

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/mm³, 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/1.73m², 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). Expedited referrals should be obtained for patients that are symptomatic or have a CD4 count < 200 cells/mm³. If patient refuses, contact the CMC Virology Clinic (UTMB sector) or designated physician (Texas Tech sector) for drug therapy and ITP recommendations.



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/mm³ 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/mm³ 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

Patient CD4 count < 500 cells/mm³, symptomatic, pregnant, HIV-associated nephropathy, or hepatitis B co-infection when HBV treatment is indicated?

Yes

No

4

Encourage starting drug therapy

5

Discuss and offer drug therapy

6

1. Discuss pros & cons of drug therapy, adherence, resistance, administration, possible adverse effects & management.
2. If patient is committed, begin HAART. Consider follow up in 2 to 4 weeks to assess medication tolerance.
3. 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.

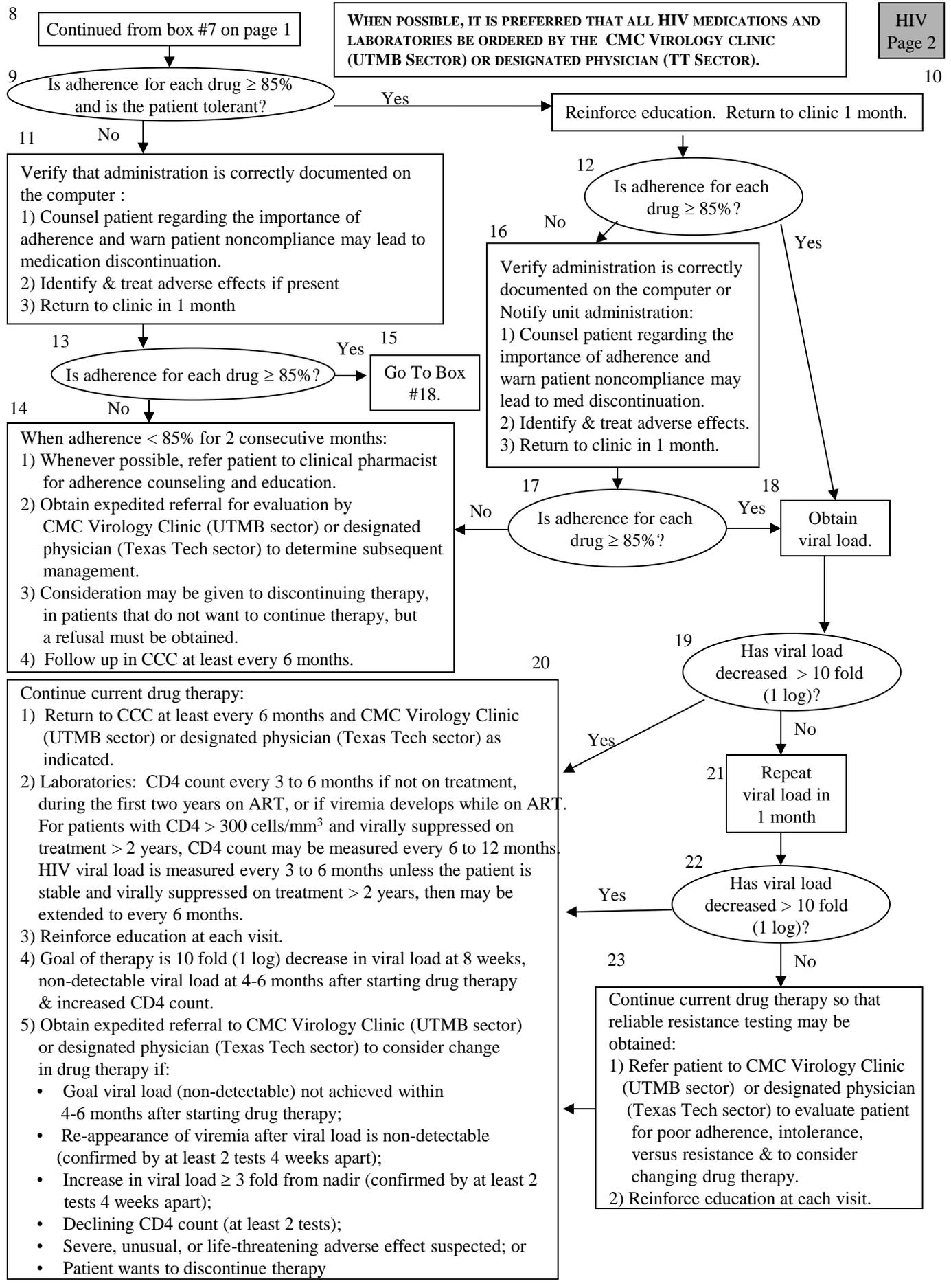
The pathways do not replace sound clinical judgment, nor are they intended to strictly apply to all patients

7

Go to box #8 on page 2



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).



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 (restart if CD4 count < 200)
< 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 (restart if CD4 count < 100-200)
< 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	<i>Pneumocystis jirovecii</i>	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 (restart if CD4 count < 200 or PCP recurrence)
Prior toxoplasmic encephalitis	<i>Toxoplasma gondii</i>	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	<i>M. avium</i> 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	<i>Cryptococcus neoformans</i>	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	<i>Histoplasma capsulatum</i>	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	<i>Coccidioides immitis</i>	Fluconazole 400mg po qd	Itraconazole 200mg po bid or Amphotericin 1mg/kg IV weekly	
Bacteremia	<i>Salmonella</i> 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	<i>Candida</i> *** (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: 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 <table border="0"> <tr> <td>CrCl</td> <td>>60kg</td> <td><60kg</td> </tr> <tr> <td>30-59</td> <td>200mg QD</td> <td>125mg QD</td> </tr> <tr> <td>10-29</td> <td>125mg QD</td> <td>100mg QD</td> </tr> <tr> <td><10 or HD</td> <td>125mg QD</td> <td>75mg QD</td> </tr> </table> Best if taken on empty stomach	CrCl	>60kg	<60kg	30-59	200mg QD	125mg QD	10-29	125mg QD	100mg QD	<10 or HD	125mg QD	75mg QD	Tenofovir, methadone	Peripheral neuropathy, rare pancreatitis, nausea, diarrhea Lactic acidosis with hepatic steatosis.
CrCl	>60kg	<60kg													
30-59	200mg QD	125mg QD													
10-29	125mg QD	100mg QD													
<10 or HD	125mg QD	75mg QD													
Emtricitabine (FTC, Emtriva ®) Nonformulary	200mg QD <table border="0"> <tr> <td>CrCl</td> <td>Dose</td> </tr> <tr> <td>30-49</td> <td>200mg q 48</td> </tr> <tr> <td>15-29</td> <td>200mg q 72</td> </tr> <tr> <td><15 or HD</td> <td>200mg q 96</td> </tr> </table>	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.				
CrCl	Dose														
30-49	200mg q 48														
15-29	200mg q 72														
<15 or HD	200mg q 96														
Lamivudine (3TC, Epivir ®)	150mg BID or 300mg QD <table border="0"> <tr> <td>CrCl</td> <td>Dose</td> </tr> <tr> <td>30-49</td> <td>150mg QD</td> </tr> <tr> <td>15-29</td> <td>100mg QD</td> </tr> <tr> <td>5-14</td> <td>50mg QD</td> </tr> <tr> <td><5 or HD</td> <td>25mg QD</td> </tr> </table>	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.		
CrCl	Dose														
30-49	150mg QD														
15-29	100mg QD														
5-14	50mg QD														
<5 or HD	25mg QD														
Stavudine (d4T, Zerit ®)	> 60kg 40mg BID < 60kg 30mg BID <table border="0"> <tr> <td>CrCl</td> <td>>60kg</td> <td><60kg</td> </tr> <tr> <td>26-50</td> <td>20mg q 12</td> <td>15mg q 12</td> </tr> <tr> <td>10-25 or HD</td> <td>20mg q 24</td> <td>15mg q 24</td> </tr> </table>	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.			
CrCl	>60kg	<60kg													
26-50	20mg q 12	15mg q 12													
10-25 or HD	20mg q 24	15mg q 24													
Zalcitabine (ddC, Hivid ®) Nonformulary	0.75mg TID <table border="0"> <tr> <td>CrCl</td> <td>Dose</td> </tr> <tr> <td>10-40</td> <td>0.75mg BID</td> </tr> <tr> <td><10</td> <td>0.75mg qd</td> </tr> <tr> <td>HD</td> <td>no data</td> </tr> </table>	CrCl	Dose	10-40	0.75mg BID	<10	0.75mg qd	HD	no data		Peripheral neuropathy, stomatitis Lactic acidosis with hepatic steatosis.				
CrCl	Dose														
10-40	0.75mg BID														
<10	0.75mg qd														
HD	no data														
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.												
Tenofovir** (TDF, Viread ®)	300mg QD best if taken with food <table border="0"> <tr> <td>CrCl</td> <td>Dose</td> </tr> <tr> <td>30-49</td> <td>300mg q 48</td> </tr> <tr> <td>10-29</td> <td>300mg twice a week</td> </tr> <tr> <td>HD</td> <td>300mg q 7 days</td> </tr> </table>	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.				
CrCl	Dose														
30-49	300mg q 48														
10-29	300mg twice a week														
HD	300mg q 7 days														

*not a complete list of drug interactions or adverse effects

**nucleotide reverse transcriptase inhibitor (NtRTI)

HD=hemodialysis

Table 2: Combination Products

Medication	Dosage	Drug Interactions*	Adverse Effect*
Combivir® (zidovudine 300 mg & lamivudine 150mg) Nonformulary	1 tablet BID Do not use if CrCl < 50	Same as single entity drugs	Same as single entity drugs
Epzicom® (lamivudine 300mg & abacavir 600mg) Nonformulary	1 tablet QD Do not use if CrCl < 50	Same as single entity drugs	Same as single entity drugs
Truvada® (emtricitabine 200mg & tenofovir 300mg) Nonformulary	1 tablet QD <u>CrCl</u> <u>Dose</u> 30-49 1 tab q 48hr < 30 do not use	Same as single entity drugs	Same as single entity drugs
Atripla® (emtricitabine 200mg, tenofovir 300mg, & efavirenz 600mg) Nonformulary	1 tablet QD Do not use if CrCl < 50	Same as single entity drugs	Same as single entity drugs
Complera® (emtricitabine 200mg, tenofovir 300mg, & rilpivirine 25mg) Nonformulary	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.
Stribild® (emtricitabine 200mg, tenofovir 300mg, elvitegravir 150mg, & cobicistat 150mg) Prior Authorization	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.
Trizivir® (zidovudine 300 mg, lamivudine 150mg, & abacavir 300mg) Nonformulary	1 tablet BID Do not use if CrCl <50	Same as single entity drugs	Same as single entity drugs
Triumeq® (dolutegravir 50mg, abacavir 600 mg, & lamivudine 300 mg) Nonformulary	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

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; BID = twice daily; cobl = 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

Table 3: Protease Inhibitors (PIs)

Medication	Dosage*	Drug Interactions**	Adverse Effects**
Atazanavir (ATV, Reyataz®)	400mg QD best if taken with food <u>Boosted or With Tenofovir or EFV</u> 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®)	<u>Treatment Naïve patient</u> DRV 800 + RTV 100 QD <u>Treatment Experienced patient</u> DRV 600 + RTV 100 BID (<u>must</u> 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 <u>Boosted</u> f-APV 1400 + RTV 100-200 QD f-APV 700 + RTV 100 BID <u>With EFV</u> 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®)	800mg q 8 hr drink plenty of fluids, best if taken on empty stomach, best if separate dosing with ddI by 1 hr <u>Boosted</u> 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 <u>With EFV or NVP</u> 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	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 (<u>must</u> 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®)	500mg + RTV 200mg BID (<u>must</u> 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
Nonformulary			

*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®) Nonformulary	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
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, avoid in pregnancy
Etravirine (ETR, Intelence®) Nonformulary	200mg BID best if taken with food	Phenytoin, carbamazepine, other NNRTIs, PIs (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*
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
Elvitegravir (EVG, Stribild®) Only as Stribild®	(EVG 150 mg + COBI 150 mg + TDF 300 mg + FTC 200 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®)	400mg BID <u>With rifampin</u> 800mg BID	rifampin	Nausea, headache, diarrhea, pyrexia, fatigue, elevated CPK

Table 6: CCR5 Antagonist

Medication	Dosage	Drug Interactions	Adverse Effect*
Maraviroc (MVC, Selzentry®) Nonformulary	Tropism testing is required before use <u>With Protease Inhibitors except tipranivir, delavirdine, itraconazole, ketoconazole, clarithromycin</u> 150mg BID <u>With all NRTI, Efavirtide, TPV, NVP</u> 300mg BID <u>With EFV, rifampin, carbamazepine, phenytoin</u> 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

Table 7: Fusion Inhibitors

Medication	Dosage	Drug Interactions*	Adverse Effect*
Enfuvirtide (T20, Fuzeon®) Nonformulary	90mg SQ BID		Local injection site reaction (e.g., pain erythema, induration, nodules, cysts), increased rate of pneumonia, hypersensitivity reaction (rechallenge is not recommended)

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/mm³), 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 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

1. 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.
2. 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.
3. 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 therapy is recommended for all HIV-infected individuals to reduce the risk of disease progression
2. Primary Care providers should refer patients to CMC Virology Clinic (UTMB Sector) or designated physician (Texas Tech Sector) for recommendations and initiation of therapy.
3. Strength of evidence for the recommendation varies by pretreatment CD4 cell count as follows:

Table 8: Indication for drug therapy*

CD4 Count	Recommendation
< 350 cells/mm ³	Strong
350 to 500 cells/mm ³	Strong
> 500 cells/mm ³	Moderate

B. Table 9: Antiretroviral Regimens or Components That Should Not Be Offered At Any Time*

	Rationale	Exception
Antiretroviral Regimens <u>Not</u> Recommended		
Monotherapy with NRTI (All)	<ul style="list-style-type: none"> • Rapid development of resistance • Inferior ARV activity when compared with combination of three or more ARV agents 	• No exception
Dual-NRTI regimens (All)	<ul style="list-style-type: none"> • Rapid development of resistance • Inferior ARV activity when compared with combination of three or more ARV agents 	• No exception
Triple-NRTI regimens (All) except for ABC/ZDV/3TC (BI) or possibly TDF + ZDV/3TC (BII)	<ul style="list-style-type: none"> • High rate of early virologic nonresponse seen when triple-NRTI combinations, including ABC/TDF/3TC and TDF/ddI/3TC, were used as initial regimen in ART-naive patients. • Other triple-NRTI regimens have not been evaluated. 	• ABC/ZDV/3TC (BI) and possibly TDF + ZDV/3TC (BII) in patients in whom other combinations are not desirable

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

Antiretroviral Components <u>Not</u> Recommended as Part of an Antiretroviral Regimen*		
ATV + IDV (AIII)	<ul style="list-style-type: none"> Potential additive hyperbilirubinemia 	<ul style="list-style-type: none"> No exception
ddl + d4T (All)	<ul style="list-style-type: none"> 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 	<ul style="list-style-type: none"> No exception
ddl + TDF (All)	<ul style="list-style-type: none"> Increased ddl concentrations and serious ddl-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 	<ul style="list-style-type: none"> Clinicians caring for patients who are clinically stable on regimens containing TDF + ddl should consider altering the NRTIs to avoid this combination.
2-NNRTI combination (AI)	<ul style="list-style-type: none"> 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. 	<ul style="list-style-type: none"> No exception
EFV in first trimester of pregnancy or in women with significant childbearing potential (AIII)	<ul style="list-style-type: none"> Teratogenic in nonhuman primates 	<ul style="list-style-type: none"> When no other ARV options are available and potential benefits outweigh the risks (BIII)
FTC + 3TC (AIII)	<ul style="list-style-type: none"> Similar resistance profiles No potential benefit 	<ul style="list-style-type: none"> No exception
ETR + unboosted PI (All)	<ul style="list-style-type: none"> ETR may induce metabolism of these PIs; appropriate doses not yet established 	<ul style="list-style-type: none"> No exception
ETR + RTV-boosted ATV or FPV (All)	<ul style="list-style-type: none"> ETR may alter the concentrations of these PIs; appropriate doses not yet established 	<ul style="list-style-type: none"> No exception
ETR + RTV-boosted TPV (All)	<ul style="list-style-type: none"> ETR concentration may be significantly reduced by RTV-boosted TPV 	<ul style="list-style-type: none"> No exception
NVP in ARV-naive women with CD4 count >250 cells/mm ³ or men with CD4 count >400 cells/mm ³ (BI)	<ul style="list-style-type: none"> High incidence of symptomatic hepatotoxicity 	<ul style="list-style-type: none"> If no other ARV option available and if used, patient should be monitored closely
d4T + ZDV (All)	<ul style="list-style-type: none"> Antagonistic effect on HIV-1 	<ul style="list-style-type: none"> No exception
Unboosted DRV, SQV, or TPV (All)	<ul style="list-style-type: none"> Inadequate bioavailability 	<ul style="list-style-type: none"> No exception

• **Acronyms:** 3TC = lamivudine, ABC = abacavir, ATV = atazanavir, d4T = stavudine, ddl = didanosine, DRV = darunavir, EFV = efavirenz, ETR = etravirine, FPV = fosamprenavir, FTC = emtricitabine, 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.

Lamivudine may substitute for emtricitabine or vice versa

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 antiretroviral therapy and 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)
3. Immunologic Failure
 - a. Failure to increase CD4 count by 25-50 cells/mm³ 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