • Recent surgery and blood loss

2. It takes at least 5-7 days for INR to reach therapeutic range. In patients with an **acute** VTE, bridging with a parenteral anticoagulant is recommended:
   a. Submit a non-formulary request for enoxaparin (Lovenox®).
   b. Assess and review INR in 2-3 days, as discussed in Table 11.
   c. Discontinue enoxaparin once INR reaches therapeutic goal.

Table 11. Warfarin Initiation Nomogram Week 1		
Day Therapy	**INR Value**	**Total Daily Dose**
Day 1	-	Refer to Section B. Warfarin Initiation Dose
In 2-3 days after initiation	< 1.5 1.5 – 1.9 2.0 – 2.5 > 2.5	Increase to 5 – 7.5 mg daily Continue 2.5 – 5 mg daily Decrease to ≤ 2.5 mg daily Hold and recheck INR next day
In additional 2-3 days after previous INR check	< 1.5 1.5 – 1.9 2.0 – 3.0 > 3.0	Increase to 7.5 – 10 mg daily Increase to 5 – 10 mg daily Continue 2.5 – 5 mg daily Hold and recheck INR in 1 – 2 days

Adapted from UW Health. Version 5. Warfarin Management CPG - Ambulatory Appendix A: Warfarin management dosing tool - Adult - Ambulatory. Created 10/28/2015. Available from https://www.uwhealth.org/files/uwhealth/docs/pdf2/Ambulatory_Warfarin_Guideline.pdf

Table 12. Frequency of INR Monitoring After Initiation of Warfarin	
Frequency	**Dose Change**
Every 2 – 3 days	Until INR within therapeutic range on 2 consecutive INR checks
Then every week	Until INR within therapeutic range on 2 consecutive INR checks
Then every 2 weeks	Until INR within therapeutic range on 2 consecutive INR checks
Then every 4 weeks	Once INR and dose are stable

Note: INRs should be scheduled to be drawn on a weekday, Monday – Friday.

3. Refer to Tables 13-15 for dose adjustment after week 1

IV. Management of Warfarin Anticoagulation Therapy

A. A stable patient is considered having ≥ 3 months of consistent INR within goal with no need to adjust dosing

B. Subtherapeutic levels increase the patient's risk for developing an embolism. If a single INR is ≤ 0.5 below the INR therapeutic goal in a usually stable patient, continue current dose and test INR within 1 to 2 weeks.

1. A 10% change in total weekly warfarin dose will result in an approximate INR change of 0.7 to 0.8.
2. A 15% change in total weekly warfarin dose will result in an approximate INR change of 1.

Table 13. Unit Management of Subtherapeutic INR, with INR Target 2.5, Goal Range 2 – 3.

Patient INR	Warfarin Dose Adjustment	Schedule Next INR To Be Drawn In:	Schedule For Reevaluation In:
1.1 to 1.4	Increase total weekly dose by 10% to 20%	2 days before next visit	7 – 14 days
1.5 to 1.9	Increase total weekly dose by 5% to 10%	2 days before next visit	7 – 14 days

C. Supratherapeutic levels increase the patient's risk for developing a severe bleed. If a single INR goal is ≤ 0.5 above the INR therapeutic goal in a usually stable patient, continue current dose and test INR within 1 to 2 weeks.

1. A 10% change in total weekly warfarin dose will result in an approximate INR change of 0.7 to 0.8.
2. A 15% change in total weekly warfarin dose will result in an approximate INR change of 1.
3. An oral Vitamin K dose of 1 to 2.5 mg may result in an INR change varying from 2 to 5 INR units. Monitoring is essential when using Vitamin K to correct supratherapeutic INR levels

Table 14. Unit Management of Subtherapeutic INR with INR Target 3, Goal Range 2.5 – 3.5

Patient INR	Warfarin Dose Adjustment	Schedule Next INR To Be Drawn In:	Schedule For Reevaluation In:
< 2	Increase total weekly dose by 10% to 20%	2 days before next visit	7 – 14 days
2 – 2.4	Increase total weekly dose by 5% to 15%	2 days before next visit	7 – 14 days

Table 15. Unit Management of Supratherapeutic INR
with INR Target 2.5, Goal Range 2 – 3 OR with INR Target 3, Goal Range 2.5 – 3.5

Bleeding Severity	INR	Oral Vitamin K	Warfarin adjustment	Next INR in	Follow up in
Without signs & symptoms of serious bleeding, and without urgent or recent surgery	More than therapeutic up to 5	None	Hold 1 dose or Decrease total weekly dose by 5- 15%.	2 days before next visit	7 – 14 days
	>5 – 8.9	None	Hold 1- 2 doses. Decrease total weekly dose by 10-20%.	1 – 2 days	1 – 2 days. Evaluation of signs of excess bleeding should be frequently performed.
	9 – 10	2.5 – 5 mg based on bleeding risk	Hold warfarin until INR is therapeutic. Then, resume at a dose that is 20-50% less than previous regimen's total weekly dose.	1 – 2 days	As soon as possible. If INR still higher than desirable, may administer another dose of Vitamin K1, 2.5 mg by mouth 24 hours after first dose.
	>10	Hold warfarin, give Vitamin K, and consider transport to higher level of care.			
Serious bleeding	Any INR	Hold warfarin, give Vitamin K, and consider transport to higher level of care.			

D. Factors That Can Result In Subtherapeutic or Supratherapeutic Warfarin Level or Alter Warfarin's Effect

Table 16: Drugs That Can Change Warfarin's Effects and/or INR	
Drugs That ↑ Warfarin's Effects and/or INR (SUPRAtherapeutic)	**Drugs that ↓ Warfarin Effects and/or INR (SUBtherapeutic)**
• Acetaminophen or aspirin > 1.3 g (1300 mg) per day X 7 days or more • Allopurinol • Amiodarone • Androgens: testosterone • Cephalosporins: cephalexin, cefazolin, ceftriaxone • Antiplatelet agents: aspirin, clopidogrel, prasugrel • CYP 2C9 inhibiting drugs : amiodarone, isoniazid, fluoxetine, metronidazole, fluconazole, voriconazole • Antihyperlipidemic agents: gemfibrozil, clofibrate, fenofibrate • NSAID Agents: aspirin, ibuprofen, indomethacin, naproxen, meloxicam • Macrolide antibiotics: clarithromycin, erythromycin • Levothyroxine • Anticonvulsants: phenytoin, valproic acid • Omeprazole • Quinidine • Quinolone antibiotics: ciprofloxacin, levofloxacin • Salicylates: aspirin, salsalate • Selective serotonin reuptake inhibitors: citalopram, fluoxetine, paroxetine, sertraline • Sulfonamide derivatives: trimethoprim / sulfamethoxazole • Tetracycline derivatives: tetracycline, doxycycline	• Antithyroid agents: propylthiouracil • Azathioprine • Bile acid sequestrants: cholestyramine resin • Bosentan • CYP2C9 inducing drugs : carbamazepine, phenobarbital, phenytoin, primidone, rifampin, rifapentine, ritonavir • Penicillin-based antibiotics: dicloxacillin, nafcillin • Hormonal Contraceptives: norethindrone / ethinyl estradiol, norgestrel / ethinyl estradiol, ethynodiol diacetate / ethinyl estradiol • Hormone Therapy: estrogens, conjugated; synthetic estrogens • Sulfasalazine • Chronic daily ethanol use • Griseofulvin • Antipsychotic Agents: haloperidol, clozapine • Spironolactone • Sucralfate • Trazodone

Note: This is not a complete list of drugs that can affect warfarin and/or INR. Providers may consult with a pharmacist and/or check the drug package insert or other drug reference if uncertain of drug-drug interactions.

Table 17: Foods That Alter the Effects of Warfarin	
Foods That ↑ Warfarin's Effects and/or INR	**Foods that ↓ Warfarin Effects and/or INR = Foods High in Vitamin K**
Beverages: • Grapefruit juice • Cranberry juice • Alcohol	**Fats & Dressings**: • Margarine • Mayonnaise • Oil (canola, vegetable, soybean, olive) • Foods containing Olestra® synthetic fats
	Vegetables: • Asparagus • Avocado • Broccoli • Brussel sprouts, cabbage • Cabbage, red • Collard greens, Mustard greens • Endives, raw • Green scallions, raw • Kale, raw leaf • Romaine Lettuce, raw • Parsley • Peas, green, cooked • Spinach, raw leaf • Turnip greens, raw • Watercress, raw
Over-the-Counter Supplements: • Vitamin E • Fish oil • Garlic oil	**Over-the-Counter Supplements:** • Vitamin supplements containing Vitamin K • Vitamin C, high-dose • Nutritional supplement beverages (e.g., Osmolite®)

Table 18: Factors That May Change Warfarin's Effects	
Factors That Can ↑ Warfarin's Effects	**Factors That Can ↓ Warfarin Effects**
• Blood dyscrasias • Cancer • Collagen vascular disease • Congestive Heart Failure (CHF) • Diarrhea • Dietary deficiencies / poor nutritional state • Elevated temperature / fever • Hepatic Disorders: Infectious hepatitis, jaundice • Hyperthyroidism • Prolonged hot weather → dehydration • Steatorrhea • Vitamin K deficiency	• Diet high in Vitamin K • Edema • Hereditary coumarin resistance • Hyperlipidemia • Hypothyroidism • Nephrotic syndrome

V. **Conversions between anticoagulants**

A. Transition from LMWH to NOAC: discontinue LMWH, start NOAC at the time the next dose of LMWH would be due

B. Transition from NOAC to LMWH: discontinue NOAC, start LMWH at the time the next dose of NOAC would be due

C. Transition between different non-vitamin K oral anticoagulants (NOAC): start the new NOAC at the time the next dose of previous NOAC would be due

D. Transition between warfarin and NOAC, see Tables 19 & 20.

Table 19. Transition from NOAC to warfarin*

NOAC	Transition Recommendation
Apixaban (Eliquis®)	Stop apixaban and start warfarin with parenteral anticoagulant (nonformulary enoxaparin). Discontinue parenteral agent when INR is in therapeutic range.
Rivaroxaban (Xarelto®)	Stop rivaroxaban and start warfarin with parenteral anticoagulant (nonformulary enoxaparin). Discontinue parenteral agent when INR is in therapeutic range.
Dabigatran (Pradaxa®)	Stop dabigatran and start warfarin with parenteral anticoagulant (nonformulary enoxaparin). Discontinue parenteral agent when INR is in therapeutic range. Or: If CrCl > 50 mL/min: start warfarin 3 days before stopping dabigatran If CrCl 30-50 mL/min: start warfarin 2 days before stopping dabigatran If CrCl 15-30 mL/min: start warfarin 1 day before stopping dabigatran
Edoxaban (Savaysa®)	Stop edoxaban and start warfarin with parenteral anticoagulant (nonformulary enoxaparin). Discontinue parenteral agent when INR is in therapeutic range. Or: Reduce edoxaban dose by 50% and start warfarin concurrently, check INR weekly, then discontinue edoxaban when INR is in therapeutic range.

*Note: NOACs can elevate the INR, complicating interpretation if overlapped with warfarin.

Table 20. Transition from warfarin to NOAC
NOAC use requires a non-formulary approval

NOAC	Transition Recommendation
Apixaban	Stop warfarin. Once INR is < 2 start apixaban.
Rivaroxaban	Stop warfarin. Once INR is < 3 start rivaroxaban.
Dabigatran	Stop warfarin. Once INR is < 2 start dabigatran.
Edoxaban	Stop warfarin. Once INR is ≤ 2.5 start edoxaban.

VI. **Periprocedural Warfarin Management**

A. Consider postponing non-urgent procedures during the acute phase (3-6 months) of a thromboembolic event.

B. For minor dermatologic surgeries or cataract surgery, continue warfarin therapy as prescribed.

C. For dental procedures, continue warfarin therapy as prescribed.

1. For patients with high risk of bleeding (Refer to Tables 3 & 4), modification to therapy prior to dental surgery should be done in consultation with the patient's medical provider.

D. For all other surgeries that require warfarin interruption:

1. Consult the surgeon and involved specialists regarding the surgical bleed risk, whether bridging is needed, and the timing of stopping and resuming anticoagulant. Providers may also consult a clinical pharmacist.

Table 21. Risk Stratification for Perioperative Thromboembolism

High Risk	• Any mechanical mitral valve • Any mechanical aortic valve • Recent (within 6 months) stroke or TIA • CHADS score of 5 or 6 • Rheumatic valvular heart disease • Recent (within 3 months) VTE • Severe thrombophilia	Consider bridging with LMWH
Moderate Risk	• Bileaflet aortic valve prosthesis and 1 or more risk factors: AF, prior stroke or TIA, hypertension, diabetes, congestive heart failure, age > 75 years • CHADS score of 3 or 4 • VTE within 3-12 months • Recurrent VTE • Active cancer	Bridging decision should be individualized based on surgical risk of bleeding and patient risk factors
Low Risk	• Bileaflet aortic valve prosthesis without atrial fibrillation and no risk factors • CHADS score of 0 – 2 with no prior stroke or TIA • VTE occurred more than 12 months previously	Consider no bridging during anticoagulation interruption

E. Resuming warfarin after perioperative temporary interruption

1. When there is adequate hemostasis, resume warfarin at previous dose 12 to 24 hours after surgery, depending on the surgical bleed risk, the patient's bleeding and thromboembolic risk, and the patient's renal and hepatic functions.
2. Monitor INR 2 weeks after restarting therapy, or sooner if needed.

F. If bridging with LMWH is recommended, provider should submit a non-formulary request for enoxaparin.

1. Pre-procedure: Start LMWH when INR is subtherapeutic. Discontinue >12-24 hours prior to the procedure based on renal function and LMWH dosing frequency (given daily or twice daily).
2. Post-procedure: When there is adequate hemostasis, may resume LMWH 24 hours after a low bleed risk procedure or 48-72 hours after a high bleed risk procedure. Discontinue LMWH when INR is therapeutic.
3. Monitor INR closely during bridging period.

VII. Patient Education

A. Who educates?

1. Any provider involved in providing clinical warfarin therapy management services
2. Providers caring for a patient on warfarin therapy.
3. Specialty clinic providers of care related to the reason for a patient's warfarin therapy.
   a. For example, Cardiology
4. Educator must document in patient's medical record.

B. When does education occur?

1. Clinical warfarin therapy management sessions
2. When patient is stable, following a thromboembolic event or a hemorrhagic event.
3. Group education if available

C. What topics are covered when educating the patient?

1. Relationship between VTE and the patient's current medical condition(s)
2. Relationship between INR and:
   a. The patient's current medical condition(s)
   b. The risk for VTE / bleed
3. Role of adherence in warfarin therapy
4. Role of drug interactions in warfarin therapy
5. Role of changes in diet in warfarin therapy
6. Importance of modifying lifestyle / risk factors in preventing VTE and related conditions, when appropriate
7. Adjusting activities of daily living to minimize the risk of experiencing a bleed while on chronic warfarin therapy
8. Signs and symptoms of VTE and/or bleed, and when to drop a sick call for either of these.
9. Any relevant topic about which the patient requests information

WOUND CARE PATHWAYS

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

Wound / Patient Characteristics	Present?	If yes,
• Located in lower extremities, below the ankle • Decreased peripheral pulses • Smooth/round edges • Wounds are usually small and deep. • Wound bed is dry or pale pink. • "Punched out" lesions • Poor hair and nail growth • Distal wounds • ABI <0.9 • Intermittent claudication	☐ Yes ☐ No	Refer to Arterial Insufficiency Wound DMG
• Callous formation • Dry skin • Decreased sensation • Located in plantar aspect of foot • Diabetes	☐ Yes ☐ No	Refer to Neuropathic Wound DMG
• Mobility impaired • Low Braden Score • Bony prominence • Located in areas of pressure • Malnourished • Moisture exposure	☐ Yes ☐ No	Refer to Pressure Wound DMG
• Located in gaited area, mostly in the medial malleolus • Positive peripheral pulses • Larger, irregular borders • Wounds are usually large and superficial. • Wound bed is beefy, red and moist. • Painful • Surrounding skin usually has stasis dermatitis and hemosiderin. • ABI >0.9 • Presence of scar tissue increases risk of re-ulceration. • Varicosities	☐ Yes ☐ No	Refer to Venous Insufficiency Wound DMG
• Caused by incisional wound dehiscence or laceration • Occurred post-op	☐ Yes ☐ No	Refer to Surgical Wound DMG

Nurses: DMGs are to assist providers in making treatment decisions and are not to be confused with or viewed as Nursing Standing Delegated Orders (SDOs). As such, **treatment recommendations in DMGs cannot be implemented independently by nursing staff without an order from a provider.**

*Prepared by the Correctional Managed Care Pharmacy & Therapeutics Committee, November 2005. Revised 1/07, 11/07, 5/10, 7/12, 3/14. 5/16 Reviewed 1/08, **3/21**.*

ARTERIAL INSUFFICIENCY WOUNDS

1

Patient Assessment:

1. Obtain Ankle Brachial Index (ABI). An ABI <0.9 is diagnostic for Arterial Insufficiency.
2. Assess the patient for symptoms of intermittent claudication. Regardless of normal ABI (0.9 to 1.2), patient may still have arterial insufficiency disease if symptomatic, and further work-up is warranted.
3. Counsel the patient on smoking cessation, to not cross legs, to avoid constrictive garments and to avoid caffeine.
4. Consider ASA 81mg to 325mg for the treatment of intermittent claudication.
5. **Know that undiagnosed arterial insufficiency wounds can lead to osteomyelitis**.
6. Manage underlying diseases that can increase risk of arterial insufficiency disease (e.g. hypertension, hyperlipidemia, cardiovascular disease and diabetes mellitus).
7. If needed, provide adequate pain control (refer to pain disease management guidelines).
8. Ensure tetanus status is up to date.
9. Evaluate the patient for any factors that may slow wound healing (e.g. medications and nutritional status).
10. Consider consultation with the Wound Care Specialist.

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

2 Does the patient have an arterial insufficiency wound that requires treatment?

No → 3
- •Educate patient on wound prevention
- •Follow the patient in Chronic Care Clinic

Yes → 4

Precautions:
- Avoid compression therapy
- Avoid elevation of lower extremities
- Avoid sharp debridement of chronic dry, eschar-covered, uninfected ulcers in pts with low ABI's.

→ 5 Treat wound according to wound bed description. Most arterial insufficiency wounds will be dry. **Go to "Dry Wound Bed".**

6

Wound Bed		Epithelialization	Granulation	Local infection/critical colonization	Necrotic/Slough
Objective		**Protect newly formed tissue**	**Support granulation and tissue growth**	**Debridement and decrease bacterial burden**	**Debridement**
OFFLOAD		**Use offloading equipment i.e., heel protectors, pressure relieving overlay, crutches and trapezes**			
CLEANSE		**Wash with soap and water or a commercial wound cleanser**		**Flush with 250cc's of normal saline or sterile water**	
PROTECT PERIWOUND		**Consider using skin prep, hydrocolloid window paning dressing, or foam with silicone adhesive.**			
Wet Wound Bed	Primary Dressing	•Hydrocolloid •Foam	•Cadexomer Iodine •Silver alginate	•Wet to moist (WTM) dressings •Collagenase (Santyl®) •Silver alginate •Cadexomer Iodine	
	Secondary Dressing	n/a	•Foam •Hydrocolloid •Permeable dressing	•Foam •Gauze	
Moist Wound Bed	Primary Dressing	•Hydrocolloid	•Silver dressing •Cadexomer Iodine	•Silver dressing •Cadexomer Iodine •WTM dressings	
	Secondary Dressing	n/a	•Foam	•Foam •Gauze	
Dry Wound Bed	**Primary Dressing**	**•Hydrogel •Cadexomer Iodine**	**•Hydrogel**	**•Hydrogel •Silver with hydrogel •Collagenase (Santyl®)**	
	Secondary Dressing	**•Hydrocolloid**	**•Hydrocolloid**	**•Foam •Hydrocolloid •Gauze**	

7 Reassess wound every 4 weeks. Is the wound healing?

No → 8 If wound is stagnant or not improving, consider dressing regimen change or referral to Wound Care Specialist.

Yes → 9 Continue care until wound is healed and educate pt on wound care prevention.

NEUROPATHIC WOUNDS

1

Patient Assessment:
1. Check feet for structural changes, bony prominences, or for painless wounds with even margins.
2. Test for sensory function using a 5.07/10gm monofilament.
3. Obtain ABI to rule out arterial insufficiency. Refer to Arterial Insufficiency disease management guidelines.
4. Manage underlying diseases that can increase risk of neuropathic wounds (e.g. diabetes mellitus, hypertension, hyperlipidemia).
5. If needed, provide adequate pain control (refer to pain disease management guidelines).
6. Ensure tetanus status is up to date.
7. Evaluate the patient for any factors that may slow wound healing (e.g., medications and nutritional status).
8. Consider consultation with a Wound Care Specialist.

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

2 Does the patient have a neuropathic wound that requires treatment?

No → 3
- Educate patient on wound prevention and early detection/screening.
- Follow the patient in Chronic Care Clinic.

Yes → 4

4 Assess wound for:
- Calluses
- Infection
- Cellulitis
- Gangrene

→ 5 Consider evaluation for osteomyelitis:
- X-ray if indicated
- Bone scan if indicated
- Ortho referral if indicated

→ 6 Treat wound according to wound bed description. Most neuropathic wounds will be dry. **Go to "Dry Wound Bed". Debridement is the mainstay of therapy.**

7

Wound Bed		Epithelialization	Granulation	Local infection/critical colonization	Callous/Necrotic/ Slough
Objective		**Protect newly formed tissue**	**Support granulation and tissue growth**	**Debridement and decrease bacterial burden**	**Debridement**
OFFLOAD		**Use offloading equipment i.e., heel protectors, pressure relieving overlay, crutches and trapezes**			
CLEANSE		**Wash with soap and water or a commercial wound cleanser**		**Flush with 250cc's of normal saline or sterile water**	
PROTECT PERIWOUND		**Consider using skin prep, hydrocolloid window paning dressing, or foam with silicone adhesive.**			
Wet Wound Bed	Primary Dressing	•Hydrocolloid •Foam	•Cadexomer Iodine •Silver alginate	•Wet to moist (WTM) dressings •Collagenase (Santyl®) •Silver alginate •Cadexomer Iodine	
	Secondary Dressing	n/a	•Foam •Hydrocolloid •Permeable dressing	•Foam •Gauze	
Moist Wound Bed	Primary Dressing	•Hydrocolloid	•Silver dressing •Cadexomer Iodine	•Silver dressing •Cadexomer Iodine •WTM dressings	
	Secondary Dressing	n/a	•Foam	•Foam •Gauze	
Dry Wound Bed	**Primary Dressing**	**•Hydrogel •Cadexomer Iodine**	**•Hydrogel**	**•Hydrogel •Silver with hydrogel •Collagenase (Santyl®)**	
	Secondary Dressing	**•Hydrocolloid**	**•Hydrocolloid**	**•Foam •Hydrocolloid •Gauze**	

8 Reassess wound every 4 weeks. Is the wound healing?

No → 9 If wound is stagnant or not improving, consider dressing regimen change or referral to Wound Care Specialist.

Yes → 10 Continue care until wound is healed and educate pt on wound care prevention.

PRESSURE WOUND

1

Patient Assessment

1. Risk for development of wounds should be determined at intake, each clinic visit and each Chronic Care Clinic visit in high risk patients (e.g., paraplegic, quadriplegic, hemiplegic, geriatric, pt with incontinence, diabetics, immunocompromised patients, patients with peripheral arterial disease, & malnourished patients) using the Braden Scale for Predicting Pressure Sore Risk (Located in the EMR Note Builder Template as "Wound – Braden Scale")
2. May consider moisturizing skin cream for patients with a Braden Scale score less than 14 to protect skin integrity.
3. Perform physical and visually inspect areas prone to wound development at each clinic visit.
4. Counsel patient regarding the importance of adequate hydration and nutrition.
5. Counsel patient regarding the importance of offloading for wound prevention.
6. If needed, provide adequate pain control (refer to pain disease management guideline).
7. Ensure tetanus status is up to date.
8. Evaluate the patient for any factors that may slow wound healing (e.g. medications and nutritional status).
9. Consider consultation with the Wound Care Specialist.

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

2 Does the patient have a pressure wound that requires treatment?

No → 3 •Educate patient on wound prevention •Follow the patient in Chronic Care Clinic

Yes

4 Treat wound according to stage

5	11	12	13	18	20
Stage 1 Non-blanchable erythema of intact skin	**Stage 2** Partial thickness skin loss involving epidermis and/or dermis	**Stage 3** Full thickness skin loss involving damage or necrosis of subcutaneous tissue that may extend to underlying fascia	**Stage 4** Full thickness loss with destruction, tissue necrosis or damage to muscle, bone, or other structures	**Deep tissue injury** Purple or maroon localized area of intact skin	**Unstageable** Full thickness tissue loss in which the base of the ulcer is covered by necrotic tissue

6 •OFFLOAD •Keep area clean and dry •PROTECT THE PERIWOUND

7 Is the skin healing?

No

8 If wound appears to be worsening, reeducate the patient on the importance of wound care (see box 6).

10 Go to box 4.

9 Yes → Go to Box 17

14

Wound Bed		Epithelialization	Granulation	Local infection/critical colonization	Necrotic/Slough
Objective		Protect newly formed tissue	Support granulation and tissue growth	Debridement and decrease bacterial burden	Debridement
OFFLOAD		Use offloading equipment i.e., heel protectors, pressure relieving overlay, crutches and trapezes			
CLEANSE		Wash with soap and water or a commercial wound cleanser		Flush with 250cc's of normal saline or sterile water	
PROTECT PERIWOUND		Consider using skin prep, hydrocolloid window paning dressing, or foam with silicone adhesive.			
Wet Wound Bed	Primary Dressing	•Hydrocolloid •Foam	•Cadexomer iodine •Silver alginate	•Wet to moist (WTM) dressings •Collagenase (Santyl®) •Silver alginate •Cadexomer Iodine	
	Secondary Dressing	n/a	•Foam •Hydrocolloid •Permeable dressing	•Foam •Gauze	
Moist Wound Bed	Primary Dressing	•Hydrocolloid	•Silver dressing •Cadexomer Iodine	•Silver dressing •Cadexomer Iodine •WTM dressings	
	Secondary Dressing	n/a	•Foam	•Foam •Gauze	
Dry Wound Bed	Primary Dressing	•Hydrogel •Cadexomer Iodine	•Hydrogel	•Hydrogel •Silver with hydrogel •Collagenase (Santyl®)	
	Secondary Dressing	•Hydrocolloid	•Hydrocolloid	•Foam •Hydrocolloid •Gauze	

19 •OFFLOAD •PROTECT THE PERIWOUND •Apply foam dressing •Monitor for worsening of wound •Consider referral to wound care specialist

21 •OFFLOAD •PROTECT THE PERIWOUND with hydrocolloid or foam dressing DO NOT DEBRIDE STABLE ESCHAR ON LOWER EXTREMITIES. • Apply foam dressing •Monitor for worsening for wound •Consider referral to wound care specialist.

15 Reassess wound every 4 weeks. Is the wound healing?

No → 16 If wound is stagnant or not improving, consider dressing regimen change or referral to Wound Care Specialist.

Yes → 17 Continue care until wound is healed and educate pt on wound care prevention.

VENOUS INSUFFICIENCY WOUNDS

1

Patient Assessment:
1. Obtain ABI to rule out arterial insufficiency. Refer to Arterial Insufficiency disease management guidelines.
2. May consider moisturizing skin cream for stasis dermatitis.
3. Manage underlying diseases that can increase risk of venous insufficiency disease (e.g. hypertension and diabetes mellitus)
4. If needed, provide adequate pain control (refer to pain disease management guidelines).
5. Ensure tetanus status is up to date.
6. Evaluate the patient for any factors that may slow wound healing (e.g. medications and nutritional status).
7. Consider consultation with the Wound Care Specialist.

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

2 Does the patient have a venous insufficiency wound that requires treatment?

No → 3
- Educate patient on wound prevention
- Follow the patient in Chronic Care Clinic

Yes → 4

4 Counsel the patient on
- Exercises and mobility training
- Lower extremity elevation

5 Use compression therapy to manage edema.
Contraindications:
- Arterial insufficiency with an ABI <0.8
- Acute infection
- Pulmonary edema
- Uncontrolled or severe CHF
- Active deep vein thrombosis

6 Treat wound according to wound bed description. Most venous insufficiency wounds will be wet or moist. **Go to "Wet or Moist Wound Bed".**

7

Wound Bed		Epithelialization	Granulation	Local infection/critical colonization	Necrotic/Slough
Objective		**Protect newly formed tissue**	**Support granulation and tissue growth**	**Debridement and decrease bacterial burden**	**Debridement**
OFFLOAD		**Use offloading equipment i.e., heel protectors, pressure relieving overlay, crutches and trapezes**			
CLEANSE		**Wash with soap and water or a commercial wound cleanser**		**Flush with 250cc's of normal saline or sterile water**	
PROTECT PERIWOUND		**Consider using skin prep, hydrocolloid window paning dressing, or foam with silicone adhesive.**			
Wet Wound Bed	**Primary Dressing**	**•Hydrocolloid •Foam**	**•Cadexomer Iodine •Silver alginate**	**•Wet to moist (WTM) dressings •Collagenase (Santyl®) •Silver alginate •Cadexomer Iodine**	
	Secondary Dressing	**n/a**	**•Foam •Hydrocolloid •Permeable dressing**	**•Foam •Gauze**	
Moist Wound Bed	**Primary Dressing**	**•Hydrocolloid**	**•Silver dressing •Cadexomer Iodine**	**•Silver dressing •Cadexomer Iodine •WTM dressings**	
	Secondary Dressing	**n/a**	**•Foam**	**•Foam •Gauze**	
Dry Wound Bed	Primary Dressing	•Hydrogel •Cadexomer Iodine	•Hydrogel	•Hydrogel •Silver with hydrogel •Collagenase (Santyl®)	
	Secondary Dressing	•Hydrocolloid	•Hydrocolloid	•Foam •Hydrocolloid •Gauze	

8 Reassess wound every 4 weeks. Is the wound healing?

No → 9 If wound is stagnant or not improving, consider dressing regimen change or referral to Wound Care Specialist.

Yes → 10 Continue care until wound is healed and educate pt on wound care prevention.

SURGICAL WOUNDS

1

Patient Assessment:
1. Address co-morbidities and optimize treatment e.g., diabetes, renal diabetes, infections (HIV, HCV, skin, bone), circulation/smoking, obesity.
2. If needed, provide adequate pain control (refer to pain disease management guideline).
3. Ensure tetanus status is up to date.
4. Evaluate the patient for any factors that may slow wound healing (e.g. medications and nutritional status).
5. Consider consultation with the Wound Care Specialist.

2 Does the patient have a surgical wound that needs treatment?

No → 3
- Educate patient on basic wound care.
- Counsel the patient on incision protection and good hygiene.
- Educate patient on signs and symptom of infection and to report complications to the medical department.
- Follow the patient for suture/staple removal.

Yes → 4

Prevent surgical complications

Surgical Site Infections	Delayed Healing	Bleeding	Dehiscence	Evisceration
• Remove surgical sutures per recommendation • Keep area dry and clean	• Off-load • Avoid mechanical stress on the wound.	• Cautious use of anticoagulants and NSAIDS • Avoid mechanical stress on the wound	• Avoid mechanical stress on the wound • Consider abdominal binders or montgomery straps	• Avoid mechanical stress on the wound • Avoid lifting **This is a surgical emergency.**

5 Treat wound according to method of closure and wound bed.

6 **Primary Intention**
Wounds that are approximated with surgical closure.

7 **Secondary Intention**
Wounds which are left open and filled in with granulation or scar tissue.

8 **Tertiary Intention**
Large or infected wounds which require debridement or drainage prior to closure.

9 See box 3

10

Wound Bed		Epithelialization	Granulation	Local infection/critical colonization	Necrotic/Slough
Objective		Protect newly formed tissue	Support granulation and tissue growth	Debridement and decrease bacterial burden	Debridement
OFFLOAD		Use offloading equipment i.e., heel protectors, pressure relieving overlay, crutches and trapezes			
CLEANSE		Wash with soap and water or a commercial wound cleanser		Flush with 250cc's of normal saline or sterile water	
PROTECT PERIWOUND		Consider using skin prep, hydrocolloid window paning dressing, or foam with silicone adhesive.			
Wet Wound Bed	Primary Dressing	•Hydrocolloid •Foam	•Cadexomer Iodine •Silver alginate	•Wet to moist (WTM) dressings •Collagenase (Santyl®) •Silver alginate •Cadexomer Iodine	
	Secondary Dressing	n/a	•Foam •Hydrocolloid •Permeable dressing	•Foam •Gauze	
Moist Wound Bed	Primary Dressing	•Hydrocolloid	•Silver dressing •Cadexomer Iodine	•Silver dressing •Cadexomer Iodine •WTM dressings	
	Secondary Dressing	n/a	•Foam	•Foam •Gauze	
Dry Wound Bed	Primary Dressing	•Hydrogel •Cadexomer Iodine	•Hydrogel	•Hydrogel •Silver with hydrogel •Collagenase (Santyl®)	
	Secondary Dressing	•Hydrocolloid	•Hydrocolloid	•Foam •Hydrocolloid •Gauze	

The pathways do not replace sound clinical judgment nor are they intended to strictly apply to all patients.

11 Reassess wound every 4 weeks. Is the wound healing?

No → 12 If wound is stagnant or not improving, consider dressing regimen change or referral to Wound Care Specialist.

Yes → 13 Continue care until wound is healed and educate pt on wound care prevention.

Purpose

1. To define different kinds of wounds and how to individualize treatment regimen per wound type
2. To define specific language for the assessment of wounds
3. To provide preventative measures and prevention education for each high-risk population
4. To provide education on specific treatment measures

Definitions/Description

I. Arterial Insufficiency Wounds
   - A. Definition: Wound caused by the partial or complete blockage of arterial blood flow to the internal organs, arms or leg as a result of atherosclerosis. Intermittent claudication (defined as pain, fatigue or cramping in the leg muscles occurring with activity) is a common symptom of arterial insufficiency. ABI is <0.9.
   - B. Description of wound: Arterial insufficiency wounds will appear small and "punched out," with round and smooth margins. Wounds are usually deep, and the wound bed is dry, pale pink or grey.

II. Neuropathic Wounds
   - A. Definition: Wound caused by peripheral neuropathy and constant pressure or repeated trauma to lower extremities, otherwise known as diabetic foot ulcers in diabetics.
   - B. Description of wound: Wound usually located on the plantar aspect of the foot on a pressure point. It will be painless, surrounded by a callous and have even wound margins. Wound bed is usually deep and dry.

III. Pressure wounds
   - A. Definition: Wound caused by localized injury to the skin and/or underlying tissue usually over a bony prominence, as a result of pressure or pressure combined with shear and/or friction.
   - B. Description of wound: Wound usually located on a pressure point and is defined by the level of tissue involved.

IV. Venous insufficiency wounds
   - A. Definition: Wound caused by improper functioning of the venous valves, usually of the legs. It is the most common type of leg ulcers, accounting for 80-85% of all cases.
   - B. Description of wound: Wound usually located on the Gaiter area, where area has been exposed to trauma and/or skin is the weakest (e.g., scar sites of skin graft). Wound will be superficial, irregular in shape, and painful. Wound bed is beefy, red and wet.

V. Surgical Wounds
   - A. Definition: Wound caused by a precise, planned break in the skin integrity or sutured laceration.
   - B. Description of wound: Wounds occurring post-surgery based on type of closure.

Prevention of Wounds

I. Manage underlying risk factors
   - A. Arterial Insufficiency Wounds:
     1. Optimize management of hypertension, hyperlipidemia and diabetes through therapeutic lifestyle changes and pharmacotherapy.
     2. Improve tissue perfusion by avoiding tobacco, caffeine, and wearing constrictive garments, not crossing legs and staying hydrated.
     3. Consider antiplatelet medication for peripheral arterial disease.
     4. Counsel patient on conducting daily inspections of skin and to notify a health care provider if any lesions start to form.
   - B. Neuropathic Wounds
     1. Assess patient for neuropathy by testing for sensory function using a 5.07/10gm monofilament
        a. Demonstrate sensation on forearm or hand.
        b. Place monofilament perpendicular to test site on plantar aspect of foot.
        c. Bow into C-shape for one second.
        d. Test minimum of four sites, avoiding calluses, scar and ulcers.
     2. Optimize glycemic control in diabetics
     3. Counsel patient to off-load lower extremities to prevent repetitive pressure and trauma to feet.
     4. Counsel patient to visually inspect feet for lesions, ulcers and calluses.
     5. Manage the risk factors for peripheral arterial disease, e.g., hypertension, hyperlipidemia, smoking.
     6. Refer for proper fitting footwear.
     7. Counsel patient on conducting daily inspections of skin and to notify a health care provider if any lesions start to form.
   - C. Pressure Wounds
     1. Assess patient's risk for the development of wounds at intake, each clinic visit, and Chronic Care Clinic visit in high-risk patients using the Braden Scale (Located in the EMR Note Builder Template as "Wound – Braden Scale")
     2. High risk patients are:
        a. Paraplegics, quadriplegics, hemiplegics
        b. Geriatric patients
        c. Patients with incontinence
        d. Diabetics
        e. Immunocompromised patients
        f. Patients with peripheral arterial disease
        g. Malnourished patients
     3. Physically and visually inspect areas prone to wound development at each clinic visit.
     4. Maintain skin integrity by keeping area clean and dry.
        a. Gentle cleansing for bed bound and/or incontinent patients.
        b. Prevent excessive moisture by changing incontinent patient frequently and using moisture barrier creams.
        c. Consider moisturizing skin cream for patients with a Braden Scale score of less than 14.
     5. Off-load
        a. Reposition at least every 2 hours or as indicated. Use turning sheets, trapeze or lifts to reposition to prevent sheer and drag.
        b. Elevate head of bed no more than 30 degrees.
        c. Raise heels off the bed by placing pillows under legs allowing the heels to hang off the edge or use heel protectors.
        d. Use pressure reducing devices, e.g., high density foam mattress overlay, as available.

6. Optimize glycemic control in diabetics.
7. Manage the risk factors for peripheral arterial disease, e.g., hypertension, hyperlipidemia, smoking.
8. Treat underlying disease to improve immune system in immunocompromised patients.
9. Counsel patient on conducting daily inspections of skin and to notify a health care provider if any lesions start to form.

D. Venous Insufficiency Wounds
1. Optimize management of hypertension, hyperlipidemia and diabetes through therapeutic lifestyle changes and pharmacotherapy
2. Counsel patient to implement therapeutic lifestyle changes with diet and exercise to maintain normal body mass index (BMI).
3. Counsel patient to decrease salt consumption.
4. Counsel patient on conducting daily inspections of skin and to notify a health care provider if any lesions start to form.
5. Counsel patient that compression therapy is the mainstay of prevention and treatment.

E. Surgical wounds
1. Counsel patient to avoid mechanical stress on the incision.
2. Counsel patient on conducting daily inspections of skin and to notify a health care provider if any lesions start to form.

II. Screen for medications that may impede wound healing
A. Anticoagulants – forms hematomas
B. Aspirin – suppresses inflammation
C. NSAIDS – suppress inflammation, protein synthesis and epithelialization

III. Evaluate nutritional status
A. Counsel patient on the importance of adequate hydration and nutrition.
B. Assure adequate protein intake.
C. Consider nutritional supplement if unintentional weight loss leads to loss of lean body mass. Evaluate for underlying cause of weight loss.

<u>Assessment of Wounds</u>

I. Determine the mechanism of injury. CONSIDER obtaining the appropriate diagnostic work-up.
A. Arterial insufficiency wounds
1. Ankle-Brachial Index (ABI) Measurement is a non-invasive tool necessary for screening arterial insufficiency. Refer to Vascular Surgery Lab.
a. How ABI is performed:
i. Equipment: blood pressure and handheld Doppler device with a vascular probe
ii. ABI = Ankle Systolic BP / Brachial Systolic BP
iii. Using a BP cuff and Doppler, measure the systolic BP in the right dorsalis pedis and right posterior tibial arteries. Use the higher SBP to calculate the ABI for the right leg.
iv. Using a BP cuff and Doppler, measure the systolic BP in the left dorsalis pedis and left posterior tibial arteries. Use the higher SBP to calculate the ABI for the left leg.
v. Using a BP cuff, measure the systolic BP in the brachial artery in both arms. Use the higher SBP for the ABI formula to calculate the ABI in both the right and left legs.
b. ABI Interpretation
i. ABI > 1.2 is not a valid test. Refer to vascular surgery due to possible stiffening of vessels secondary to diabetes or hypertension.
ii. ABI 0.9 to 1.2 is normal
iii. ABI 0.6 to 0.8 is borderline perfusion. Manage wound according to Arterial Insufficiency DMG.
iv. ABI of < 0.5 is critical ischemia and requires immediate referral to vascular surgery

B. Neuropathic wounds
1. Check ABI to screen for arterial insufficiency, which may co-exist with peripheral neuropathy.
2. Screen for infection with wound culture, and screen for osteomyelitis with x-ray.
3. Classify the wound according to the Wagner Grading System
a. Grade 0 – No open foot lesions
b. Grade 1 – Presence of superficial ulcer, partial or full thickness
c. Grade 2 – Ulcer extends to ligaments, tendon, join capsule or deep fascia without abscess or osteomyelitis
d. Grade 3 – Presence of deep ulcer with abscess, osteomyelitis or joint sepsis
e. Grade 4 – Gangrene localized to the forefoot or heel
f. Grade 5 – Extensive gangrene

C. Pressure wounds
1. Screen for infection with wound culture, and screen for osteomyelitis with x-ray.
2. Stage the wound based upon the level of tissue involved. ONLY pressure wounds are staged.
a. Stage 1 – non-blanchable erythema
b. Stage 2 – partial thickness skin loss involving the epidermis and possibly the dermis
c. Stage 3 – full thickness skin loss involving damage or necrosis of subcutaneous tissue that may extend down but not through underlying fascia
d. Stage 4 – full thickness skin loss involving damage to muscle, bone, or supporting structures.
e. Deep Tissue Injury - Purple or maroon localized area of intact skin
f. Unstageable - Full thickness tissue loss in which the base of the ulcer is covered by necrotic tissue

D. Venous insufficiency wounds
1. Screen for concomitant arterial insufficiency by checking the ABI. Compression should not be used with ABI <0.8.
2. Screen for DVT (deep vein thrombosis) by checking ultrasonography.

E. Surgical wounds – screen for infection with wound culture, and screen for osteomyelitis with x-ray.

II. Identify any underlying co-morbidities – diabetes, hypertension, hyperlipidemia or chronic infections.

III. Review medication profile.
A. Optimize control of underlying comorbidities.
B. Identify medications that may impair wound healing.

IV. Review vitals, including weight.

V. Wound documentation (document using the EMR Note Builder Template "Wound – Wound Care Assessment Form")
- A. Type of wound
- B. Location of wound
- C. Measurement of wound
  1. What is the size of the wound (measure in centimeters)?
     - a. Measure actual ulcer. Do not include the periwound in the measurement.
     - b. Measure the longest length (cm) x widest width (cm) x deepest depth (cm).
  2. Document tunneling (development of sinus tract)
  3. Document undermining (when the tissue erodes under the wound edges)
- D. Describe the wound bed
  1. Red/pink – healthy granulating tissue
  2. Yellow/tan – slough
  3. Black – eschar
  4. Pale – decreased circulation (often seen in arterial insufficiency wounds)
- E. Describe the periwound (wound edges)
  1. Describe structure and quality: calloused, rolled, healing with epithelization, scarred, or pigmented.
  2. Temperature: cool or warm
  3. Edematous
- F. Describe the wound drainage
  1. Amount (mild, moderate, copious) in the wound, NOT on the dressing
  2. Color
  3. Type
     - a. Serous – inflammatory phase of wound healing
     - b. Sanguineous – from bleeding
     - c. Purulent – from infection
  4. Consistency of drainage: thick or thin
- G. Note odor

<u>Treatment of Wounds</u>

Step 1: Cleanse the wound, then pat dry.
- A. Superficial wounds – cleanse with soap and water or use a commercial cleanser
- B. Deeper wounds – flush with 250cc's of normal saline or sterile water
- C. Do not use iodine or betadine as these are cytotoxic to healing skin.
- D. Do not soak the wound.

Step 2: Protect the periwound (skin surrounding the edges of the wound). Options include:
- A. Copolymer skin prep – do not use with silicone adhesive
- B. Hydrocolloid window paning
- C. Silicone adhesive

Step 3: Apply primary dressing directly to the wound bed. Options include:
- A. Gauze (wet to moist) dressing (refer to Debridement on page 10, section IV.C.)
- B. Alginate - for moderate to highly draining wounds (refer Debridement on page 10, section IV. A.).
- C. Hydrogel - for minimally or moderately draining wounds (refer to Debridement on page 10, section IV. A.).
- D. Silver dressing (refer to Management of Infection on page 10, section II.C. and D.)
  1. Silver infused sheets or gel for dry or moist wounds
  2. Silver with alginate for wet wounds
- E. Cadexemer iodine dressing (refer to Management of Infection on page 10, section II.C. and D.)
- F. Chemical debrider - collagenase for debridement of calloused and necrotic wounds (refer to Debridement on page 10, section IV.B.)

Step 4: Apply secondary dressing to wound bed. Options include:
- A. Gauze dressing – use with hydrogel, wet to moist dressings or chemical debrider
- B. Foam dressing – use with silver dressing or cadexomer iodine
- C. Hydrocolloid dressing – use with silver dressing or cadexomer iodine
- D. Permeable dressing – use with hydrogel, wet to moist dressing or chemical debrider

<u>Debridement</u>

I. Purpose
- A. Decreases bacterial load and reduces risk of infection, as devitalized material is a medium for infection and supports the growth of organisms that retard wound healing
- B. Increases effectiveness of topical treatments
- C. Decreases wound odor

II. Indication – for removal of necrotic tissue, debris, callus, foreign material, eschar and slough.

III. Special considerations – recommend to Wound Care Clinic
- A. Hypergranulating wounds
- B. Heel ulcers with eschar without edema, erythema, fluctuance or drainage.
- C. Patient factors:
  1. Co-morbidities (e.g., uncontrolled diabetes)
  2. Thrombocytopenia
  3. Anticoagulation use
  4. Patient setting (e.g., hospice)

IV. Different types of debridement
- A. Autolytic debridement - uses body's endogenous enzymes to debride necrotic tissue with moisture-retentive dressing (example: Alginate dressings and hydrogel dressings)
  1. Indicated for non-infected wounds with necrotic tissue
  2. Advantages
     a. Moist wound healing
     b. Dressing changes are fast/easy and can be every 72 to 96 hours
  3. Disadvantage – patients often complain of odor.
- B. Enzymatic debridement - uses prescribed enzymes to debride necrotic tissue with moisture –retentive dressing (example: collagenase with hydrocolloid dressing; do not use iodine or silver containing dressings as silver and iodine deactivates the collagenase.)
  1. Indicated for infected and non-infected wounds with necrotic tissue
  2. Advantages
     a. Moist wound healing
     b. Dressing changes are fast/easy
  3. Disadvantage – dressing changes are up to BID to TID
- C. Mechanical debridement - uses force to remove devitalized tissue (example: gauze (wet to moist) dressings)
  1. Advantages
     a. Dressing changes are fast/easy
     b. Decreases odor
     c. Decreases drainage in highly exudative wounds
  2. Disadvantages
     a. Nonselective debridement
     b. Painful
     c. Periwound maceration
     d. Dressing changes up to BID to TID
- D. Sharp debridement - uses forceps, scissors or scalpel to remove devitalized tissue
- E. Surgical debridement – debridement in a sterile operating room environment.
- F. Biological debridement – uses maggot larvae for debridement of necrotic tissue.

<u>Management of Infection</u>

I. Prevention of infection
- A. Wash hands with soap, water and friction.
- B. Open supplies just prior to use.
- C. Keep wound always covered except during examination.
- D. Treat most infected wound last.
- E. Change gloves between dressings.

II. Stages of infection
- A. Contamination
  1. Description: Existence of non-replicating bacteria within a wound. All chronic wounds are contaminated.
  2. Management: irrigate or cleanse with sterile water or normal saline
- B. Colonization
  1. Description: Presence of replicating bacteria but does not adversely affect the individual (no odor, no drainage).
  2. Management: irrigate or cleanse with sterile water or normal saline
- C. Critical colonization
  1. Description: Theoretical point when the bacteria becomes a bioburden. Wound may start exuding serous fluid, have an odor and/or have friable or red granulation tissue.
  2. Management: Consider a wound culture using the Levine technique, and topical antimicrobial treatment (e.g., antimicrobial dressings such silver or cadexomer iodine dressings or triple antibiotic cream).
- D. Infection
  1. Description: When bacteria invade the body tissue of the host. A wound culture will have bacterial levels greater than 10^5 organisms per gram. Wound healing becomes stalled or reverses. Wound will be warm to touch, edematous and erythemetous. Bacteria may gain access to systemic circulation. Patient may start exhibiting systemic symptoms of infection.
  2. Management: Consider clinical work-up for infection (monitor vitals, obtain labs such as CBC and cultures via the Levine technique, and order appropriate x-rays if needed). Use appropriate systemic antibiotics plus topical antimicrobial treatment (e.g., antimicrobial dressings such silver or cadexomer iodine dressings or triple antibiotic cream).
  3. SYSTEMIC antibiotics are only indicated when the wound is INFECTED.

III. Culture using the Levine technique
- A. Cleanse the wound with sterile water or normal saline to wash away any slough, necrotic tissue or dried exudate.
- B. Moisten the culture tip.
  1. If the wound is moist, a sterile swab can be used straight from the packaging.
  2. If the wound is dry, then the swab tip should be moistened with sterile water to increase the chances of recovering organisms from the site.
- C. Collect in a zig-zag motion – the swab should be moved across the wound surface in a zig-zag motion, at the same time, being rotated between the fingers.
- D. Send to lab – immediately following the collection, the swab should be returned to its container (placed into the transport medium) and accurately labeled.

Braden Scale For Predicting Pressure Sore Risk

Located in the EMR Note Builder template as "Wound-Braden Scale"

Directions: Assessment should be done upon intake, every clinic visit, and Chronic Care Clinic visit for high-risk patients (defined on page 3). Note: Patients with a total score of 16 or less are considered to be at risk for developing pressure ulcers (15-16 = low risk, 13-14 = moderate risk, 12 or less = high risk).

				Date of Assessment	
Sensory Perception Ability to respond meaningfully to pressure-related discomfort.	1. **Completely Limited**. Unresponsive (does not moan, flinch or grasp) to painful stimuli, due to diminished level of consciousness or sedation **or** limited ability to feel pain over most of body	2. **Very Limited**. Responds only to painful stimuli. Can't communicate discomfort except by moaning or restlessness **or** has a sensory impairment which limits ability to feel pain or discomfort over ½ of body.	3. **Slightly Limited**. Responds to verbal commands but can't always communicate discomfort or the need to be turned **or** has some sensory impairment which limits ability to feel pain or discomfort in 1 or 2 extremities.	4. **No Impairment**. Responds to verbal commands. Has no sensory deficit which would limit ability to feel or voice pain or discomfort.	
Moisture Degree to which skin is exposed to moisture	1. **Constantly Moist**. Skin is kept moist almost constantly by perspiration urine, etc. Dampness is detected every time patient is moved or turned.	2. **Very Moist**. Skin is often, but not always moist. Linen must be changed at least once a shift.	3. **Occasionally Moist**. Skin is occasionally moist requiring an extra linen change once a day.	4. **Rarely Moist**. Skin is usually dry; linen only requires changing at routine intervals.	
Activity Degree of physical activity	1. **Bedfast**. Confined to bed.	2. **Chairfast**. Ability to walk severely limited or non-existent. Can't bear own weight, and/or must be assisted into chair or wheelchair.	3. **Walks Occasionally**. Walks occasionally during day, but for very short distances, with or without assistance. Spends majority of each shift in bed or chair.	4. **Walks Frequently**. Walks outside room at least twice a day & inside room at least once every 2 hours during waking hours.	
Mobility Ability to change & control body position	1. **Completely Immobile**. Does not make slight changes in body or extremity position without assistance.	2. **Very Limited**. Makes occasional slight changes in body or extremity position but unable to make frequent or significant changes independently.	3. **Slightly Limited**. Makes frequent though slight changes in body or extremity position independently.	4. **No Limitation**. Makes major & frequent changes in position without assistance.	
Nutrition Usual food intake pattern	1. **Very Poor**. Never eats a complete meal. Rarely eats more than 1/3 of food offered. Eats 2 servings or less of protein (meat or dairy) per day. Takes fluids poorly. Doesn't take a liquid dietary supplement **or** is NPO and/or maintained on clear liquids or IV for more than 5 days.	2. **Probably Inadequate**. Rarely eats a complete meal & generally eats only ½ of food offered. Protein intake includes only 3 servings of meat or dairy products per day. Occasionally will take a dietary supplement **or** receives less than optimum amount of liquid diet or tube feeding.	3. **Adequate**. Eats over ½ of most meals. Eats a total of 4 servings of protein per day. Occasionally will refuse a meal but will usually take a supplement when offered **or** is on a tube feeding or TPN regimen which probably meets most of nutritional needs.	4. **Excellent**. Eats most of every meal. Never refuses a meal. Usually eats a total of 4 or more servings of meat & dairy products. Occasionally eats between meals. Does not require supplementation.	
Friction & Shear	1. **Problem**. Requires moderate to maximum assistance in moving. Complete lifting without sliding against sheets is impossible. Frequently slides down in bed or chair requiring frequent repositioning with maximum assistance. Spasticity, contractures or agitation leads to almost constant friction.	2. **Potential Problem**. Moves feebly or requires minimum assistance. During a move, skin probably slides to some extent against sheets, chair, restraints or other devices. Maintains relatively good position in chair or bed most of the time but occasionally slides down.	3. **No Apparent Problem**. Moves in bed and in chair independently & has sufficient muscle strength to lift completely during move. Maintains good position in bed or chair.		
				Total Score	

WOUND CARE ASSESSMENT FORM
Located in the EMR Note Builder Template as "Wound – Wound Care Assessment Form"

Patient Name: _____ TDCJ#:
Date and time of evaluation: _____
Admit Date: _____
Patient Diagnosis: _____
Braden Score: _____
Location of Wound: 1. _____
2. _____
3. _____

DESCRIPTION OF WOUND	WOUND 1	WOUND 2	WOUND 3
SKIN AROUND WOUND			
Skin color around wound			
1. Normal			
2. Bright red or blanches to touch			
3. Dark red or purple, non-blanchable			
4. White or gray pallor, macerated			
5. Irritated, dermatitis or reaction			
Peripheral tissue edema (press 5 seconds)	**WOUND 1**	**WOUND 2**	**WOUND 3**
1. Minimal swelling around wound			
2. Non-pitting edema, skin shiny and taunt			
3. Pitting edema			
Peripheral tissue firmness (induration)	**WOUND 1**	**WOUND 2**	**WOUND 3**
1. Minimal firmness			
2. Cannot gently pinch tissue			
3. Firmness extends to surrounding tissue			
DRAINAGE OF THE WOUND			
Exudate type	**WOUND 1**	**WOUND 2**	**WOUND 3**
1. None			
2. Sanguinous (bloody)			
3. Serous (clear)			
4. Serosanguinous (watery pink)			
5. Purulent			
6. Odor			
Exudate amount	**WOUND 1**	**WOUND 2**	**WOUND 3**
1. None or dry wound tissue			
2. Scant or moist wound tissue			
3. Small or wet wound tissue			
4. Moderate or saturated wound tissue			
5. Large or draining obvious			

DESCRIPTION OF WOUND	WOUND 1	WOUND 2	WOUND 3
ARCHITECTURE OF UNHEALED WOUND			
Measurements in centimeters (cm)			
1. Length (vertical dimension) in cm			
2. Width (horizontal dimension) in cm			
3. Depth (deepest, do not include tunnel) in cm			
WOUND BED CHARACTERISTICS	**WOUND 1**	**WOUND 2**	**WOUND 3**
Necrotic type			
1. None visible			
2. Non-adherent yellow slough			
3. Loosely adherent yellow slough			
4. Adherent soft, eschar			
5. Firmly adherent, hard eschar			
Granulation tissue type	**WOUND 1**	**WOUND 2**	**WOUND 3**
1. Skin intact			
2. Bright, beefy red			
3. Pink or dull, dusky red			
4. Combination of #2 and #3			
5. Obscured			

Undermining/Tunneling Wound	**Location of undermining/tunneling (use clock as reference)**	**Depth of tunnel in cm**
For example, right ischial wound with tunnel	Tunnel at 3 o'clock	3 cm

GOALS	GOALS MET	NOT MET
1. Facilitate granulation and re-epithelialization through use of clean technique during cleansing and dressing change		
2. Promote granulation tissue of wound bed		
3. Soften and remove non-viable tissue		
4. Patient will express understanding and importance of the educational information presented		

PLAN:

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