HIV DISEASE MANAGEMENT

1

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. Perform pelvic exam every 6 months for HIV+ female patients.
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.
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 Selzentry® or Fuzeon® 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 patient meets the following criteria: not on treatment, during the first two years on ART, or if viremia develops while on ART. For patients with CD4 > 300 cells/mm^3 and virally suppressed on treatment > 2 years, CD4 count may be measured every 6 to 12 months. HIV viral load is measured every 3 to 6 months unless the patient is stable and virally suppressed on treatment > 2 years, then can be extended to every 6 months. Obtain CBC with differential every 3 to 6 months and Chemistries including LFTs, serum creatinine, blood sugar, lipid profile at least 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

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

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 for each drug ≥ 80% and is the patient tolerant?

Yes → 7 Reinforce education. Return to clinic 1 month.

No → 8

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 for each drug ≥ 80%?

Yes → 12 Go To Box #15.

No → 11

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 for each drug ≥ 80%?

No → 13

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.

Yes → 15

14 Is adherence for each drug ≥ 80%?

No → 11

Yes → 15 Obtain viral load.

16 Has viral load decreased > 10 fold (1 log)?

Yes → 17

17 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, during the first two years on ART, or if viremia develops while on ART. For patients with CD4 > 300 cells/mm^3 and virally suppressed on treatment > 2 years, CD4 count may be measured every 6 to 12 months. HIV viral load is measured every 3 to 4 months unless the patient is stable and virally suppressed on treatment > 2 years, then may be extended to every 6 months.
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

No → 18 Repeat viral load in 1 month

19 Has viral load decreased > 10 fold (1 log)?

Yes → 17

No → 20

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.

Box A: Primary Prophylaxis of Opportunistic Infections				
Initiate based on CD4 count	Organism	Recommended Regimen	Alternative Regimen	Discontinuation Criteria*****
All (regardless of CD4 count)	M. tuberculosis PPD ≥ 5 mm	INH 5mg/kg/day (max 300mg) or 900mg twice a week x 9 months	Rifampin 600mg po qd or Rifabutin 300mg po qd 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 patients (2 dose series)		
	Hepatitis B virus*	Hepatitis B vaccine (3 dose series)		
< 200**	**Pneumocystis jirovecii**	TMP-SMX DS Once daily or three times weekly	Dapsone 100mg qd or Atovaquone 1500mg qd (nonformulary approval is required)	CD4 count > 200 for > 3 months Can consider 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)**
< 100***	**Toxoplasma gondii**	TMP-SMX DS Once daily or three times weekly	Dapsone 100mg qd + pyrimethamine 50mg q week + leucovorin 25mg q week	CD4 count > 200 for > 3 months Can consider 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)**
< 50	M. avium complex	Azithromycin 1200 mg q week	Clarithromycin 500mg bid or rifabutin 300mg qd	CD4 count > 100 for ≥ 3 months **(restart if CD4 count < 50)**

* all susceptible (anti-HBc negative) patients
** start prophylaxis if have oropharyngeal candidiasis regardless of CD4 count
***if also antibody positive
****primary prophylaxis for CMV and deep fungal infections is generally not recommended
*****in response to ART and virally suppressed

Box B: Secondary Prophylaxis of Opportunistic Infections				
Indication	Organism	Recommended Regimen	Alternative Regimen	Discontinuation Criteria****
Prior PCP	Pneumocystis jirovecii	TMP-SMX DS qd	TMP-SMX DS three times weekly, Dapsone 100mg qd or Atovaquone 1500mg daily (Nonformulary approval required)	CD4 count > 200 for > 3 months Can consider 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 1000mg to 2000mg po bid + Pyrimethamine 25-50mg po qd + Leucovorin 10-25mg po qd	Clindamycin 600mg po q 6 hr + Pyrimethamine 25-50mg po qd + Leucovorin 10-25mg po qd	CD4 count > 200 for > 6 months* **(restart if CD4 count < 200)**
Prior disseminated disease	M. avium complex	Clarithromycin 500mg po bid + Ethambutol 15mg/kg po qd +/- Rifabutin 300mg po qd	Azithromycin 500mg po qd + Ethambutol 15mg/kg po qd +/- Rifabutin 300mg po qd	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 1gm po TID + SR implant q 6-9 months	Foscarnet IV 90mg/kg/day , Cidofovir 5mg/kg IV q 2 weeks, or Valganciclovir 900mg po qd	CD4 count > 100 for > 3-6 months** **(restart if CD4 count < 100)**
Prior disease	Cryptococcus neoformans	Fluconazole 200mg po qd	Itraconazole 200mg po qd, or Amphotericin 0.6-1mg/kg IV weekly – 3 times weekly	CD4 count ≥ 100 for > 3 months* **(restart if CD4 count < 100)**
Prior disease	Histoplasma capsulatum	Itraconazole 200mg po bid	Amphotericin 1mg/kg IV weekly or Fluconazole 800mg qd	Histoplasma antigen < 2ng/mL, CD4 count > 150 for ≥ 6 months* **(restart CD4 count ≤ 150)**
Prior disease	Coccidioides immitis	Fluconazole 400mg po qd	Itraconazole 200mg po bid or Amphotericin 1mg/kg IV weekly	
Bacteremia	Salmonella species	Ciprofloxacin 500mg po bid x several months		CD4 count > 200
Frequent/ severe recurrences	Herpes simplex virus***	Acyclovir 400mg po bid	Valacyclovir 500mg po bid or famciclovir 250mg bid	
Frequent/ severe recurrences	Candida*** (oropharyngeal, vulvovaginal, esophageal)	Fluconazole 100-200mg po qd	Itraconazole 200mg po qd	

*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

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 offenders 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

Table 1: Combination Products

Medication	Dosage	Drug Interactions*	Adverse Effect*
Atripla®** (emtricitabine 200mg, tenofovir 300mg, & efavirenz 600mg) Non-formulary	1 tablet QD Do not use if CrCl < 50	Same as single entity drugs	Same as single entity drugs
Biktarvy® (bictegravir 50mg, emtricitabine 200mg, & tenofovir alafenamide 25mg) Non-formulary	1 tablet QD Do not use if CrCl < 30	Same as single entity drugs	Headache, skin rash, diarrhea, nausea, increased LDL cholesterol
Cimduo®** (lamivudine 300mg, & tenofovir 300mg) Non-formulary	1 tablet QD Do not use if CrCl < 50	Same as single entity drugs	Same as single entity drugs
Combivir®** (zidovudine 300 mg & lamivudine 150mg) Non-formulary	1 tablet BID Do not use if CrCl < 50	Same as single entity drugs	Same as single entity drugs
Complera®** (emtricitabine 200mg, tenofovir 300mg, & rilpivirine 25mg) Non-formulary	1 tablet QD 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 100mg, lamivudine 300mg, & tenofovir 300mg) Non-formulary	1 tablet QD 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
Epzicom®** (lamivudine 300mg & abacavir 600mg) Non-formulary	1 tablet QD Do not use if CrCl < 50	Same as single entity drugs	Same as single entity drugs
Genvoya® (emtricitabine 200mg, tenofovir 300mg, elvitegravir 150mg, & cobicistat 150mg) Prior Authorization	1 tablet QD 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 50mg, & rilpivirine 25mg) Non-formulary	1 tablet QD	Same as single entity drugs	Same as single entity drugs

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; BID = twice daily; cobi = cobicistat; d4T = stavudine; ddI = didanosine; 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

**See "Nonformulary Conversion DMG" for formulary substitutions.

Table 1: Combination Products Continued

Medication	Dosage	Drug Interactions*	Adverse Effect*
Stribild®** (emtricitabine 200mg, tenofovir 300mg, elvitegravir 150mg, & cobicistat 150mg) Non-formulary	1 tablet QD 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.
Symfi®** (efavirenz 600mg, lamivudine 300mg, & tenofovir 300mg) Symfi Lo®** (efavirenz 400mg, lamivudine 300mg, & tenofovir 300mg) Non-formulary	1 tablet QD with food Do not use if CrCl < 50	Same as single entity drugs	Same as single entity drugs
Symtuza®** (darunavir 800mg, cobicistat 150mg, emtricitabine 200mg, & tenofovir 10mg) Non-formulary	1 tablet QD Do not use if CrCl < 30	Same as single entity drugs	Same as single entity drugs
Triumeq®** (dolutegravir 50mg , abacavir 600 mg, & lamivudine 300 mg) Non-formulary	1 tablet QD with or without food. 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 150mg, & abacavir 300mg) Non-formulary	1 tablet BID Do not use if CrCl <50	Same as single entity drugs	Same as single entity drugs
Truvada®** (emtricitabine 200mg & tenofovir 300mg) Non-formulary	1 tablet QD 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; d4T = stavudine; ddI = didanosine; 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

**See "Nonformulary Conversion DMG" for formulary substitutions

Table 2: Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

Medication	Dosage	Drug Interactions*	Adverse Effects*
Abacavir (ABC, Ziagen®)	300mg BID or 600mg QD		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.
Didanosine EC (ddI, Videx EC®)	> 60kg 400mg QD or < 60kg 250mg QD CrCl >60kg <60kg 30-59 200mg QD 125mg QD 10-29 125mg QD 100mg QD <10 or HD 125mg QD 75mg QD Best if taken on empty stomach	Tenofovir, methadone	Peripheral neuropathy, rare pancreatitis, nausea, diarrhea Lactic acidosis with hepatic steatosis.
Emtricitabine (FTC, Emtriva®) Non-formulary	200mg QD CrCl Dose 30-49 200mg q 48 15-29 200mg q 72 <15 or HD 200mg q 96		Nausea, vomiting, diarrhea, headache, hyperpigmentation of palms & soles Lactic acidosis with hepatic steatosis.
Lamivudine (3TC, Epivir®)	150mg BID or 300mg QD CrCl Dose 30-49 150mg QD 15-29 100mg QD 5-14 50mg QD <5 or HD 25mg QD		Minimal effects Lactic acidosis with hepatic steatosis.
Stavudine (d4T, Zerit®) Non-formulary	> 60kg 40mg BID < 60kg 30mg BID CrCl >60kg <60kg 26-50 20mg q 12 15mg q 12 10-25 or HD 20mg q 24 15mg q 24	Zidovudine, methadone	Peripheral neuropathy, lipodystrophy, hyperlipidemia, pancreatitis Lactic acidosis with hepatic steatosis.
Tenofovir** (TDF, Viread®)	300mg QD best if taken with food CrCl Dose 30-49 300mg q 48 10-29 300mg twice a week HD 300mg q 7 days	Didanosine, atazanavir	GI upset, flatulence, headache, asthenia, renal insufficiency Lactic acidosis with hepatic steatosis.
Zidovudine (AZT, ZDV, Retrovir®)	300mg BID CrCl < 15 or HD 100mg TID or 300mg QD	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)
HD=hemodialysis

Table 3: Protease Inhibitors (PIs)

Medication	Dosage*	Drug Interactions**	Adverse Effects**
Atazanavir (ATV, Reyataz®)	400mg QD best if taken with food Boosted or With Tenofovir or EFV ATV 300 + RTV 100 QD	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 QD 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®)	1400mg BID Boosted f-APV 1400 + RTV 100-200 QD f-APV 700 + RTV 100 BID With EFV f-APV 700 + RTV 100 BID f-APV 1400 + RTV 300 QD	Lovastatin, rifampin, rifabutin, rifapentine, ergotamine	Diarrhea, nausea, vomiting, rash hyperglycemia, fat redistribution, lipid abnormalities, increased bleeding in hemophilia
Indinavir (IDV, Crixivan®) Non-formulary	800mg q 8 hr drink plenty of fluids, best if taken on empty stomach, best if separate dosing with ddI by 1 hr Boosted IDV 800 + RTV 100-200 q 12 hr	Carbamazepine, lovastatin, rifampin, rifabutin, rifapentine, ergotamine	Nephrolithiasis, GI intolerance, nausea, metallic taste hyperglycemia, fat redistribution, lipid abnormalities, increased bleeding in hemophilia
Lopinavir 200mg + Ritonavir 50mg (LPV/r, Kaletra®)	2 tabs BID or 4 tabs QD 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®)	1250mg 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*
Delavirdine (DLV, Rescriptor®) Non-formulary	400mg TID	Lovastatin, rifampin, rifapentine, rifabutin, H-2 antagonists (ranitidine), proton pump inhibitors (omeprazole), ergotamine, dapsone, phenytoin, warfarin, carbamazepine, quinidine, clarithromycin	Rash, elevated LFTs, headache
Doravirine (DOR, Pifeltro®) Non-formulary	100mg QD	Carbamazepine, oxcarbazepine, phenobarbital, phenytoin, and rifampin	Nausea, headache, fatigue, diarrhea, abdominal pain, dizziness, abnormal dreams
Efavirenz (EFV, Sustiva®)	600mg 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	200mg 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®)	200mg QD x 14 days then 200mg BID or 400mg QD	Ketoconazole, rifampin, phenytoin, carbamazepine	Rash, elevated LFTs, hepatitis
Ripilvirine (RPV, Edurant®) Prior Authorization	25 mg QD with a meal	Acid suppression therapy, rifampin, rifabutin, carbamazepine, primidone, phenobarbital, phenytoin	Rash, depression, insomnia, headache, hepatotoxicity

Table 5: Integrase Inhibitors

Medication	Dosage	Drug Interactions*	Adverse Effect*
Bictegravir (BIC, Only as Biktarvy®) Non-formulary	bictegravir 50mg, emtricitabine 200mg, & tenofovir alafenamide 25mg 1 tablet QD Do not use if CrCl < 30	Rifampin, phenytoin, carbamazepine	Headache, skin rash, diarrhea, nausea, increased LDL cholesterol
Dolutegravir (DTG, Tivicay®)	50mg QD <u>With certain resistance or drug interactions</u> 50mg 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 300mg, elvitegravir 150mg, & cobicistat 150mg) Stribild® (emtricitabine 200mg, tenofovir 300mg, elvitegravir 150mg, & cobicistat 150mg) 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®)	400mg BID <u>With rifampin</u> 800mg BID	rifampin	Nausea, headache, diarrhea, pyrexia, fatigue, elevated CPK

Table 6: Entry Inhibitors

Medication	Dosage	Drug Interactions*	Adverse Effect*
CCR5 Antagonist			
Maraviroc (MVC, Selzentry®) Non-formulary	Tropism testing is required before use. With Protease Inhibitors except tipranivir, delavirdine, itraconazole, ketoconazole, clarithromycin 150mg BID With all NRTI, Enfuvirtide, TPV, NVP 300mg BID With EFV, rifampin, carbamazepine, phenytoin 600mg 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	90mg 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	2000mg IV loading dose followed by 800mg IV every 2 weeks		Dizziness, skin rash, diarrhea, nausea, decreased neutrophils, leukopenia, increased serum creatinine

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; BID = twice daily; cobi = cobicistat; d4T = stavudine; ddI = didanosine; 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

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 offender'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 the 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 setpoint
         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/cmm 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.
4. The following ART drugs are no longer recommended for use because of suboptimal antiviral potency, unacceptable toxicities, high pill burden, or pharmacologic concerns: delavirdine (DLV), didanosine (ddI), indinavir (IDV), nelfinavir (NFV), and stavudine (d4T).

B.Table 7: Antiretroviral Regimens or Components That Should Not Be Offered At Any Time*

	Rationale
Antiretroviral Regimens Not Recommended	
Monotherapy (AI)	• NRTI monotherapy is inferior to dual-NRTI therapy • PI monotherapy is inferior to combination ART • INSTI monotherapy has resulted in virologic rebound and INSTI resistance
Dual-NRTI regimens (AI)	• Rapid development of resistance • Inferior ARV activity when compared with combination of three or more ARV agents
Triple-NRTI regimens (AI)	• Triple-NRTI regimens have suboptimal virological activity

*adapted from Guidelines for the use of antiretroviral agents in HIV-1 infected adults and adolescents

Table 7: Antiretroviral Regimens or Components That Should Not Be Offered At Any Time* (continued)

Antiretroviral Components Not Recommended as Part of an Antiretroviral Regimen*	
ATV + IDV (AIII)	• Potential additive hyperbilirubinemia
COBI + RTV	• This combination may be prescribed inadvertently, which may result in additive CYP3A4 enzyme inhibition and may further increase the concentrations of ARV drugs or other concomitant medications
ddI + d4T (AII)	• High incidence of toxicities: peripheral neuropathy, pancreatitis, and hyperlactatemia • Reports of serious, even fatal, cases of lactic acidosis with hepatic steatosis with or without pancreatitis in pregnant women
ddI + TDF (AII)	• Increased ddI concentrations and serious ddI-associated toxicities • Potential for immunologic nonresponse and/or CD4 cell count decline • High rate of early virologic failure • Rapid selection of resistance mutations at failure
2-NNRTI combination (AI)	• When EFV combined with NVP, higher incidence of clinical adverse events seen when compared with either EFV- or NVP-based regimen. • Both EFV and NVP may induce metabolism and may lead to reductions in ETR exposure; thus, they should not be used in combination with ETR.
FTC + 3TC (AIII)	• Similar resistance profiles • No potential benefit
ETR + unboosted PI (AII)	• ETR may induce metabolism of these PIs; appropriate doses not yet established
ETR + RTV-boosted FPV (AII)	• ETR may alter the concentrations of these PIs; appropriate doses not yet established
ETR + RTV-boosted TPV (AII)	• ETR concentration may be significantly reduced by RTV-boosted TPV
NVP in ARV-naive women with CD4 count >250 cells/mm^3 or men with CD4 count >400 cells/mm^3 (BI)	• High incidence of symptomatic hepatotoxicity
d4T + ZDV (AII)	• Antagonistic effect on HIV-1
Unboosted DRV, SQV, or TPV (AII)	• The virologic benefit of these PIs has been demonstrated only when they were used with concomitant RTV, or in the case of DRV, also with COBI
TAF + TDF	• This combination may be prescribed inadvertently, especially during transition from one formulation to another. There is no data supporting any potential additive efficacy or toxicity if TAF and TDF are used in combination.

•**Acronyms:** 3TC = lamivudine, ABC = abacavir, ATV = atazanavir, COBI = cobicistat, d4T = stavudine, ddI = didanosine, DRV = darunavir, EFV = efavirenz, ETR = etravirine, FPV = fosamprenavir, FTC = emitricitabine, IDV = indinavir, NVP = nevirapine, RTV = ritonavir, SQV = saquinavir, TDF = tenofovir, TPV = tipranavir, ZDV = zidovudine

*adapted from Guidelines for the use of antiretroviral agents in HIV-1 infected adults and adolescents.

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. Should not be performed if viral load < 1,000 copies/mL because amplification of virus is unreliable

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