



# **Pocket Guide**

## **Adult HIV/AIDS Treatment**

### **2010-2011**

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**Compliments of:**  
**The Johns Hopkins AIDS Service**  
*<http://hopkins-hivguide.org>*

**Pocket Guide to Adult HIV/AIDS Treatment**  
**2010-2011**

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### **AIDSinfo**

Guidelines for the treatment of HIV/AIDS from the NIH Office of AIDS Research

<http://www.aidsinfo.nih.gov/>

### **New York State Department of Health AIDS Institute HIV Clinical Guidelines Program**

<http://www.hivguidelines.org/>

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- **Antimicrobial Resistance Testing:** 2008 Recommendations of IAS-USA *Top HIV Med* 2008;16:266

## Important Information for the Users of This Pocket Guide

This document is provided as an information resource for physicians and other health care professionals to assist in the appropriate treatment of patients with HIV/AIDS. Recommendations for care and treatment change rapidly, and opinion can be controversial; therefore, physicians and other health care professionals are encouraged to consult other sources, especially manufacturers' package inserts, and confirm the information contained on these tables. The individual physician or other health care professional should use his/her best medical judgment in determining appropriate patient care or treatment because no reference or guideline can trump provider judgment, based on individual patient issues, available resources and updated information. The document was completed August 5, 2010. Although these tables have been carefully prepared and reviewed the author makes no warranty as to the reliability, accuracy, timeliness, usefulness or completeness of the information. The data presented herein is for informational purposes only. Determination of appropriate treatment is the responsibility of the treating physician.

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The Pocket Guide has been developed as a resource primarily for the AIDS Education and Training Centers (AETC) with Gilead, Inc sponsorship for the Corrections Edition. For US colleagues, requests for individual copies or small quantities of the Pocket Guide may, therefore, be addressed to your local AETC. The locations of your local AETC may be found at <http://www.aids-ed.org>.

An electronic version of the Pocket Guide is available at <http://hopkins-hivguide.org>.

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## Table of Contents

References for the Pocket Guide.....	5
Important Information for Users .....	6
Table of Contents .....	7
Drug Abbreviations .....	10
Miscellaneous Abbreviations.....	10
Formulas: Child-Pugh Score and Creatinine Clearance.....	12
<b>Baseline Evaluation</b>	
Baseline Evaluation Table 1. Laboratory Tests.....	13
Baseline Evaluation Table 2. Laboratory Monitoring Before and During ART.....	15
Baseline Evaluation Table 3. Prevention of HIV for HIV Providers.....	16
<b>Drug Information</b>	
Drug and Treatment Information Resources.....	19
Drug Table 1. Antiretroviral Agent Characteristics.....	20
Drug Table 2. Antiretroviral Agents, Adverse Reactions.....	30
Drug Table 3. Antiretroviral Agents, Black Box Warnings.....	36
Drug Table 4. National Cholesterol Education Program .....	37
Drug Table 5. Drug Therapy for Hyperlipidemia .....	38
Drug Table 6. Drug Interactions: Combinations That Should Not Be Used.....	39
Drug Table 7. Drug Interactions: Combinations With PIs, or NNRTIs or CCR5 Antagonists Requiring Dose Modifications.....	41
Drug Table 8. Drug Interactions: Nucleosides .....	45
Drug Table 9. Co-administration of PIs and NNRTIs: Dose Adjustments.....	46
Drug Table 10. Co-administration of PIs: Dose Adjustments.....	47
<b>Antiretroviral Therapy</b>	
Adult ART Table 1A. Indications for ART: DHHS Guidelines .....	48
Adult ART Table 1B. Indications for ART: IAS-USA Guidelines .....	49
Adult ART Table 2A. Starting Regimens for Antiretroviral Naïve Patients: DHHS Guidelines .....	49
Adult ART Table 2B-1. Starting Regimens for Antiretroviral Naïve Patients: IAS-USA Guidelines .....	50
Adult ART Table 2B-2. Starting Regimens in Patients with Co-Morbidities.....	50

## Table of Contents (Cont'd)

Adult ART Table 2C-1 When to Start Antiretroviral Therapy: WHO Guidelines .....	50
Adult ART Table 2C-2. What Antiretroviral Therapy to Start: WHO Guidelines .....	51
Adult ART Table 2C-3. When to Change ART Regimens: WHO Guidelines .....	51
Adult ART Table 2C-4. What ART Regimen to Change to .....	52
Adult ART Table 3. Advantages and Disadvantages of Initial Antiretroviral Regimens .....	52
Adult ART Table 4. Methods to Achieve Readiness to Start HAART and Maintain Adherence .....	55
Adult ART Table 5. Therapeutic Failure-Definitions .....	55
Adult ART Table 6. Management of Virologic Failure .....	56
Adult ART Table 7. Indications for Resistance Testing .....	57
Adult ART Table 8. Resistance Mutations .....	57

## Pregnancy and HIV

Pregnancy Table 1. Antiretroviral Drugs in Pregnancy: DHHS Guidelines .....	59
Pregnancy Table 2. Antiretroviral Drugs and Concerns for Pregnancy .....	59
Pregnancy Table 3. Recommendations for the Use of Antiretroviral Agents in Pregnant Women .....	61
Pregnancy Table 4. Recommendations for Clinical Scenarios .....	62
Pregnancy Table 5. Mode of Delivery .....	63
Pregnancy Table 6. Drugs for Opportunistic Infections in Pregnancy .....	63
Pregnancy Table 7. Drugs to Avoid During Pregnancy .....	65

## Opportunistic Infections

Adult OI Table 1. 2008 USPHS/IDSA Guidelines for Prevention of Opportunistic Infections .....	67
Adult OI Table 2. Treatment of Opportunistic Infections .....	72
Adult OI Table 3. Immune Reconstitution Syndrome .....	80
Adult OI Table 4. Latent TB and HIV Co-Infection .....	81
Adult OI Table 5. Treatment of Drug-Susceptible Active Tuberculosis .....	82
Adult OI Table 6. Special Considerations for TB Treatment With HIV Co-Infection .....	82

## Table of Contents (Cont'd)

Adult OI Table 7. Doses of Antituberculosis Drugs: First Line Drugs .....	83
Adult OI Table 8. Treatment of Hepatitis C .....	84

## Guidelines for Sexually Transmitted Disease Co-Morbidity

STD/HIV Table 1. Sexually Transmitted Disease Identification and Treatment ...	86
STD/HIV Table 2. Management of Syphilis Co-Infection: Summary .....	90

## Occupational Exposure

Occupational Post-Exposure Prophylaxis .....	93
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## Abbreviations Used in This Pocket Guide to HIV/AIDS Treatment

Drugs	
ABC: Abacavir ( <i>Ziagen</i> )	LPV/r: Lopinavir/Ritonavir ( <i>Kaletra</i> )
ATV: Atazanavir ( <i>Reyataz</i> )	MVC: Maraviroc ( <i>Selzentry</i> )
AZT: Zidovudine ( <i>Retrovir</i> )	NFV: Nelfinavir ( <i>Viracept</i> )
ddI: Didanosine ( <i>Videx</i> )	NNRTI: Non-nucleoside Reverse Transcriptase Inhibitor
d4T: Stavudine ( <i>Zerit</i> )	NRTI: Nucleoside Reverse Transcriptase Inhibitor
DLV: Delavirdine ( <i>Rescriptor</i> )	NVP: Nevirapine ( <i>Viramune</i> )
DRV: Darunavir ( <i>Prezista</i> )	/r: Ritonavir <400 mg/d
EFV: Efavirenz ( <i>Sustiva</i> )	RAL: Raltegravir ( <i>Isentress</i> )
ENF: Enfuvirtide ( <i>Fuzeon, T-20</i> )	RBT: Rifabutin ( <i>Mycobutin</i> )
ETR: Etravirine ( <i>Intence</i> )	RTV: Ritonavir ( <i>Norvir</i> )
FPV: Fosamprenavir ( <i>Lexiva</i> )	SQV: Saquinavir ( <i>Invirase</i> )
FTC: Emtricitabine ( <i>Emtriva</i> )	3TC: Lamivudine ( <i>Epivir</i> )
IDV: Indinavir ( <i>Crixivan</i> )	TDF: Tenofovir ( <i>Viread</i> )
INH: Isoniazid	TMP-SMX: Trimethoprim sulfamethoxazole
INV: Inivirase (saquinavir, HGC)	TPV: Tipranavir ( <i>Aptivus</i> )
IVIG: Intravenous Immune Globulin	VZIG: Varicella Zoster Immune Globulin

Miscellaneous	
ADR: Adverse Drug Reaction	CrCl: Creatinine Clearance
ART: Antiretroviral Therapy	D/C: Discontinue
AUC: Area Under the Curve (total drug exposure)	DOT: Directly Observed Therapy
bid: twice per day	Dx: Diagnosis
biw: twice per week	EC: Enteric Coated
CBC: Complete Blood Count	EE: Ethinyl Estradiol
CDC: Center for Disease Control	ESRD: End-stage Renal Disease
CPS: Child-Pugh Score	ETOH: Alcohol

## Abbreviations Used in This Pocket Guide to HIV/AIDS Treatment (Cont'd)

Miscellaneous (Cont'd)	
FBS: Fasting Blood Glucose	PML: Progressive Multifocal Leukoencephalopathy
HAV: Hepatitis A Virus	po: by mouth
HBV: Hepatitis B Virus	q: every
HCV: Hepatitis C Virus	qd: daily
HAART: Highly Active Antiretroviral Therapy	qid: four times per day
HIVAN: HIV - associated nephropathy	qm: monthly
HPV: Human Papilloma Virus	qod: every other day
HSV-2: Herpes Simplex Type 2 (usually genital)	qw: every week
hs: bedtime (hour of sleep)	R5 Trophic Virus: HIV strain that uses the CCR5 receptor
IM: Intramuscular	Rx: Treatment
IV: Intravenous	std: Standard (dose)
KS: Kaposi sarcoma	STD: Sexually Transmitted Disease
MAC: Mycobacterium avium	soln: solution
MDRTB: Multidrug Resistant TB	Sx: Symptoms
mo: month	tid: three times per day
MTCT: Maternal to Child Transmission	tw: three times per week
NAAT: Nucleic Acid Amplification Test	TAMs: Thymidine Analogue Resistance Mutations
OI: Opportunistic infection	TMP/SMX: Trimethoprim-Sulfamethoxazole
PCP: Pneumocystis Pneumonia	VL: Viral Load
PEP: Post-exposure prophylaxis	ULN: Upper Limit of Normal
PrEP: Pre-exposure prophylaxis	VZV: Varicella Zoster Virus
PI: Protease Inhibitor	

## Formulas

Child-Pugh Score (CPS) for Hepatic Disease

Component			
Encephalopathy	None	1-2	3-4
Ascites	None	Mild	Mod/refractory
Albumin (g/dL)	>3.5	2.8-3.5	<2.8
Total bilirubin (mg/dL)	<2	2-3	>3
Pro-time sec. or INR	<4 <1.7	4-6 1.7-2.3	>6 >2.3

5-6 points = C-P A

7-9 points = C-P B

> 9 points = C-P C

## Creatinine Clearance

Males:  $\frac{\text{Weight (kg)} \times (140\text{-age})}{72 \times \text{Serum creatinine (mg/dL)}}$

Females: Value for males x 0.85

Note: Assumes stable renal function.

## Baseline Evaluation

Baseline Evaluation Table 1. Laboratory Tests [Aberg J, Clin Inf Dis (2009;49:651-81)]

Test	Comment
HIV Serology	<ul style="list-style-type: none"> <li>• Sensitivity and specificity standard serology is &gt;99%</li> <li>- False positives: Human error</li> <li>- False negatives: Usually "window period"</li> <li>• Acute HIV: HIV RNA level &gt;10,000 c/mL; confirm seroconversion</li> <li>• Rapid tests: Confirm positives with Western blot</li> </ul>
CD4 count and %	<ul style="list-style-type: none"> <li>• Reproducibility: 95% CI = 30%</li> <li>• False high levels – splenectomy (use CD4%) concurrent HTLV-1</li> <li>• Repeat every 3-6 mos</li> <li>• % - CD4 &gt;500 = &gt;29%, 200-500 = 14-28%, &lt;200 = &lt;14%</li> </ul>
HIV Viral Load	<ul style="list-style-type: none"> <li>• Reproducibility: 95% CI = 0.3 log<sub>10</sub> c/mL or 50%</li> <li>• Repeat at 2-6 wks after starting or changing ART, then q3-4mos</li> </ul>
Genotypic Resistance Test	<ul style="list-style-type: none"> <li>• Genotypic resistance test at baseline with or without ART and with virologic failure while on ART or within 4 wks of stopping ART if possible</li> </ul>
CBC	<ul style="list-style-type: none"> <li>• Repeat every 3-6 mos; more frequently as indicated</li> <li>• Macrocytosis with AZT and d4T</li> </ul>
Chemistry Profile (Creatinine, BUN, ALT, AST, Alk phos, electrolytes)	<ul style="list-style-type: none"> <li>• Include LFT and renal function</li> <li>• Repeat LFT with all PIs and NNRTIs, ETOH and hepatitis q3-6mos</li> <li>• Repeat renal function with IDV &amp; TDF q3-6mos</li> </ul>
Hepatitis Screen Anti-HAV, Anti-HCV, Anti- HBsAg, Anti-HBcAg, and HBsAg	<ul style="list-style-type: none"> <li>• Standard screen: anti-HCV, anti-HAV, HBsAg, anti-HBs and anti-HBc</li> <li>• Abnormal LFT: get anti-HCV &amp; HBsAg</li> <li>• Neg anti-HCV-not infected</li> <li>• Positive anti-HCV only: get quantitative HCV RNA</li> <li>• Neg anti-HBs: Vaccinate for HBV unless HBs pos</li> <li>• Pos HBsAg indicates acute or chronic HBV- get HBV DNA &amp; HBeAg</li> <li>• Neg anti-HAV: HAV vaccine; Pos anti-HAV: immune</li> </ul>
Fasting Lipid Profile and FBS or Hgb A1c	<ul style="list-style-type: none"> <li>• Patient at risk for CVD</li> <li>• Baseline for HAART; repeat at 3-6 mos based on initial results</li> </ul>
Toxoplasma IgG	<ul style="list-style-type: none"> <li>• 10-15% positive in U.S.</li> <li>• If neg repeat when symptomatic or when CD4&lt;100 (if positive, give prophylaxis)</li> </ul>
PPD or Gamma Interferon Release Assay	<ul style="list-style-type: none"> <li>• Indicated if no history of TB or prior pos. PPD</li> <li>• Induration &gt;5 mm is indication for INH x 9 mos</li> </ul>
PAP smear	<ul style="list-style-type: none"> <li>• Baseline, at 6 mos and then annual; if "inadequate" – repeat; if atypia – refer to gynecologist</li> </ul>
Chest x-ray	<ul style="list-style-type: none"> <li>• Indicated with pulmonary sx, positive PPD or history of chest disease; some do baseline X-ray routinely</li> </ul>

**Baseline Evaluation Table 1. Laboratory Tests [Aberg J, Clin Inf Dis (2009;49:651-81)] (Cont'd)**

Test	Comment
Urinary NAAT for Gonorrhea & Chlamydia and Wet Mount for Trichomoniasis	<ul style="list-style-type: none"> <li>All women should be screened for trichomoniasis</li> <li>Women &lt;25 yrs should be screened for C. trachomatis</li> <li>Consider: in sexually active patients (see STD/HIV Table 1)</li> <li>Repeat at 6-12 mos intervals depending on risk</li> </ul>
HLA-B 5701 Test	• Screening for ABC Treatment
Tropism Assay	• If plan to use CCR5 antagonist (MVC). Expensive
VDRL, RPR	<ul style="list-style-type: none"> <li>Baseline and repeat annually in sexually active patients</li> <li>Confirm positives with FTA-ABS, TPPA or MHA-TP; LP if positive screen and: neurologic or ocular signs, late, latent syphilis (&gt;1 yr), CD4 count &lt;350, early syphilis and titer &gt;1:32 and when penicillin is not used for treatment</li> </ul>
Renal Screen	<ul style="list-style-type: none"> <li>Urinalysis and creatinine; repeat annually – more often with TDF or renal disease</li> <li>If ≥1+ proteinuria or elevated creatinine: quantify urine protein and do renal ultrasound</li> </ul>
G6PD Level	• Consider: most susceptible are men of African, Mediterranean, Asian, or Sephardic Jewish descent. If pos, avoid oxidant drugs-dapsone and primaquine; ? sulfonamides. African-American patients have the milder form of G6PD deficiency and can often tolerate TMP/SMX.
<b>General Health Screens</b>	
Mammography	Female >50 years
Prostate Specific Antigen	Males >50 years
Colonoscopy	Age >50 years
Bone Densitometry	If other risks for osteoporosis

**Baseline Evaluation Table 2. Laboratory Monitoring Before and During ART (Based on DHHS Guidelines–December 1, 2009)**

Test	Baseline	Before ART	ART Baseline	wk 2-8	Every 3-6 Mo	Every 12 Mo	Viral Failure
CD4	+	q 3-6 mo	+		+		+
Viral Load	+	q 3-6 mo	+	+	+		+
Genotypic resistance test	+		+				+
HBsAg	+		+				+
Chem profile	+	q 6-12 mo	+	+	+		
LFT's	+	q 6-12 mo	+	+	+		
CBC	+	q 6-12 mo	+	+(AZT)	+		
Lipids/FBS	+	q 12mo	+	(+)*	(+)*	+	
Urinalysis	+		+		+(HIVAN)	+(TDF)	

**Baseline Evaluation Table 3. Prevention of HIV for HIV Providers**  
(DHHS Prevention Guidelines)

**Prevention-Three Steps**

**Step 1: Screen for risk behaviors**

- Behaviors and clinical factors associated with HIV, other STDs, and IV drug use (repeat at every visit)
- STD symptoms: Most are asymptomatic (repeat query at every visit)
- Pregnancy test (if indicated)
- Screening tests

Patients	Test
<b>Routine</b>	
All patients	Syphilis serology - RPR or VDRL*
All women	Trichomonas wet mount or culture
All women $\leq$ 25 yrs & sexually active	Cervical specimen or urinary NAAT for <i>C. trachomatis</i>
<b>Consider</b>	
All men and women, if sexually active	Screening for GC and <i>C. trachomatis</i> by urethral (men) or cervical (women) specimen or first catch urine for NAAT*
Anal receptive sex	Consider anal swab for GC culture and, if available, for <i>C. trachomatis</i>
Oral receptive sex	Consider pharyngeal culture for GC
Possible pregnancy	Pregnancy test

\* Repeat RPR or VDRL annually. Consider repeating screening tests for *N. gonorrhoeae* and *C. trachomatis* annually or more frequently if sexually active, if previous screening test positive, or other high risk.

**Step 2: Behavioral Interventions**

- **Prevention messages** should be provided with each visit
- **Communicate factors that influence transmission** and risk reduction: i.e. abstinence, sex with condoms, sex exclusively with HIV-infected person(s) (with precautions to prevent superinfection). Also stress reduced efficacy of oral contraceptives with PIs and NNRTIs. Stress proper condom use.
- **IDU (Risk of needle sharing is 67 transmissions per 10,000 exposures)**
  - Encourage to stop using drugs  $\pm$  enter substance abuse treatment
  - **If patient continues to use drugs:**
    - Never reuse or share needles, water, or drug preparation equipment.
    - Use only syringes from reliable sources (pharmacies).
    - Use new syringe; if not possible-boil or disinfect with bleach (<http://www.cdcnpin.org>).

**Step 2: Behavioral Interventions – IDU (Cont'd)**

- Use sterile water to prepare drugs; otherwise use tap water.
- Use new or disinfected cooker and new cotton
- Clean injection site with new alcohol swab.
- Safely dispose of needle.

• **Sexual Activity**

- **The per coital act risk of HIV transmission (assumes no condom use)** [*MMWR Recomm and Rep* 2005;54(RR-2); *Lancet* ID 2008;8:553; *Lancet* ID 2009;9:118)

Female to male: 0.04% / act

Male + female: 0.08% / act

Receptive anal intercourse: 1.7% / act

Probabilities in early and late stage HIV: 7.3-9.2x

increased (vs asymptomatic stage)

Genital ulcer (either partner): 5.2x increased

- **Condom vs no condom:** Risk is 20X greater without condoms.
- **Viral load:** Each  $\log_{10}$  reduction in viral load reduces probability of transmission 2.5 fold.
- **Early stage disease:** Risk is increased about 10-fold per coital act during acute HIV infection (prior to seroconversion).
- **HAART recipients:** Decreases in VL reduces risk; with VL<50 c/mL, transmission is extremely low but not eliminated-- safe sex still advocated. If treatment is discontinued for any reason, warn patient that viral load increases within weeks to pre-treatment levels and this substantially increases risk of transmission.

**Step 3: Partner Counseling and Notification**

- **Laws:** Follow local and state laws for reporting sex and needlesharing partners.
- **Initial Visit:** Ask if all sex and needle-sharing partners have been notified.
- **Follow-ups:** Ask about new sex or needle-sharing partners who have not been notified.
- **Referrals:** All contacts should be referred to the health department to arrange for notification and testing without identifying source. Patients who elect not to notify partners should be referred to the health department to conduct these activities.

## Drug and Treatment Information Resources

Resource	Information and source
AIDSInfo <a href="http://www.aidsinfo.nih.gov/">http://www.aidsinfo.nih.gov/</a>	DHHS Guidelines for ART in adults, pediatrics, and pregnancy.
AETC <a href="http://www.aids-ed.org/aidsetc?page=cm-00-00">http://www.aids-ed.org/aidsetc?page=cm-00-00</a>	Clinical Manual for Management of the HIV-Infected Adult
AETC <a href="http://www.aids-ed.org/">http://www.aids-ed.org/</a>	Training resources, slide sets, self study, and more.
HIV InSite <a href="http://www.hivinsite.org/">http://www.hivinsite.org/</a>	Knowledge base, drug interactions, global country profiles, and more.
Johns Hopkins HIV Guide <a href="http://www.hopkins-hivguide.org/">http://www.hopkins-hivguide.org/</a>	Clinical database, handheld HIV, publications, Q&A forum
Medscape HIV/AIDS <a href="http://www.medscape.com/hiv">http://www.medscape.com/hiv</a>	News, conference coverage, reviews, CME and more
The National HIV/AIDS Clinicians' Consultation Center <a href="http://www.nccc.ucsf.edu/">http://www.nccc.ucsf.edu/</a>	AETC clinical resource, contact to warm line and PEPline.
International AIDS Society-USA <a href="http://www.iasusa.org/">http://www.iasusa.org/</a>	CME, resistance mutation chart, cases
VA National HIV/AIDS Program <a href="http://www.hiv.va.gov/">http://www.hiv.va.gov/</a>	Information for providers and patients
International Training and Education Center on HIV <a href="http://www.go2itech.org/">http://www.go2itech.org/</a>	International AETC with training material.
HIV Web Study <a href="http://depts.washington.edu/hiv aids/">http://depts.washington.edu/hiv aids/</a>	University of Washington cases, tables, images.
Stanford University HIV Drug Resistance Database <a href="http://hivdb.stanford.edu/">http://hivdb.stanford.edu/</a>	Resistance mutations and interpretations.
Clinical Care Options <a href="http://www.clinicaloptions.com/">http://www.clinicaloptions.com/</a>	Reviews, CME, and conference summaries.
STD Guidelines [MMWR 2006;55 (RR-11):1-94] <a href="http://www.cdc.gov/std/treatment/2006/rr5511.pdf">http://www.cdc.gov/std/treatment/2006/rr5511.pdf</a>	CDC STD guidelines 2006
New York State Department of Health AIDS Institute <a href="http://www.hivguidelines.org/clinical-guidelines/hiv-and-mental-health/">http://www.hivguidelines.org/clinical-guidelines/hiv-and-mental-health/</a>	HIV and Mental Health
New York State Department of Health AIDS Institute <a href="http://www.nyhealth.gov/diseases/aids/standards/">http://www.nyhealth.gov/diseases/aids/standards/</a>	Guidelines for ART, organ systems
Hyperlipidemia <a href="http://www.journals.uchicago.edu/doi/pdf/10.1086/378131">http://www.journals.uchicago.edu/doi/pdf/10.1086/378131</a>	HIVMA of IDSA and ACTG guidelines
HIV Testing [MMWR Recomm Rep. 2006;55 (RR-14):1-17] <a href="http://www.cdc.gov/mmwr/pdf/rr/rr5514.pdf">http://www.cdc.gov/mmwr/pdf/rr/rr5514.pdf</a>	CDC recommendations for HIV testing 2006

**Drug Table 1. Antiretroviral Agent Characteristics**

(Most common and/or important toxicities are in *italics*.)

Drug Name	Form	Usual Adult Dose			Food Effects	Renal Failure Dosing			Liver Failure Dosing	Toxicity (main toxicity – <i>italics</i> )
						CrCl 30-59 mL/min	CrCl 10-29 mL/min	CrCl <10 or dialysis		
<b>Nucleoside Reverse Transcriptase Inhibitors (NRTIs)</b>										
<b>Abacavir (ABC, Ziagen)</b>	300 mg tab; (see also: <i>Trizivir and Epzicom</i> ) 20 mg/mL po soln	300 mg bid or 600 mg qd			No effect ETOH ↑ ABC 41% Clinical significance unknown.	Standard dose			Std Dose	<i>Hypersensitivity- fever, rash, GI sx, dyspnea§ ¶¶</i> Screen for HLA-B* 5701 Possible CVD risk
<b>Atripla (EFV/TDF/FTC)</b>	TDF 300 mg + FTC 200 mg + EFV 600 mg	1 tab qd			Take on an empty stomach during the first 2 weeks.	Fixed formulation not recommended w/ CrCl <50 mL/min			Std Dose	TDF renal toxicity HBV flare## EFV CNS toxicity
<b>Combivir (CBV) (AZT/3TC)</b>	AZT 300 mg + 3TC 150 mg (tab)	1 bid			No effect	Fixed formulation not recommended			Std Dose	AZT side effects§ HBV flare##
<b>Didanosine (Videx; Videx EC; ddI) †‡</b>	EC caps: 125, 200, 250, and 400 mg		>60 kg	<60 kg	Take 1/2 h before or 2 h after meal Separate dosing of IDV, RTV, DLV, ATV, NFV	>60 kg - 200 mg/d	>60 kg - 150 mg/d	>60 kg - 100 mg/d	Std Dose	<i>Pancreatitis, peripheral neuropathy, GI intolerance§, lactic acidosis non-cirrhotic portal hypertension, hepatic failure</i>
		EC Caps	400 mg qd	250 mg qd (pref)		<60 kg - 150 mg/d	<60 kg - 100 mg/d	<60 kg - 75 mg/d¶		
		With TDF	250 mg qd‡	200 mg qd‡						
<b>Emtricitabine (Emtriva, FTC)</b>	200 mg cap 10 mg/mL po soln (see also: <i>Truvada and Atripla</i> )	200 mg qd (cap) 24 mL (240 mg) qd (liquid)			No effect	200 mg q48h 120 mg qd (liquid)	200 mg q72h 80 mg qd (liquid)	200 mg q96h¶ 60 mg qd (liquid)	Std Dose	Minimal. Skin hyperpigmentation§ HBV flare##
<b>Epzicom (ABC/3TC)</b>	ABC 600 mg + 3TC 300 mg	1 tablet qd			No effect	Fixed formulation not recommended in renal failure			Std Dose	ABC hypersensitivity¶¶. Screen for B-5701. HBV flare##
<b>Lamivudine (Epivir; 3TC)</b>	150, 300 mg tabs (see also: <i>Combivir, Trizivir &amp; Epzicom</i> ) 10 mg/mL po soln	150 mg bid or 300 mg qd			No effect	150 mg qd	150 mg x 1 then 100 mg/d	150 mg x 1 then 25-50 mg/d¶	Std Dose	Minimal. HBV flare##
<b>Stavudine (Zerit; d4T) †‡</b>	15, 20, 30, 40 mg cap; 1 mg/mL po soln	Wt >60 kg: 40 mg bid (30 mg bid is recommended by WHO and author for all pts) Wt <60 kg: 30 mg bid			No effect	>60 kg-20 mg q12h <60 kg-15 mg q12h	>60 kg-20 mg q24h <60 kg-15 mg q24h	Dose after dialysis on days of HD¶	Std Dose	<i>Peripheral neuropathy, Pancreatitis, hyperlipidemia, lactic acidosis, lipoptrophy, ascending paresis (rare)§</i>
<b>Tenofovir (Viread, TDF) †‡</b>	300 mg tab (see also: <i>Truvada and Atripla</i> )	300 mg qd			No effect	Avoid	Avoid	300 mg q7d**	Std Dose	Renal failure - avoid w/ CrCl<50 ml/min, HBV flare##

† The combination of ddI & d4T should be avoided, especially in pregnant women.

‡ The combination of ddI and TDF should be avoided.

§ Class adverse reactions – lactic acidosis with steatosis. (see page 30)/most common with AZT, d4T, ddI.

## Patients with chronic HBV (HBsAg) may have flare if TDF, 3TC, or FTC are discontinued if HBV becomes resistant or with IRIS

¶ Give post dialysis

¶¶ Registry for hypersensitivity reactions (HSR) 800-270-0425; Screen for HLA-B\* 5701; with HSR – do not re-challenge

\*\* Not recommended if renal failure is reversible

### Drug Table 1. Antiretroviral Agent Characteristics (Cont'd)

(Most common and/or important toxicities are in *italics*.)

Drug Name	Form	Usual Adult Dose	Food Effects	Renal Failure Dosing			Liver Failure Dosing	Toxicity (main toxicity – <i>italics</i> )
				CrCl 30-59 mL/min	CrCl 10-29 mL/min	CrCl <10 or dialysis		
<b>Trizivir</b> (AZT/3TC/ABC)	AZT 300 mg + 3TC 150 mg + ABC 300 mg (tab)	1 bid	No effect	Fixed formulation not recommended in renal or hepatic failure				<i>Hypersensitivity reaction (ABC), ¶¶. Screen for B 5701 bone marrow suppression (AZT), GI intolerance (ATZ)§. HBV flare## (3TC)</i>
<b>Truvada</b> (TDF/FTC)	TDF 300 mg + FTC 200 mg	1 tablet qd	No effect	1 tab q48h	Not recommended		Std dose	<i>Renal toxicity (TDF) HBV flare##</i>
<b>Zidovudine</b> (Retrovir, AZT, ZDV)	100 cap, 300 mg tab; (see also: <i>Combivir &amp; Trizivir</i> ) 10 mg/ mL IV soln 10 mg/ mL po soln	300 mg bid 200 mg tid	No effect	300 mg bid	300 mg bid	300 mg qd	Std dose	<i>Anemia, neutropenia, headache, asthenia, GI intolerance§, lactic acidosis</i>
<b>Protease Inhibitors (PIs) Doses with/without RTV Boosting (see Drug Table 10, pg 47)</b>								
<b>Atazanavir</b> (Reyataz, ATV)	100, 150, 200, and 300 mg caps	400 mg qd; ATV 300 mg/RTV 100 mg qd (preferred) RTV boosting is usually desired and is required if ATV is combined with TDF (ATV/r 300/100 mg qd) or with EFV (ATV/r 400/100 mg qd) in treatment – naïve pts. H2 antagonist – do not exceed equivalent of 40 mg Famotidine 40mg bid (treatment naïve) or 20 mg bid (treatment experienced)	Take with food. Avoid concurrent buffered ddl, antacids, PPIs H2 blocker (Needs food & gastric acid)	Standard dose			CPS** 7-9: 300 mg qd CPS** >9: Avoid boosted ATV.	<i>Benign increase in indirect bilirubin, increase in ALT/AST, GI intolerance, prolongation of QTc; caution with conduction defects with drugs that do this (eg clarithromycin); fat redistribution††, Nephrolithiasis (rare)</i>
<b>Darunavir</b> (Prezista, DRV)	75, 150, 400 and 600 mg tabs 50 mg/mL oral suspension	DRV 800 mg/RTV 100 mg qd (treatment-naïve) DRV 600 mg/RTV 100 mg bid (treatment experienced)	Take with food	Standard dose			Mild/Mod disease-std dose severe-avoid	<i>Skin rash (sulfonamide moiety), GI intolerance, increased ALT/AST and hepatotoxicity, fat redistribution, Lipodystrophy††</i>
<b>Fosamprenavir</b> (Lexiva, FPV)	700 mg tabs 50 mg/ml oral suspension	treatment - naïve - 1400 mg bid or 700 mg/RTV 100 mg bid (preferred) or 1400 mg/RTV 100 or 200 mg qd treatment experienced – FPV 700/RTV100 bid	No effect	Standard dose			¶	<i>Rash (caution with severe sulfa allergy), increase in ALT/AST, GI intolerance, headache, hepatiti§, fat redistribution, Lipodystrophy††</i>

STD=standard dose

\*\* CPS=Child-Pugh Score; limited clinical data on dose adjustment with liver failure (see page 11)

§§ More frequent monitoring required. Drug change or dose change could be considered on a case-by-case basis noting the risk of resistance with underdosing

¶ CPS\*\* 5-7: FPV 700 mg bid (naïve) RTV 100 qd + FPV 700 bid (experienced) CPS\*\* 7-9: FPV 700 mg bid (naïve) 100 mg RTV qd + FPV 450 bid (experienced) CPS\*\* 10-15: 350 mg bid (naïve) RTV 100 qd + FPV 300 (experienced) Limited data. Use with caution.

†† Class adverse effects include lipodystrophy with hyperglycemia, fat redistribution, hyperlipidemia, and possible increased bleeding with hemophilia. ATV does not cause hyperlipidemia or hyperglycemia. All PIs and NNRTIs may cause increase in ALT/AST (see Drug Table 2).

**Drug Table 1. Antiretroviral Agent Characteristics (Cont'd)**

(Most common and/or important toxicities are in *italics*.)

Drug Name	Form	Usual Adult Dose	Food Effects	Renal Failure Dosing			Liver Failure Dosing	Toxicity (main toxicity – <i>italics</i> )
				CrCl 30-59 mL/min	CrCl 10-29 mL/min	CrCl <10 or dialysis		
<b>Indinavir</b> ( <i>Crixivan, IDV</i> )	100, 200, 333, 400 mg caps	800 mg q8h; separate buffered ddl ≥1 h; IDV 800 mg/RTV 100-200 mg bid Take w/48oz of water	1 h before or 2 h after meal With RTV no food effect	Standard dose			600 mg q8h§§	<i>GI intolerance</i> <i>Nephrolithiasis</i> , increase in ALT/AST, benign increase in indirect bilirubin, paronychia††, fat redistribution
<b>Lopinavir/ Ritonavir</b> ( <i>Kaletra, LPV/r</i> )	LPV 200 mg + RTV 50 mg tab; LPV 100 + RTV 25 tab; LPV 80 mg + RTV 20 mg/ mL po soln (42% alcohol)	400 mg LPV + 100 mg RTV (2 tabs) bid or 800 mg LPV + 200 mg RTV (4 tabs) qd (in PI-naïve only)§ Soln: 5 mL bid or 10 mL qd (treatment naïve only) With EFV or NVP: LPV/r 500/125 mg bid	No effect w/tablet take liquid w/ food	Standard dose			Caution§§	<i>GI Intolerance</i> , (esp. diarrhea), increase in ALT/AST, asthenia††, fat redistribution, hypertriglyceridemia, hyperglycemia QTc & PR interval prolongation
<b>Nelfinavir</b> ( <i>Viracept, NFV</i> )	250, 625 mg tabs 50 mg/g powder	1250 mg bid or 750 mg tid	Take with fatty meal	Standard dose			Caution§§	<i>Diarrhea</i> , increased ALT/AST, Lipodystrophy††
<b>Ritonavir</b> ( <i>Norvir, RTV</i> )	100 mg caps, 100 mg tab 600 mg/ 7.5 mL po soln Note: Refrigerate capsules, but they can be left at room temperature at up to 77° F (25°C) for ≤ 30 days. Do not refrigerate oral soln.	100-200 mg q12-24h coadministered with a second PI as a pharmacokinetic enhancer or 600 mg q12h (rarely used)#; separate ddl ≥2 h	Food improves GI tolerance	Standard dose			Caution No adjust- ment for mild to mod.	<i>GI intolerance</i> , paresthesia, increased ALT/AST, taste perversion, Lipodystrophy†† PR and QTc prolongation (RTV 400 bid)
<b>Saquinavir</b> ( <i>Invirase, SQV</i> )	200 mg caps 500 mg tabs	SQV 1000 mg + RTV 100 mg bid	Take within 2 h of meal	Standard dose			Caution§§	<i>GI intolerance</i> , increased ALT/AST, Lipodystrophy††

† Efavirenz should be avoided in first trimester of pregnancy and avoid in women with reproductive potential.

# See Drug Tables 9 & 10 (pgs 46 & 47) for dosing recommendations when using dual PI or PI plus NNRTI.

§§ More frequent monitoring required. Drug change or dose change could be considered on a case-by-case basis noting the risk of resistance with underdosing

†† Class adverse effects include lipodystrophy with hyperglycemia, fat redistribution, hyperlipidemia, and possible increased bleeding with hemophilia. ATV does not cause hyperlipidemia or insulin resistance.

### Drug Table 1. Antiretroviral Agent Characteristics (Cont'd)

(Most common and/or important toxicities are in *italics*.)

Drug Name	Form	Usual Adult Dose	Food Effects	Renal Failure Dosing			Liver Failure Dosing	Toxicity (main toxicity – <i>italics</i> )
				CrCl 30-59 mL/min	CrCl 10-29 mL/min	CrCl <10 or dialysis		
Tipranavir (Aptivus, TPV)	250 mg caps 100 mg/ml po soln Note: Refrigerate capsules, but they can be at room temperature at up to 77° F (25°C) for up to 60 days. Do not refrigerate or freeze oral soln.	500 mg bid + RTV 200 mg bid	Fatty meal ↑TPV AUC 31%. But can be given with or without food.	Standard dose			Caution CPS 7-9	<i>Severe hepatitis</i> , increased ALT/AST, rash (caution w/ severe sulfa allergy), GI intolerance, Lipodystrophy <sup>‡‡</sup> , intracranial bleed (rare) ##
<b>Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)</b>								
Delavirdine (Rescriptor, DLV)	100, 200 mg tabs	400 mg tid Separate buffered ddl or antacid ≥1 h	No effect	Standard dose			§§	Rash, increased ALT/AST
Efavirenz † (Sustiva, EFV)	50, 100, 200 mg caps, 600 mg tabs (see also: <i>Atripla</i> )	600 mg hs	Take on an empty stomach during the first 2-3 wks	Standard dose			§§	CNS x 2-3 wk, rash, increased ALT/AST, lipoatrophy, false + cannabinoid and benzodiazepine test, <i>teratogenic</i>
Etravirine (Intelligence, ETR)	100 mg tabs	200 mg bid after a meal	Take with meal	Standard dose			Child-Pugh Class C: No data Child Pugh Class A and B: Standard dose	Hypersensitivity - rash ± constitutional sx ± hepatic failure; Nausea Avoid concurrent unboosted PI, ATV/r, FPV/r, TPV/r
Nevirapine§§ (Viramune, NVP)	200 mg tabs 50 mg/5 mL po susp.	200 mg qd x 14 d, then 200 mg bid Continue 200 mg/d up to 28d if rash without constitutional symptoms. Repeat lead-in regimen if stopped > 7 days	No effect	Standard dose	Standard; give post dialysis		Avoid with moderate to severe hepatic disease	Rash, increased ALT/AST, <i>hepatic necrosis</i> , esp. in females with a baseline CD4 >250 cells/mm <sup>3</sup> §§

† Efavirenz should be avoided in first trimester of pregnancy and avoid in women with reproductive potential.

§§ Nevirapine should be avoided as initial therapy in women with a baseline CD4 count >250 cells/mm<sup>3</sup> and in men with CD4 counts >400 cells/mm<sup>3</sup> due to high rate of symptomatic hepatitis (11% in women and 6% in men).

# See Drug Tables 9 & 10 (pgs 46 & 47) for dosing recommendations when using dual PI or PI plus NNRTI.

§§ More frequent monitoring required. Drug change or dose change could be considered on a case-by-case basis noting the risk of resistance with underdosing

‡‡ Class adverse effects include lipodystrophy with hyperglycemia, fat redistribution, hyperlipidemia, and possible increased bleeding with hemophilia. ATV does not cause hyperlipidemia or insulin resistance.

## Avoid antiplatelet drug co-administration.

### Drug Table 1. Antiretroviral Agent Characteristics (Cont'd)

(Most common and/or important toxicities are in *italics*.)

Drug Name	Form	Usual Adult Dose	Food Effects	Renal Failure Dosing			Liver Failure Dosing	Toxicity (main toxicity – <i>italics</i> )
				CrCl 30-59 mL/min	CrCl 10-29 mL/min	CrCl <10 or dialysis		
<b>Fusion Inhibitors</b>								
Enfuvirtide ( <i>Fuzeon</i> , ENF, T-20)	90 mg single-use vials to be reconstituted with 1.1 mL H <sub>2</sub> O	90 mg (1 mL) SQ q12h into upper arm, anterior thigh or abdomen (Rotate sites)	N/A	Standard dose			Standard dose	<i>Site reactions</i> (nodules), bacterial pneumonia
<b>CCR5 Antagonist</b>								
Maraviroc ( <i>Selzentry</i> , MVC)	150 and 300 mg tabs	150-600 mg bid** Dosing regimen based on concurrent medicines: 150 mg bid with PIs except TPV/r, and strong CYP3A4 inhibitor (e.g. <i>Kitocoragole</i> , <i>itracomzole</i> , <i>clarithromycin</i> ). 300 mg bid with ENF, TPV, NVP, RAL †600 mg bid with EFV, ETR ** and strong CYP3A4 inducer (e.g. <i>rifampin</i> , <i>phenobarbital</i> , <i>phenytoin</i> <i>carbamazepine</i> ).	No effect	Use with caution; with CrCl < 50/ min and CYP3A inhibitor. Monitor for postural hypotension.			Standard dose, levels ↑	Abdominal pain, upper respiratory tract infections, hepatotoxicity preceded by rash and ↑IgE. Rash, cough, rash, abd pain
<b>Integrase Inhibitors</b>								
Raltegravir ( <i>Isentress</i> , RAL)	400 mg tabs	400 mg bid	No effect	Standard dose			Standard dose with mod liver disease	Nausea, headache, diarrhea, fever, rhabdomyolysis (all rare) CPK ↑

† Note: if MVC is co-administrative with both a CYP3A4 inducer and inhibitor, dose MVC 150 mg bid.

\*\* MVC dose with DRV/r/ETR - 150 mg bid.

# See Drug Tables 9 & 10 for dosing recommendations when using dual PI or PI plus NNRTI.

**Drug Table 2. Adverse Reactions to Antiretroviral Agents**

LIFE THREATENING REACTIONS	
<b>Hepatic necrosis</b>	
<b>Agent</b>	NVP
<b>ADR Features</b>	Abrupt onset flu-like illness with GI symptoms, fever, rash (50%), eosinophilia and hepatic necrosis usually in first 6 wks and up to 18 wks of NVP; may be drug rash, eosinophilia, and systemic symptoms.
<b>Frequency</b>	1-2% of all NVP recipients. Rate of symptomatic hepatitis is 11% in treatment-naïve women with baseline CD4 count >250 cells/mm <sup>3</sup> and 6% in men with baseline CD4 count >400 cells/mm <sup>3</sup> . No risk with single dose for PMTCT.
<b>Monitor</b>	Warn patient. ALT: Baseline and at 2 wks and 4 wks then monthly x 3 mos, then q3mos.
<b>Intervention</b>	Promptly discontinue ART, but may progress despite this. Supportive care (steroids, antihistamines appear useless). Do not rechallenge. Safety of EFV switch unknown.
<b>Cutaneous: Steven-Johnson Syndrome and Toxic Epidermal Necrolysis</b>	
<b>Agent</b>	NVP, less common is EFV + ETR (reported with FPV, DRV, TPV, ABC, ddl, LPV, AZT, ATV and IDV).
<b>ADR Features</b>	Usually first few weeks with fever, myalgia, skin rash with blistering ± mucous membrane involvement with NVP may also cause hepatic necrosis.
<b>Frequency</b>	NVP 0.5-1%, EFV 0.1%, ETR <0.1%.
<b>Monitor</b>	Warn patient.
<b>Intervention</b>	Promptly discontinue ART if mucous membrane involved, conjunctivitis, blisters, bullae, and/or system symptoms. Intensive care of wounds including pain meds and antibiotics and IVs; may require treatment in a burn center. Use of steroids is controversial. Role of steroids and IVIG unclear.
<b>Lactic acidosis</b>	
<b>Agent</b>	d4T+ddl>AZT (Rare or never with ABC, TDF, 3TC, and FTC); long duration use.
<b>ADR Features</b>	GI symptoms, wasting, fatigue, ± multiorgan failure, pancreatitis, respiratory failure.
<b>Frequency</b>	1-10 per 1,000 patient-years for d4T or ddl. Risk: d4T>ddl>AZT; Female, obesity; dose and duration related.
<b>Monitor</b>	Clinical symptoms. No routine lactate levels, but obtain if clinically indicated; normal level is <2.0 mmol/L. Surrogate for lactic acid levels: High CPK and ALT; low HCO <sub>3</sub> <sup>-</sup> ; anion gap.
<b>Intervention</b>	Promptly discontinue ART; supportive care with mechanical ventilation, dialysis, HCO <sub>3</sub> <sup>-</sup> infusion, hemofiltration. Role of steroids, carnitine, thiamine, IVIG, plasmapheresis, or riboflavin: unclear. Recovery may take months. Long-term residual effects are common. For ART avoid NRTI or use ABC, 3TC, FTC, and/or TDF. Case reports of benefit from L-carnitine, riboflavin.

LIFE THREATENING REACTIONS (CONT'D)	
<b>Hypersensitivity</b>	
<b>Agent</b>	ABC
<b>ADR Features</b>	Symptoms (in rank order): high fever, diffuse skin rash, nausea, headache, abdominal pain, diarrhea, arthralgias, pharyngitis, and dyspnea. Virtually all have ≥2 systems involved (may help distinguish common intercurrent illnesses). Always progresses with continued ABC. Median onset: day 9 of ABC; 90% in first 6 wks.
<b>Frequency</b>	6-7% of ABC recipients; very rare if screening test for HLA-B* 5701 is negative. Rates are less in African-Americans.
<b>Monitor</b>	Warn patient. (In questionable cases may want to administer next dose under observation – this reaction always progresses with next dose).
<b>Intervention</b>	D/C ABC. Never re-challenge (if dx is probable). Supportive care (steroids and antihistamines are not useful). Symptoms usually resolve in 48 h after D/C ABC.
<b>SERIOUS REACTIONS</b>	
<b>Pancreatitis</b>	
<b>Agent</b>	ddl + d4T > ddl > d4T
<b>ADR Features</b>	Abdominal pain with elevated amylase and/or lipase.
<b>Frequency</b>	ddl 1-7%. Appears to be less frequent in HAART era. More frequent with other risks—especially alcoholism, hx pancreatitis, concurrent d4T, ddl and TDF without ddl dose adjustment, ddl + ribavirin (contraindicated).
<b>Monitor</b>	Warn patient. Amylase with clinical symptoms.
<b>Intervention</b>	Supportive care, pain meds and bowel rest (NPO).
<b>Nephrotoxicity – Fanconi syndrome</b>	
<b>Agent</b>	TDF
<b>ADR Features</b>	Renal failure ± Fanconi syndrome. Note: increased creatinine, proteinuria, hypophosphatemia, glycosuria, hypokalemia, non-anion gap, metabolic acidosis. May be asymptomatic or signs of diabetes insipidus. Risks: Advanced age; low BMI, low CD4; avoid TDF with CrCl < 50 ml/min.
<b>Frequency</b>	Low, but increase with long term use and possibly w/ boosted PI co-administration.
<b>Monitor</b>	Monitor urinalysis, creatinine clearance, serum K, and phosphorus at baseline, then at 6-12 mo, intervals. If proteinuria or decreased CrCl then measure 24 h protein.



Drug Table 2. Adverse Reactions to Antiretroviral Agents (Cont'd)

MISCELLANEOUS REACTIONS (CONT'D)	
<b>CNS Toxicity</b>	
<b>Agent</b>	EFV
<b>ADR Features</b>	"Disconnected syndrome" with bad dreams, somnolence, impaired concentration reduced attention etc. Begins with first dose.
<b>Frequency</b>	>50% with EFV.
<b>Monitor</b>	Warn patient. May wish to avoid heavy machinery operation or similar type jobs for 1 <sup>st</sup> 2-3 wks.
<b>Intervention</b>	Usually resolves in 2-3 wks.
<b>Insulin resistance</b>	
<b>Agent</b>	PIs (especially IDV) except ATV
<b>ADR Features</b>	FBS >126 mg/dL ± symptoms of diabetes.
<b>Frequency</b>	3-5%; higher frequency with family history of diabetes.
<b>Monitor</b>	FBS at baseline, 3 mos, and then q3-6mos
<b>Intervention</b>	Diet and exercise, metformin or rosiglitazone (no drug interactions with PIs) if indicated; may need insulin. May switch to NNRTI regimen.
<b>Hyperlipidemia</b>	
<b>Agent</b>	PIs (except ATV), EFV, and d4T. Rank order for PIs: TPV/r>LPV/r=FPV/r>IDV/r>SQV/r ~DRV/r >>ATV/r.
<b>ADR Features</b>	Increase total and LDL cholesterol and triglycerides; triglycerides esp high with RTV, LPV/r and TPV/r. Begins within weeks.
<b>Frequency</b>	Variable.
<b>Monitor</b>	Fasting lipid profile at baseline, 3-6 mos and then annually.
<b>Intervention</b>	Based on National Cholesterol Education Program [JAMA 2001;285:2486] See Drug Tables 4 & 5. Preferred statins: pravastatin, atorvastatin, or rosuvastatin (with dose adjustment for coadministration with ARV if necessary.) Consider ART regimen change to avoid d4T and PIs other than ATV.

MISCELLANEOUS REACTIONS (CONT'D)	
<b>Fat atrophy</b>	
<b>Agent</b>	d4T>AZT, ddl, and EFV
<b>ADR Features</b>	Thinning of buccal fat in face; extremities and buttocks.
<b>Frequency</b>	Common with long term use.
<b>Monitor</b>	Self image is most important.
<b>Intervention</b>	Discontinue d4T or AZT early if possible – changes are either slow to reverse or are irreversible. Injectable agents: poly-L-lactic acid ( <i>Sculptra</i> ).
<b>Fat accumulation</b>	
<b>Agent</b>	PIs
<b>ADR Features</b>	Increase abdominal girth, breast size, buffalo hump.
<b>Frequency</b>	20-80% of those receiving HAART.
<b>Monitor</b>	Self image is most important.
<b>Intervention</b>	May change to NNRTI based regimen for cosmetic reasons; restorative surgery.

**Drug Table 3. Antiretroviral Agents, “Black Box” Warnings**

Agent	Reaction
Abacavir	<ul style="list-style-type: none"> <li>• Fatal hypersensitivity reactions: Do not restart if hypersensitivity reaction cannot be ruled out.</li> <li>• Lactic acidosis and steatosis*</li> </ul>
Atazanavir	None
Darunavir	None
Delavirdine	None
Didanosine	<ul style="list-style-type: none"> <li>• Fatal and nonfatal pancreatitis: Do not restart</li> <li>• Lactic acidosis with steatosis</li> <li>• Fatal lactic acidosis when combined with stavudine in pregnancy</li> </ul>
Efavirenz	None
Emtricitabine	<ul style="list-style-type: none"> <li>• Lactic acidosis with steatosis*</li> <li>• Flare of hepatitis B (HBsAg) when antiretroviral is stopped. May need to treat HBV.</li> <li>• Safety and efficacy for HBV treatment is not established.</li> </ul>
Enfuvirtide	None
Indinavir	None
Lamivudine	<ul style="list-style-type: none"> <li>• Lactic acidosis with steatosis.*</li> <li>• Patients with HIV infection should receive only dosage and formulations appropriate for treatment of HIV.</li> <li>• Flare of hepatitis B (HBsAg) when antiretroviral is stopped. May need to treat HBV.</li> </ul>
Lopinavir	None
Mavavirac	<ul style="list-style-type: none"> <li>• Hepatotoxicity with systemic allergic response (rash, ↑IgE)</li> </ul>
Nelfinavir	None
Nevirapine	<ul style="list-style-type: none"> <li>• Hepatotoxicity including fulminant and cholestatic hepatitis &amp; hepatic necrosis, especially in females with baseline CD4 count &gt;250 cells/mm<sup>3</sup>; monitor intensively in first 18 wks of therapy.</li> <li>• Severe, life-threatening skin reaction including toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome, etc.</li> <li>• Do not restart if there is serious liver injury or serious drug reaction.</li> </ul>
Raltegravir	None*
Ritonavir	<ul style="list-style-type: none"> <li>• Potentially serious drug interactions with non-sedating antihistamines, sedative hypnotics, antiarrhythmics, or ergot alkaloids. (see Table 7, pg 41-43).</li> </ul>
Saquinavir	None

\* Described with NRTI class, however unlikely to occur with ABC, FTC, 3TC, and TDF.

**Drug Table 3. Antiretroviral Agents, “Black Box” Warnings (Cont’d)**

Agent	Reaction
Stavudine	<ul style="list-style-type: none"> <li>• Lactic acidosis with steatosis</li> <li>• Fatal and non-fatal pancreatitis when used with ddI.</li> <li>• Fatal lactic acidosis when combined with Didanosine in pregnancy</li> </ul>
Tenofovir	<ul style="list-style-type: none"> <li>• Lactic acidosis and steatosis*</li> <li>• Flare of hepatitis B (HBsAg) when antiretroviral is stopped. May need to treat HBV.</li> </ul>
Tipranavir	<ul style="list-style-type: none"> <li>• Clinical reports of hepatitis and hepatic decompensation with death. Increased risk of hepatitis in patients with chronic hepatitis due to HBV or HCV.</li> <li>• Fatal and non-fatal intracranial bleed.</li> </ul>
Zidovudine	<ul style="list-style-type: none"> <li>• Hematologic toxicity-- anemia &amp; leukopenia</li> <li>• Prolonged use may cause myopathy.</li> <li>• Lactic acidosis and steatosis*</li> </ul>

\* Described with NRTI class, however unlikely to occur with ABC, FTC, 3TC, and TDF since they are least likely to cause mitochondrial toxicity *in vitro*.

**Drug Table 4. National Cholesterol Education Program: Indications for Dietary or Drug Therapy for Hyperlipidemia**

Coronary Heart Disease Risk Status	Goal	Threshold for diet Rx	Threshold for drug Rx
No CHD & 0-1 Risks*	LDL <160 mg/dL	LDL ≥130 mg/dL	LDL >190 mg/dL (LDL 160-190 Drug therapy optional)
No CHD & ≥2 Risks*	LDL <130 mg/dL	LDL ≥100 mg/dL	10 Yr CHD Risk <10%‡ LDL >160 mg/dL
			10 yr CHD Risk 10-20%‡ LDL >130 mg/dL
CHD or CHD equivalent: • Clinical ASCVD† • Diabetes mellitus • Multiple Risk Factors conferring 10 yr risk of CHD of >20%‡	LDL <100 mg/dL	LDL ≥70 mg/dL	LDL >130 mg/dL (100-129 mg/dL: drug optional)

**Drug Table 4. National Cholesterol Education Program: Indications for Dietary or Drug Therapy for Hyperlipidemia (Cont'd)**

**Triglycerides are an independent consideration**

- For patients with serum triglycerides >500 mg/dL the primary goal is reduction of triglycerides to prevent Pancreatitis and reduce risk of cardiovascular disease
- For patients with serum triglycerides 200-499 mg/dL reduction of non-HDL cholesterol becomes a secondary goal after reaching LDL goal.

Adapted from: *JAMA* 2001; 285:2486-2497. Updated - *Circulation* 2004;110:227.

Editors Note: This table is a basic condensation of complex guidelines. Readers should consult the National Heart, Lung, and Blood Institute's web site: <http://www.nhlbi.nih.gov/guidelines/cholesterol/>

\* CHD Risk Factors: Age (men >45 yrs; women >55 yrs or premature menopause without estrogen replacement); hypertension, current smoking, hx of cardiovascular disease in first degree relative (<55 yrs for male relative and <65 yrs for female relative), or serum HDL cholesterol <40 mg/dL. If high HDL (>60 mg/dL) subtract one risk factor.

† Atherosclerotic Cardiovascular Disease (ASCVD) includes peripheral artery disease, symptomatic carotid artery disease, and abdominal aortic aneurysm.

‡ Calculation of 10 year risk of CHD requires tables which may be found in the *JAMA* 2001;285:2486 or the National Heart, Lung, and Blood Institute's website: <http://www.nhlbi.nih.gov/guidelines/cholesterol/index.htm>

**Drug Table 5. Drug Therapy for Hyperlipidemia: Recommendations of the ACTG [Dube MP. et al, Clin Inf Dis 2000;31:1216]**

Lipid Problem	Preferred	Alternative	Comment
Isolated high LDL	Statin*	Fibrate†	Start low doses and titrate up. With PIs watch for myopathy
High cholesterol and triglycerides	Statin* or fibrate†	Start one and add other	Combination may increase risk of myopathy
Isolated high triglycerides	Fibrate†	Statin*	Combination may increase risk of myopathy

NOTE: Optimal management of hyperlipidemia should begin with specific risk factor reduction interventions such as: low fat diet; regular exercise; moderation of alcohol intake; smoking cessation, blood pressure control, and diabetes control (where applicable). The likelihood of success with drug therapy for hyperlipidemia is substantially reduced in the absence of such interventions.

\* Statin: Pravastatin 20 mg/d (max. 40 mg/d), fluvastatin 20-40 mg/d, or atorvastatin 10 mg/d (max 40 mg) with PI co-administration. Use particular caution when giving LPV/r, TPV/r, or NFV with atorvastatin; rosuvastatin (start w/ 5 mg/d with PI co-administration; max 40 mg/d) also see Drug Table 6

† Fibrate: Gemfibrozil 600 mg bid ≥30 minutes before meal or

Fenofibrate tablets (eg Tricor) 160 mg qd

Micronized fenofibrate (capsules) 67 mg qd to start, max. dose 201 mg qd

**Drug Table 6. Drug Interactions: Combinations That Should Not Be Used**

Class	Contraindicated Agent	ART Agents	Alternatives
Ca++ channel blocker	Bepidil	RTV, TPV/r, SQV/r, DRV/r. All PIs * EFV	-----
Antiarrhythmics	Flecainide, Propafenone	LPV/r, RTV, TPV/r, DRV/r, SQV/r. All PIs*	-----
	Amiodarone, quinidine	IDV, NFV, RTV, SQV/r, DRV/r, TPV. All PIs*	
Lipid lowering	Simvastatin, Lovastatin	All PIs*, DLV	Pravastatin or Fluvastatin, possibly Atorvastatin Rosuvastatin
Antimycobacterials	Rifampin	All PIs, MVC††, & NNRTIs contraindicated except EFV (600 or 800 mg/d) using standard doses of rifampin.	Use Rifabutin with PIs**
	Rifabutin	DLV	Clarithromycin, azithromycin
	Rifapentine	All PIs*, NVP*, DLV*, EFV*, ETR*	Rifabutin
Antihistamine	Astemizole, Terfenadine	All PIs, DLV, EFV	Loratadine, Fexofenadine, Cetirizine, or Desloratadine
Antineoplastics	Irinotecan	ATV; caution with other PIs	-----
GI	Cisapride	All PIs, DLV, EFV	Reglan
	Proton pump inhibitors	ATV, NFV	
Neuroleptic	Pimozide	All PIs and DLV, EFV	-----
Psychotropic	Midazolam†, Triazolam	All PIs, DLV, EFV	Temazepam or Lorazepam
	Alprazolam	DLV, IDV	
Ergot alkaloids	Ergotamine	All PIs, DLV, EFV	Consider sumatriptan
Herbs	St. John's wort	All PIs & EFV, DLV, ETR, NVP	Alternative antidepressants
Intranasal steroid	Fluticasone	FPV/r, LPV/r, RTV, SQV/r, TPV/r, ATV, DRV/r, all PIs*	Beclomethasone
Alpha adrenergic blockers	Alfuzosin	RTV, All PIs*, DLV*	Consider tamsulosin or doxazosin
Anti-angina	Ranolazine	All PIs, DLV	-----

\* Added by author based on pharmacokinetic principles and/or high potential for toxicity

\*\* See Drug Table 7 for rifabutin and antiretroviral dose adjustments

† Midazolam may be used with caution as a single dose given for a procedure (w/ LPV/r, ATV/r, TPV/r).

†† MVC 600 mg bid can be considered (limited data)

**Drug Table 6. Drug Interactions: Combinations That Should Not Be Used (Cont'd)**

Class	Contraindicated Agent	ART Agents	Alternatives
<b>B<sub>2</sub>-Agonist</b>	Salmeterol	RTV, LPV/r, PI/r	Fomoterol
<b>Anit-gout</b>	Allopurinol	ddl	
<b>Pulmonary HTV Agent</b>	High dose Sildenafil	RTV, LPV/r, all PI/r	Dose adjusted bosentan
<b>Anti-Hep C</b>	Ribavirin	ddl	Use alt. NRTI.

\* Added by author based on pharmacokinetic principles and/or high potential for toxicity

\*\* See Drug Table 7 for rifabutin and antiretroviral dose adjustments

† Midazolam may be used with caution as a single dose given for a procedure (w/ LPV/r, ATV/r, TPV/r).

†† MVC 600 mg bid can be considered (limited data)

**Drug Table 7. Drug Interactions: Combinations with PIs, NNRTIs or CCR5 Antagonists Requiring Dose Modifications**

Class	Agent	ART
<b>Antifungal</b>	Itraconazole	All PIs: monitor for toxicities LPV/r: max. itraconazole dose ≤200 mg bid IDV- Use IDV dose of 600 mg tid (unless boosted) + max. Itraconazole dose ≤200 mg bid MVC: 150 mg bid
	Ketoconazole	IDV- IDV/r 800/100 mg bid (do not exceed Ketoconazole ≤200 mg/d) MVC: 150 mg bid LPV/r, RTV, TPV/r, FPV/r- Ketoconazole ≤200 mg/d, FPV ≤400 mg/d NVP- Consider Fluconazole as an alternative
	Voriconazole	IDV is OK; EFV 300 mg qhs + voriconazole 400 q12h; LPV/r, TPV/r generally not recommended unless benefit outweighs risk; RTV ≥400 mg bid is contraindicated. Limited data for other PIs or NVP but potential for bidirectional inhibition. Monitor for toxicities. Lower dose RTV may be considered with voriconazole or use alternative. ETR AUC ↑36%.
	Posaconazole	ATV and Posaconazole levels are increased. Monitor posaconazole
<b>Oral contraceptives</b>	-----	Additional method of contraception recommended with: DRV/r, EFV, FPV, LPV/r, NFV, NVP, RTV, and TPV/r. ATV/r: use at least 35 mg EE (IDV & ATV: do not exceed 30 mg EE); ETR MVC and RAL: no interaction; consider additional form of contraception No data- SQV
<b>Anticonvulsants</b>	Phenobarbital, Phenytoin, Carbamazepine	Carbamazepine ↓IDV and potentially other PIs (except DRV) and NNRTIs. Phenytoin ↓NFV, ↓LPV, and potentially other PIs and NNRTIs. Phenobarbital may decrease all PIs and NNRTIs. Combinations of NNRTIs or PIs & designated anticonvulsants should be given with caution and monitoring of anticonvulsant and PI levels or consider valproic acid or levetiracetam (Keppra) MVC: 600 mg bid; RAL: close monitoring with phenytoin and phenobarbital
	Valproic Acid	LPV ↑75%
	Lamotrigine	Lamotrigine ↓50% w/ LPV/r
<b>Methadone</b>	-----	NVP and EFV may decrease methadone substantially; monitor for withdrawal. IDV and ATV have no interaction; other PIs (TPV, LPV/r, SQV/r, DRV/r) may decrease methadone levels and require monitoring for withdrawal but clinical significance is unclear. Methadone decreases buffered ddl levels - consider ddl EC (no interaction). MVC: No interaction; RAL: interaction unlikely

**Drug Table 7. Drug Interactions: Combinations with PIs, NNRTIs or CCR5 Antagonists Requiring Dose Modifications (Cont'd)**

Class	Agent	ART
Antibiotics	Clarithromycin	DLV, DRV/r, LPV/r, RTV, TPV/r-. Decrease clarithromycin dose in renal failure. MVC: 150 mg bid
		ETR, EFV: consider azithromycin as an alternative. ATV: decrease clarithromycin 50%
Erectile Dysfunction Agents	Sildenafil	PIs & DLV: ≤25 mg q48h and monitor; MVC and RAL: No data; interaction unlikely
	Vardenafil	PIs & DLV: ≤2.5 mg q72h
	Tadalafil	PIs & DLV: start with 5 mg and do not exceed 10 mg/72h
Anti-Mycobacterials	Rifabutin	All PIs with RTV boosting: standard dose PI/r + RBT 150 mg qod or 150 mg 3x/wk
		LPV/r 400/100 mg bid + RBT 150 qod (monitor RBT serum concentrations)
		FPV 1400 mg bid + RBT 150 mg/d or 300 mg 3x/wk
		ATV 400 mg/d + RBT 150 mg qod or 150 mg 3x/wk
		EFV 600 mg/d + RBT 450-600 mg/d or 600 mg 3x/wk
		IDV 1000 mg q8h + RBT 150 mg/d or 300 mg 3x/wk
		NFV 1250 mg bid + RBT 150 mg/d or 300 mg 3x/wk
		NVP standard + RBT standard (no adjustment)
		RTV 600 mg bid (no longer recommended) + RBT 150 mg qod or 150 mg 3x/wk
		MVC 300 mg bid; MVC 150 mg bid with PI co-administration
		RAL: use standard doses - No interaction
Rifampin	All PIs & NNRTIs contraindicated except EFV (600 mg/d) using standard doses of rifampin. NVP - if necessary, use with caution and monitor LFTs (not recommended by manufacturer, but good clinical data with standard dose) MVC: 600 mg bid or use rifabutin RAL: Avoid or use RAL800 mg bid	
Antiviral	Ribavirin	ddl + ABC: use other NRTI as an alternative

**Drug Table 7. Drug Interactions: Combinations with PIs, NNRTIs or CCR5 Antagonists Requiring Dose Modifications (Cont'd)**

Class	Agent	ART
Lipid Lowering	Simvastatin	EFV: may require simvastatin dose increase. Contraindicated with PI
	Atorvastatin	All PIs may substantially increase atorvastatin levels. Consider pravastatin or rosuvastatin (start with 5 mg/d) as an alternative. With co-administration use lowest possible dose of atorvastatin (10 mg). EFV may reduce atorvastatin levels. Co-administration of EFV may require atorvastatin dose increase with close monitoring of LFTs and CPK. MVC: No data; use standard doses. RAL: interaction unlikely
	Pravastatin	No dose change for most agents. EFV, NFV, & SQV/r 400/400 mg bid: pravastatin decreased; clinical significance unknown, may need to increase pravastatin dose; with DRV/r, pravastatin AUC increases in some patients 81%, but can be up to 5X in others; with LPV/r Pravastatin AUC ↑33%. Use with caution. MVC: No data; use standard doses. RAL: interaction unlikely
	Rosuvastatin	With LPV/r: Rosuvastatin AUC ↑108% With ATV: Rosuvastatin AUC ↑213% With TPV/r: Rosuvastatin AUC ↑26% Start with Rosuvastatin 5mg/d with slow titration. Interaction unlikely with RAL, MVC No interaction w/ FPV

**Drug Table 7. Drug Interactions: Combinations with PIs, NNRTIs or CCR5 Antagonists Requiring Dose Modifications (Cont'd)**

Class	Agent	ART
Miscellaneous	Antacids	APV, ATV, ddC, DLV, TPV/r- separate dosing by 2 h before or 1 h after to avoid reduced ARV bioavailability
	Ca++ channel blockers	
	Bepiridil	Contraindicated with all PIs and DLV
	Diltiazem	All PIs (especially ATV/r and RTV ≥400 mg bid)- start diltiazem with 50% dose and monitor EKG. EFV decreased diltiazem 69%; Titrate to effect.
	All Other Ca channel blockers	All PIs and DLV require dose titration and close monitoring
	Desipramine and other TCAs	RTV- Avoid desipramine co-administration Boosted PI may ↑TCA concentrations.
	Bupropion	LPV/r ↓ bupropion 46% EFV ↓ bupropion 55%
	Grapefruit juice	IDV ↓, SQV ↑ Not likely to be significant with boosted PIs
	H2 Blockers	Administer ATV 2 h before or 10 h after H2 blocker or use ATV/r 300/100 (in PI-naïve patients); in treatment experienced pts boost with RTV and give H2 blocker separately; consider alternative PI
	Opidogrel	ETR may decrease the efficacy of Isosipodogrel. Avoid
	Sertraline	EFV ↓ sertraline 39%
Theophylline	RTV- Monitor theophylline levels	
Trazodone	RTV- Lowest trazodone dose & monitor CNS LPV/r ↑ trazodone 240%. Monitor.	
Warfarin	Monitor INR closely if given with any PI or NNRTI (especially EFV or RTV)	
<b>Pulmonary Hypertension</b>	Bosentan	Significant ↑ bosentan levels co-administer bosentan (62 mg) only after PI/r has been given for at least 10 days.

**Drug Table 8. Drug Interactions: Nucleosides**

Drug	AZT	d4T	ddl	TDF
<b>Methadone</b>	AZT AUC ↑40%; no dose change. Monitor CBC	d4T ↓27%; no dose change	ddl EC- no interaction	No change in methadone or TDF levels
<b>ddl</b>	Limited clinical data	Increased toxicity: pancreatitis, peripheral neuropathy and lactic acidosis Avoid	-	ddl ↑44% >60 kg: 250 mg/d ddl EC <60 Kg: 200 mg/d ddl EC. Avoid Co-administration
<b>Ribavirin</b>	Monitor for severe anemia. <i>In vitro</i> inhibition of AZT activation; not shown <i>in vivo</i>	<i>In vitro</i> antagonism, but not clinically significant	Magnifies ddl toxicity; contraindicated.	Ribavirin unchanged; no data on TDF level.
<b>ATV</b>	AZT AUC unchanged but C <sub>min</sub> ↓30%; significance unknown	No interaction based on clinical data	Buffered ddl- take ATV 2 h before or 1 h after ddl or use ddl EC- separate dosing due to food restrictions.	ATV AUC ↓25%; TDF AUC ↑24%; Avoid concomitant use unless ATV combined with RTV (ATV/r)
<b>IDV</b>	Interaction unlikely based on clinical data.	d4T ↑25%	Buffered ddl - take 1 h apart	IDV C <sub>max</sub> ↑14%; clinical significance unknown
<b>Cidofovir, Gancyclovir, Valgancyclovir</b>	Gancyclovir + AZT increases marrow toxicity Monitor CBC	No interaction between d4T and Gancyclovir	ddl and oral gancyclovir ddl AUC ↑111% (po) and 50-70% (IV); use with caution or avoid	Combination of cidofovir + TDF may increase levels of both drugs - monitor for toxicity
<b>LPV/r</b>	No PK data but interaction unlikely due to favorable clinical data	No data. Interaction unlikely	No data	TDF AUC ↑34%. Use standard doses and monitor for TDF toxicity.
<b>TPV/r</b>	AZT ↓33-43%; clinical significance unknown	No interaction	Separate dose of ddl EC by ≥2 h	TPV AUC ↓9-18%; clinical significance unknown.
<b>DRV/r</b>	Interaction unlikely	Interaction unlikely	Take DRV 2 h before ddl	TPV AUC ↑22%. DRV no change

**Drug Table 9. Co-administration of PIs and NNRTIs: Dose Adjustments**

	EFV	NVP	ETR
ATV/r	ATV 400 mg + RTV 100 mg (with food) + EFV SD (avoid co-administration in PI-experienced patients)	Avoid	Avoid
DRV/r	DRV/r 600/100 bid + EFV 600 mg qhs (PI experienced); consider TDM	DRV/r SD + NVP SD (dose not established; consider TDM) DRV↑ & NVP↑	DRV/r 600/100 bid ETR 200 bid
FPV	• FPV 1400 mg qd + RTV 300 mg qd + EFV SD • FPV 700 mg bid + RTV 100 mg bid + EFV SD	FPV 700 mg + RTV 100 mg bid + NVP SD	Avoid
IDV	• IDV 1000 mg q8h + EFV SD or • IDV 800 mg q12h + RTV 200 mg bid + EFV SD	• IDV 1000 mg q8h + NVP SD • IDV 800 mg q12h + RTV 200 mg q12h + NVP SD	Avoid
LPV/r	LPV/r 500/125 mg bid + EFV SD	LPV/r 500/125 mg bid + NVP SD	ETR 200 bid LPV/r 400/100 bid
NFV	NFV SD + EFV SD	NVP SD + NFV SD	Avoid
SQV	SQV/r 1000/100 mg bid + EFV SD	• SQV 1000 mg bid + RTV 100 mg bid + NVP SD	SQV/r 1000/100 mg bid ETR-SD
TPV/r	TPV 500 mg bid + RTV 200 mg bid + EFV SD	ID, NVP may decrease TPV	Avoid

All Doses in mg

Abbreviations: ID= Inadequate Data, SD= Standard Dose, TDM=Therapeutic drug monitoring

**Drug Table 10. Co-administration of PIs: Dose Adjustments**

Drug	DRV	FPV	IDV	LPV/r	NFV	RTV	SQV
ATV	ATV 300 mg qd + DRV/r 600/100 bid	ID; ↓ATV AUC, avoid	Avoid	ATV 300 mg qd + LPV/r 400/100 mg bid	ID	ATV 300 mg qd + RTV 100 mg qd	ID. Poor virologic response in clinical trial
DRV		ID; avoid	ID	ID. DRV AUC ↓53%; avoid	ID	DRV 600 mg bid + RTV 100 mg bid <b>or</b> DVR/r 800/100 mg qd (PI-naïve)	ID. DRV AUC ↓26%; Avoid
FPV			ID	↓LPV/r ↓FPV; avoid	ID	• FPV 700 mg bid + RTV 100 mg bid <b>or</b> • FPV 1400 mg qd + RTV 100-200 mg qd	ID. APV ↓
IDV				IDV 600 mg bid + LPV/r 400/100 mg bid	• IDV 1200 mg bid + NFV 1250 mg bid • Limited clinical data.	• IDV 800 mg bid + RTV 100 mg bid	ID
LPV/r					ID, avoid		LPV/r 400/100 mg bid + SQV 1000 mg bid
NFV						Limited clinical data and limited boosting effect.	NFV 1250 mg bid + SQV 1200 mg bid
RTV							• RTV 400 mg bid + SQV 400 mg bid <b>or</b> • RTV 100 mg bid + SQV 1000 mg bid

All Doses in mg


Abbreviations: ID= Inadequate Data, SD= Standard Dose

Co-administration of TPV/r with other PIs is not recommended

The following foldout chart is  
A Dosing Guide to Currently  
Approved Drugs for HIV  
(antiretroviral medications).

The chart includes pill photos,  
regimens, and dietary  
considerations.

**A DOSAGE GUIDE TO CURRENTLY APPROVED DRUGS FOR HIV – This chart does not include dose adjustments or limitations on using these medicines in combination.**

DRUG/MANUFACTURER (Pills not actual size)		ADULT DOSING		DIETARY CONSIDERATIONS
<b>ONCE-DAILY SINGLE TABLET REGIMEN</b>				
ONCE DAILY	<b>ATRIPLA™</b> (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg, EFV/FTC/TDF) Bristol-Myers Squibb & Gilead Sciences, LLC		One tablet (contains 600 mg EFV, 200 mg FTC, and 300 mg TDF) once a day (a total of one tablet a day) (multiclass).†	Take on an empty stomach, preferably at bedtime. May be taken with food after 2 weeks.
<b>NUCLEOTIDE/NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS</b>				
ONCE DAILY	<b>TRUVADA®</b> (emtricitabine/tenofovir disoproxil fumarate, FTC/TDF or TVD) Gilead Sciences, Inc		One tablet (contains 200 mg FTC and 300 mg TDF) once a day (a total of one tablet a day).	No food restrictions.
	<b>VIREAD®</b> (tenofovir disoproxil fumarate, TDF) Gilead Sciences, Inc		One 300-mg tablet once a day (a total of one tablet a day).	No food restrictions.
	<b>EMTRIVA®</b> (emtricitabine, FTC) Gilead Sciences, Inc		One 200-mg capsule once a day (a total of one capsule a day).	No food restrictions.
	<b>Epzicom™</b> (abacavir sulfate/lamivudine, ABC/3TC or EPZ) GlaxoSmithKline		One tablet (contains 600 mg ABC and 300 mg 3TC) once a day (a total of one tablet a day).	No food restrictions.
	<b>Videx® EC</b> (didanosine, ddI EC) Bristol-Myers Squibb Company		For patients weighing at least 132 lb (60 kg): one 400-mg capsule once a day (a total of one capsule a day). For patients weighing less than 132 lb (60 kg): one 250-mg capsule once a day (a total of one capsule a day).	Take on an empty stomach. Must be swallowed whole.
1 OR 2 TIMES DAILY	<b>Epivir®</b> (lamivudine, 3TC) GlaxoSmithKline		One 150-mg tablet twice a day (a total of two tablets a day), or one 300-mg tablet once a day (a total of one tablet a day)	No food restrictions
	<b>Ziagen®</b> (abacavir sulfate, ABC) GlaxoSmithKline		One 300-mg tablet twice a day or two 300-mg tablets once a day (a total of two tablets a day).	No food restrictions.
2 TIMES DAILY	<b>Combivir®</b> (lamivudine/zidovudine, AZT/3TC, ZDV/3TC or CBV) GlaxoSmithKline		One tablet (contains 150 mg 3TC and 300 mg AZT) twice a day (a total of two tablets a day).	No food restrictions.
	<b>Retrovir®</b> (zidovudine, AZT or ZDV) GlaxoSmithKline		One 300-mg tablet twice a day (a total of two tablets a day).	No food restrictions.
	<b>Trizivir®</b> (abacavir sulfate/lamivudine/zidovudine, ABC/3TC/AZT) GlaxoSmithKline		One tablet (contains 300 mg ABC, 150 mg 3TC, and 300 mg AZT) twice a day (a total of two tablets a day).	No food restrictions.
	<b>Zerit®</b> (stavudine, d4T) Bristol-Myers Squibb Company		For patients weighing at least 132 lb (60 kg): one 40-mg capsule every 12 hours (a total of two capsules a day). WHO recommends 30-mg every 12 hours. For patients weighing less than 132 lb (60 kg): one 30-mg capsule every 12 hours (a total of two capsules a day).	No food restrictions.
<b>NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS</b>				
ONCE DAILY	<b>Sustiva®</b> (efavirenz, EFV) Bristol-Myers Squibb Company		One 600-mg tablet once a day (a total of one tablet a day).	Take on an empty stomach, preferably at bedtime. May be taken with food after 2 weeks.
2 TIMES DAILY	<b>Viramune®</b> (nevirapine, NVP) Boehringer Ingelheim Pharmaceuticals, Inc.		One 200-mg tablet once a day for 14 days, then one 200-mg tablet twice a day (a total of two tablets a day).	No food restrictions.
	<b>Intence™</b> (etravirine, ETV) Tibotec, Inc.		Two 100-mg tablets twice a day (a total of four tablets a day).	Take following a meal. Tablets may be dispersed in water.
3 TIMES DAILY	<b>Rescriptor®</b> (delavirdine mesylate, DLV) Pfizer Inc		Two 200-mg tablets three times a day (a total of six tablets a day) or four 100-mg tablets three times a day (a total of 12 tablets a day).	No food restrictions. 100-mg tablet may be dispersed in water. 200-mg tablet must be taken intact.






\* Indications, safety, dosing considerations, and efficacy may vary. This chart does not include dose adjustments or limitations on using these medicines in combination. Alternative formulations or dosage forms are available for some products.

† Used alone or in combination.

Please refer to the full Prescribing Information for each medication contained in this chart.

The brands listed are trademarks of their respective owners.

**A DOSAGE GUIDE TO CURRENTLY APPROVED DRUGS FOR HIV (continued) – This chart does not include dose adjustments or limitations on using these medicines in combination.**

DRUG/MANUFACTURER (Pills not actual size)		ADULT DOSING	DIETARY CONSIDERATIONS
<b>PROTEASE INHIBITORS</b>			
<b>ONCE DAILY</b>	<b>Reyataz®</b> (atazanavir sulfate, ATV) Bristol-Myers Squibb Company 	<b>Therapy-naïve patients:</b> two 200-mg capsules once a day (a total of two capsules 400-mg a day). <b>Therapy-experienced patients:</b> one 300-mg capsule plus one 100-mg ritonavir capsule once a day (a total of two capsules a day) or two 150-mg capsules plus one 100-mg ritonavir capsule once a day (a total of three capsules a day).	Take with food.
<b>1 OR 2 TIMES DAILY</b>	<b>Kaletra®</b> (lopinavir/ritonavir, LPV/RTV or LPV/r) Abbott Laboratories 	<b>Adults, therapy-naïve patients:</b> two 200/50-mg tablets twice a day or four 200/50-mg tablets once a day (a total of four tablets a day). <b>Therapy-experienced patients:</b> two 200/50-mg tablets twice a day (a total of four tablets a day). Once-daily administration of Kaletra is not recommended in therapy-experienced patients.	No food restrictions. Must be swallowed whole.
	<b>Lexiva®</b> (fosamprenavir calcium, FPV) GlaxoSmithKline 	<b>Therapy-naïve patients:</b> two 700-mg tablets twice a day (without ritonavir) (a total of four tablets a day) or two 700-mg tablets plus two 100-mg ritonavir capsules once a day (a total of four pills a day) or two 700-mg tablets plus one 100-mg ritonavir capsule once a day (a total of three pills a day) or one 700-mg tablet plus one 100-mg ritonavir capsule twice a day (a total of four pills a day). <b>Protease inhibitor-experienced patients:</b> one 700-mg tablet plus one 100-mg ritonavir capsule twice a day (a total of four pills a day). Once-daily administration of Lexiva plus ritonavir is not recommended in protease inhibitor-experienced patients. <b>Adjustment of ritonavir dose when Lexiva plus ritonavir are administered with efavirenz:</b> an additional 100 mg/day (300 mg total) of ritonavir is recommended when EFV is administered with Lexiva plus ritonavir once daily. No change in the ritonavir dose is required when EFV is administered with Lexiva plus ritonavir twice daily.	No food restrictions.
<b>2 TIMES DAILY</b>	<b>Aptivus®</b> (tipranavir, TPV) Boehringer Ingelheim Pharmaceuticals, Inc. 	Two 250-mg capsules plus two 100-mg ritonavir capsules twice a day (a total of eight capsules a day).	Take with food.
	<b>Prezista™</b> (darunavir, DRV or PRZ) Tibotec, Inc. 	<b>Therapy-naïve:</b> two 400-mg tabs (800 mg) + 100-mg ritonavir tab once daily. <b>Therapy-experienced:</b> one 600-mg tab + 100-mg ritonavir tab bid.	Take with food.
	<b>Norvir®</b> (ritonavir, RTV) Abbott Laboratories 	RTV 600-mg bid no longer recommended. RTV 100-200 mg once to twice daily enhances co-administration Protease inhibitors pharmacokinetic.	Take with food.
<b>2-3 TIMES DAILY</b>	<b>Invirase®</b> (saquinavir mesylate, SQV-HGC) Roche Laboratories Inc. 	Five 200-mg capsules twice a day plus one 100-mg ritonavir capsule twice a day (a total of 12 capsules a day) or two 500-mg tablets twice a day plus one 100-mg ritonavir capsule twice a day (a total of six pills a day).	Take within two hours after a full meal.
	<b>Viracept®</b> (nelfinavir mesylate, NFV) Agouron Pharmaceuticals, Inc. 	Two 625-mg tablets twice a day (a total of four tablets a day) or three 250-mg tablets three times a day (a total of nine tablets a day) or five 250-mg tablets twice a day (a total of 10 tablets a day).	Take with food. (Fatty food) May be dispersed in water.
<b>3 TIMES DAILY</b>	<b>Crixivan®</b> (indinavir sulfate, IDV) Merck & Co., Inc. 	Two 400-mg capsules every eight hours (a total of six capsules a day) or two 800-mg capsules + one 100-mg Ritonavir twice a day.	Take w/o food but w/water 1 hr before or 2 hrs after a meal for optimal absorption.
<b>INTEGRASE INHIBITORS</b>			
<b>2 TIMES DAILY</b>	<b>Isentress™</b> (raltegravir, RAL) Merck & Co., Inc. 	One 400-mg tablet twice a day (a total of two tablets a day).	No food restrictions.
<b>ENTRY INHIBITORS</b>			
<b>2 TIMES DAILY</b>	<b>Selzentry™</b> (maraviroc, MVC) Pfizer Inc 	<b>For patients taking CYP3A inhibitors with or without CYP3A inducers:</b> one 150-mg tablet twice a day (a total of two tablets a day). <b>For patients taking other concomitant medications, including tipranavir/ritonavir, nevirapine, all NRTIs, and enfuvirtide:</b> two 150-mg tablets twice a day (a total of four tablets a day) or one 300-mg tablet twice a day (a total of two tablets a day). <b>For patients taking CYP3A inducers without a strong CYP3A inhibitor:</b> four 150-mg tablets twice a day (a total of eight tablets a day) or two 300-mg tablets twice a day (a total of four tablets a day).	No food restrictions.
	<b>Fuzeon®</b> (enfuvirtide, T-20) Roche Laboratories Inc. 	90 mg (1 mL) twice a day injected subcutaneously into the upper arm, anterior thigh, or abdomen.	N/A

## Antiretroviral Therapy

### Adult ART Table 1A. Indications for ART: DHHS Guidelines (December 1, 2009)

Indications for ART:

- AIDS-defining diagnosis
- CD4 count <500 cells/mm<sup>3</sup>
- Pregnant woman
- HIV-associated nephropathy
- HBV co-infection when HBV is treated with agents active vs HIV

Note 1: Assumes patient readiness to commit to lifelong ART.

Note 2: Panel was divided on indication to treat with CD4 >500 cells/mm<sup>3</sup> considering it should be offered (50%) or should be optional (50%).

### Adult ART Table 1B. Indications for ART: IAS-USA Guidelines [JAMA 2010;304:321]

Clinical Category	CD4 Count (cells/mm <sup>3</sup> )	Recommendation
Symptomatic HIV or AIDS	Any	ART recommended*
Asymptomatic	<500	ART recommended*
Asymptomatic	>500	ART should be considered unless elite controller*
Associated conditions**	Any	ART recommended*

\* Assumes patient readiness

\*\* Pregnancy; HIV viral load >100,000 c/ml; active hepatitis B or C; HIV-associated nephropathy (HIVAN); age >60 years; active or high risk cardiovascular disease; CD4 slope >100 cells/mm<sup>3</sup>/yr; symptomatic acute HIV; discordant couple; active TB

### Adult ART Table 2A. Starting Regimens for Antiretroviral Naïve Patients: DHHS Guidelines (December 1, 2009)

Preferred (no order)	Alternative regimens
<ul style="list-style-type: none"> <li>• EFV/TDF/FTC</li> <li>• ATV/rt * TDF/FTC</li> <li>• DRV/rt * TDF/FTC</li> <li>• RAL/TDF/FTC</li> </ul> Pregnancy: LPV/rt/AZT/3TC	<ul style="list-style-type: none"> <li>• EFV/ABC or AZT/3TC</li> <li>• NVP/AZT/3TC</li> <li>• ATV/rt/ABC or AZT/3TC</li> <li>• FPV/rt + either TDF/FTC or ABC/3TC or AZT/3TC</li> <li>• LPV/rt + either TDF/FTC or ABC/3TC or AZT/3TC</li> <li>• SQV/rt * TDF/FTC</li> </ul>
Possibly acceptable (need more data)	Use with caution
<ul style="list-style-type: none"> <li>• MVC/AZT/3TC</li> <li>• RAL/ABC or AZT/3TC</li> <li>• DRV/rt * ABC or AZT * 3TC</li> <li>• SQV/rt * ABC or AZT * 3TC</li> </ul>	<ul style="list-style-type: none"> <li>• NVP/ABC/3TC</li> <li>• NVP/TDF/FTC</li> <li>• FPV/ABC or AZT/3TC</li> <li>• FPV/TDF/FTC</li> </ul>

**Adult ART Table 2B-1. Starting Regimens for Antiretroviral Naïve Patients:  
IAS-USA Guidelines [JAMA 2010;304:321]**

Component	Preferred	Alternatives
NRTI	TDF/FTC	ABC/3TC
3 <sup>rd</sup> agent	EFV	LPV/r
	ATV/r	FPV/r
	DRV/r	MVC
	RAL	

**Adult ART Table 2B-2. Starting Regimens in patients with co-morbidities:  
IAS-USA Guidelines [JAMA 2010;304:321]**

Comorbidity	NRTI	3 <sup>rd</sup> agent	Avoid
Cardiovascular disease	TDF, 3TC, FTC	EFV, NVP, ATV, RAL	ABC, FPV, LPV
Renal disease	ABC, 3TC, FTC	EFV, RAL, NVP, MVC, PI/r	TDF, ATV
Chronic HBV	TDF/FTC, TDF/3TC	EFV, RAL, PI/r*, MVC*	NVP*
Chronic HCV	TDF/FTC, TDF/3TC	EFV, RAL, PI/r*	NVP*, AZT, ddl, d4T, ABC

\* PI/r monitor LFTs; NPV-restrict to females with baseline CD4 <250 and males with <400; MVC-use with caution.

**Adult ART Table 2C-1. When to Start Antiretroviral Therapy  
[WHO Guidelines 2010: [http://whqlibdoc.who.int/publications/2010/9789241599764\\_eng.pdf](http://whqlibdoc.who.int/publications/2010/9789241599764_eng.pdf)]**

CD4 count ≤ 350 cells/mm <sup>3</sup>
WHO clinical stage 3 or 4 regardless of CD4 count
All patients with active TB regardless of CD4 count (start ART as soon as possible)
HBV/HIV co-infection with requirement to treat HBV

\* Clinical Stages:

- Clinical stage 1: Asymptomatic or PGL, and/or normal activity
- Clinical stage 2: Weight loss <10%, minor mucocutaneous conditions, zoster <5 years, recurrent URIs, and/or symptomatic plus normal activity
- Clinical stage 3: Weight loss >10%, unexplained diarrhea >1 mo, unexplained fever >1 mo, thrush, oral hairy leukoplakia, pulmonary TB in past year, or severe bacterial infection, and/or bed-ridden <50% of days in the past month
- Clinical stage 4: CDC-defined AIDS and/or bed-ridden >50% of days in the past month

† Treat all pregnant women, patients with TB or severe bacterial infection in this category.

**Adult ART Table 2C-2. What Antiretroviral Therapy to Start  
[WHO Guidelines 2010: [http://whqlibdoc.who.int/publications/2010/9789241599764\\_eng.pdf](http://whqlibdoc.who.int/publications/2010/9789241599764_eng.pdf)]**

ARV naive: AZT or TDF + 3TC (or FTC) + EFV or NVP
TB: Use EFV based HAART-Start ART as soon as possible (within 8 weeks of anti-TB treatment)
HBV co-infection: use TDF + (FTC or 3TC) + ATV/r or LPV/r

**Adult ART Table 2C-3. When to Change ART Regimens  
[WHO Guidelines 2010: [http://whqlibdoc.who.int/publications/2010/9789241599764\\_eng.pdf](http://whqlibdoc.who.int/publications/2010/9789241599764_eng.pdf)]**

- **Definition of clinical failure:** New or recurrent stage 4 condition. Exceptions are lymph node or pleural TB, candida esophagitis, and recurrent bacterial pneumonia; must rule-out IRIS.
- **Definition of CD4 count failure:** Fall to baseline level; 50% fall from treatment peak; or levels persistently <100 cells/mm<sup>3</sup>
- **Definition of virologic failure:** VL >5,000 c/mL because this level is associated with clinical progression and rapid CD4 decline.
- **Criteria to change therapy**

*Clinical disease progression:* events occurring >6 mos after starting ARV because events in the first 6 mos often represent IRIS. New or recurrent events in the first 6 mos meriting change in therapy are AIDS defining conditions (WHO clinical stage 4). Consider changing therapy for these WHO clinical stage 3 conditions: weight loss >10%, unexplained diarrhea or fever >1 mo, oral hairy leukoplakia, severe bacterial infection or bedridden >50% of days in past month.

*Integration of CD4 and Viral Load Criteria:*

Laboratory Criteria	WHO Staging (see footnote Adult ART Table 2C-1)			
	1	2	3	4
CD4 (see criteria above)	No change; repeat CD4 in 3 mos	No change; repeat CD4 in 3 mos	Consider change	Change
CD4 (above) + VL >10,000 after 6 mos	Consider change	Consider change	Change	Change

**Adult ART Table 2C-4. What ART Regimen to Change to [WHO Guidelines 2010  
http://whqlibdoc.who.int/publications/2010/9789241599764\_eng.pdf]**

Initial Regimen	Second Line
(NVP or EFV) + one of the 3 NRTI pairings below	PI/r including LPV/r, ATV/r, FPV/r, IDV/r, SQV/r (NFV can be considered but is less potent)
(AZT or d4T) + 3TC †	TDF + 3TC (±AZT)# + ATV/r or LPV/r
TDF + (3TC or FTC) †	AZT + (3TC or FTC) + ATV/r or LPV/r

† 3TC and FTC are considered interchangeable because they are structurally related and share pharmacological properties and resistance profiles.

# 3TC can be considered to be maintained in second-line regimens to potentially reduce viral fitness, confer residual antiviral activity and maintain pressure on the M184V mutation to improve viral sensitivity to AZT or TDF. AZT continuation may prevent or delay the emergence of the K65R mutation.

**Adult ART Table 3. Advantages and Disadvantages of Initial Antiretroviral Regimens (2009 DHHS guidelines)**

Drugs	Advantages	Disadvantages
Non-Nucleoside Reverse Transcriptase Inhibitors		
Class	<ul style="list-style-type: none"> <li>• Extensive experience</li> <li>• Saves PI option</li> <li>• Less drug interactions compared to PIs</li> </ul>	<ul style="list-style-type: none"> <li>• Low genetic barrier to resistance</li> <li>• Class resistance except ETR with single mutation</li> <li>• Drug interactions, esp methadone</li> <li>• ADR– skin rash, esp NVP</li> </ul>
EFV	<ul style="list-style-type: none"> <li>• Potent &amp; never beaten in a clinical trial</li> <li>• Low pill burden (coformulated with TDF and FTC), once daily dosing (1/d)</li> </ul>	<ul style="list-style-type: none"> <li>• CNS side effects (2-3 weeks)</li> <li>• Teratogenic - avoid use in pregnancy or pregnancy potential</li> <li>• Compared to LPV/r: lower CD4 response, more resistance mutations and increased lipotrophy</li> </ul>
NVP	<ul style="list-style-type: none"> <li>• Single dose to prevent perinatal transmission is safe and effective</li> <li>• Low pill burden</li> <li>• ART potency comparable to EFV</li> </ul>	<ul style="list-style-type: none"> <li>• ADR–rash &amp; hepatotoxicity including hepatic necrosis</li> <li>• Contraindicated in women with baseline CD4 &gt;250 and men with CD4 &gt;400</li> <li>• Single dose may cause class resistance</li> </ul>

**Adult ART Table 3. Advantages and Disadvantages of Initial Antiretroviral Regimens (Cont'd)**

Drugs	Advantages	Disadvantages
Protease Inhibitors		
Class	<ul style="list-style-type: none"> <li>• Extensive experience</li> <li>• Saves NNRTI option</li> <li>• High genetic barrier to resistance with RTV boosting</li> </ul>	<ul style="list-style-type: none"> <li>• ADR– metabolic complications</li> <li>• Multiple drug interactions</li> <li>• GI intolerance</li> </ul>
ATV	<ul style="list-style-type: none"> <li>• Superior to LPV/r</li> <li>• Potency</li> <li>• Once daily dosing</li> <li>• Low pill burden</li> <li>• No hyperlipidemia</li> <li>• RTV boosting not required (preferred)</li> <li>• Less GI intolerance</li> </ul>	<ul style="list-style-type: none"> <li>• ADR– Jaundice (harmless) &amp; PR interval prolongation (usually inconsequential)</li> <li>• Drug interaction with TDF and EFV (can be overcome by ATV/r 400/100 qd with EFV)</li> <li>• Absorption requires food and gastric acid</li> </ul>
LPV/r	<ul style="list-style-type: none"> <li>• Coformulated with RTV</li> <li>• No food effect</li> <li>• Option for once daily therapy in treatment naive patients</li> <li>• Preferred in pregnancy</li> </ul>	<ul style="list-style-type: none"> <li>• ADR– GI intolerance</li> <li>• RTV boosting required (coformulated)</li> <li>• Hyperlipidemia (may ↑ risk of CAD)</li> <li>• Possible QTC &amp; PR prolongation</li> <li>• Less potent than EFV, ATV/r and DRV/r</li> </ul>
FPV/r	<ul style="list-style-type: none"> <li>• No food effect</li> <li>• Option for once daily dosing</li> <li>• RTV boosting not required in naive patients (preferred)</li> <li>• Appears equivalent to LPV/r</li> </ul>	<ul style="list-style-type: none"> <li>• ADR– skin rash</li> <li>• Cross-resistance with DRV/r</li> <li>• Less data w/ once-daily dosing compared to ATV/r and DRV/r</li> </ul>
IDV/r	<ul style="list-style-type: none"> <li>• No food requirement with RTV</li> <li>• BID dosing with RTV boosting</li> </ul>	<ul style="list-style-type: none"> <li>• ADRs– Nephrolithiasis, sicca syndrome</li> <li>• Requirement for ≥1500 mL/d fluid intake</li> </ul>
NFV	<ul style="list-style-type: none"> <li>• Substantial and favorable experience in pregnancy (1250 mg bid)</li> </ul>	<ul style="list-style-type: none"> <li>• ADR– diarrhea</li> <li>• High rate virologic failure</li> <li>• Fatty food requirement</li> <li>• No boosting with RTV</li> </ul>
SQV/r	<ul style="list-style-type: none"> <li>• Potency similar to LPV/r</li> <li>• Reduced pill burden with Invirase</li> <li>• 500 mg tab</li> <li>• Can be considered an alternative in pregnant patients</li> </ul>	<ul style="list-style-type: none"> <li>• ADR– GI intolerance</li> <li>• Boosting with RTV required</li> </ul>
DVR/r	<ul style="list-style-type: none"> <li>• Potency</li> <li>• Superior to LPV/r</li> <li>• Once-daily dosing</li> <li>• Good GI tolerance</li> </ul>	<ul style="list-style-type: none"> <li>• Rash (esp w/ sulfa allergy)</li> <li>• Food requirement</li> <li>• RTV boosting required</li> </ul>

**Adult ART Table 3. Advantages and Disadvantages of Initial Antiretroviral Regimens (Cont'd)**

Drugs	Advantages	Disadvantages
<b>Nucleoside Reverse Transcriptase Inhibitors</b>		
AZT/3TC/ABC	<ul style="list-style-type: none"> <li>• Co-formulated</li> <li>• Minimal drug interactions</li> <li>• Low pill burden</li> </ul>	<ul style="list-style-type: none"> <li>• ABC may be associated with risk of cardiovascular disease and higher rate of viral failure in patients with baseline VL &gt;100,000</li> <li>• ADR– ABC hypersensitivity and AZT marrow suppression, and GI intolerance</li> <li>• HBV flare §</li> </ul>
<b>Nucleoside Reverse Transcriptase Inhibitor Pairs</b>		
AZT/3TC	<ul style="list-style-type: none"> <li>• Extensive experience</li> <li>• Co-formulated</li> <li>• No food effect</li> </ul>	<ul style="list-style-type: none"> <li>• ADR-GI intolerance and marrow suppression (AZT)</li> <li>• HBV flare §</li> <li>• Requires bid dosing (AZT)</li> </ul>
d4T/3TC or FTC	<ul style="list-style-type: none"> <li>• No food effect</li> <li>• Once daily</li> </ul>	<ul style="list-style-type: none"> <li>• ADR of d4T †</li> <li>• HBV flare §</li> </ul>
TDF/FTC*	<ul style="list-style-type: none"> <li>• Well tolerated</li> <li>• Co-formulated</li> <li>• Long half-life of each drug may give pharmacologic barrier to resistance.</li> <li>• No TAMs</li> <li>• Extensive experience</li> </ul>	<ul style="list-style-type: none"> <li>• HBV flare §</li> <li>• Rare cases of nephrotoxicity</li> </ul>
ddI/3TC or FTC	<ul style="list-style-type: none"> <li>• Once daily</li> </ul>	<ul style="list-style-type: none"> <li>• ADR-ddI †</li> <li>• HBV flare §</li> <li>• Must take on empty stomach</li> </ul>
ABC/3TC*	<ul style="list-style-type: none"> <li>• Co-formulated</li> <li>• Once daily</li> <li>• No food effect</li> </ul>	<ul style="list-style-type: none"> <li>• ADR-ABC hypersensitivity</li> <li>• HBV flare §</li> <li>• Risk of cardiovascular disease</li> </ul>
<b>Nucleoside Combinations to Avoid</b>		
d4T/ddI	–	ADRs– peripheral neuropathy, lipoatrophy, pancreatitis, lactic acidosis.
ABC/TDF/3TC TDF/ddI/3TC	–	High rate of virologic failure
NNRTI/ddI/TDF	–	High rate of virologic failure
d4T/AZT	–	Antagonistic
TDF/ddI	–	Drug interaction requiring dose adjustment; avoid with NNRTI

\* FTC and 3TC are similar except for convenience of co-formulations; FTC has longer intracellular half-life and has less extensive experience

§ HBV co-infection (HBsAg pos) - hepatitis flare due to discontinuation of agent or HBV resistance to NRTI (3TC, FTC, TDF)

† ADRs– d4T lipoatrophy, hyperlipidemia, lactic acidosis, peripheral neuropathy; ddI-peripheral neuropathy, pancreatitis and lactic acidosis

**Adult ART Table 4. Methods to Achieve Readiness to Start HAART and Maintain Adherence**

**Patient-related:**

- Negotiate a plan or regimen that the patient understands and to which she/he commits
- Take time needed, >2 visits, to ensure readiness before 1<sup>st</sup> prescription
- Recruit family, friends, peer and community support
- Use memory aids– timers, pagers, written schedule, pill boxes/medication organizers
- Plan ahead– keep extra meds in key locations, obtain refills
- Use missed doses as opportunities to prevent future misses
- Active drug and alcohol use and mental illness predict poor adherence; race, sex, age, educational level, income, and past drug use do not

**Provider/Health team-related:**

- Educate patient re: goals of therapy, pills, food effects, and side effects
- Assess adherence potential before HAART; monitor at each visit
- Ensure access at off-hours and weekends for questions or addressing problems
- Utilize full health care team; ensure med refills at pharmacy
- Consider impact of new diagnoses and events on adherence
- Provide training updates on adherence for all team members and utilize team to reinforce adherence
- Monitor adherence and intensify management in periods of low adherence
- Educate volunteers, patient community representatives

**Regimen-related:**

- Avoid adverse drug interactions
- Simplify regimen re: dose frequency, pill burden, and food requirements
- Inform patient about side effects
- Anticipate and treat side effects

**Adult ART Table 5. Therapeutic Failure – Definitions**

<b>Virologic Failure</b>	Failure to achieve VL <400 c/mL by 24 wks or <50 c/mL by 48 wks or consistent (2 consecutive measurements) >50 c/mL after VL <50 c/mL. Note: Most patients will have a decrease in VL of $\geq 1 \log_{10}$ c/mL at 1-4 wks.
<b>Immunologic Failure</b>	Failure to increase CD4 count 25-50 cells/mm <sup>3</sup> during first year. Note: Mean increase is about 150 cells/mm <sup>3</sup> in first year with HAART in treatment naive patients.
<b>Clinical Failure</b>	Occurrence or recurrence of HIV-related event $\geq 3$ mos after start of HAART. Note: Must exclude immune reconstitution syndromes.

## Adult ART Table 6. Management of Virologic Failure

Virologic Failure
<ul style="list-style-type: none"> <li><b>Definition:</b> Failure to decrease viral load by <math>\geq 1</math> log at 1-2 wks, to <math>&lt; 400</math> c/mL at 24 wks, to <math>&lt; 50</math> c/mL at 48 wks or any confirmed viral load <math>&gt; 50</math> c/mL after 48 wks</li> <li><b>Assessment:</b> Adherence, intolerance, pharmacokinetic issues and resistance</li> <li><b>Resistance:</b> Boosted PIs (LPV/r, ATV/r, SQV/r, FPV/r, DRV/r) all have a high genetic barrier to resistance. All other classes have a low barrier (except some NRTIs). Thus, most patients with viral failure on PI/r-based HAART who fail will have sensitive strains of HIV unless the drug is continued for prolonged periods. Other antiretrovirals usually develop resistance more rapidly when there is virologic failure.</li> <li><b>Rule of two:</b> There always needs to be two drugs that are active <i>in vitro</i>, and preferably 3</li> <li><b>3TC:</b> Resistance (184V) develops early with a failing regimen. This drug (or FTC) renders the virus "less fit" with the 184V mutation and does not risk further NRTI mutations so it is commonly retained in the regimen, but it can't be counted as one of the active agents.</li> <li><b>Immunologic failure:</b> Arbitrarily defined as the failure to increase the CD4 count by <math>&gt; 350</math>-<math>500</math> mm<sup>3</sup> over 4-7 years despite good viral suppression. Cause is usually unknown, intervention also unknown.</li> </ul>
Resistance Tests (see Adult ART Table 7. Indications for Resistance Testing)
<ul style="list-style-type: none"> <li>Usually genotypic test, especially with early sequence failure.</li> <li>Testing should be done during therapy or within 4 wks if possible of cessation of the failed regimen.</li> <li>A viral load of <math>&gt; 500</math>-<math>1,000</math> c/mL is usually required for the currently available resistance tests.</li> <li>Virologic failure of recommended first-line regimens are generally due to transmitted resistance or poor adherence.</li> <li>Phenotypic resistance assay often augments genotypic resistance tests in patients with multiple resistance mutations after multiple virologic failures.</li> </ul>
Using Resistance Test Results
<ul style="list-style-type: none"> <li>Interpretation of resistance tests results is complex and is sometimes best done by an expert.</li> <li>Interpretation should include the history of prior antiretroviral treatments and results of prior resistance tests. Past resistance mutations, even if not detected on the most recent test, remain relevant.</li> <li>Failure to detect resistance mutations in the presence of failed treatment usually indicates non-adherence</li> <li>Resistance tests are best at indicating drugs that will not work rather than those that will work.</li> </ul>
Blips
Blips are defined as single VL measurements of 50-200 c/mL. Tests should be repeated but interpreted as a laboratory error and therapeutically inconsequential if VL $> 50$ c/mL is not confirmed. They may also indicate lapses in adherence. Sustained elevated results should be considered virologic failure.
Sequences
Expectations vary with the number of treatment regimens given for virologic failure. Best results are with the first and second regimens; subsequent regimens are less efficacious if adherence is not addressed.

## Adult ART Table 7. Indications for Resistance Testing

<b>Indicated</b>	<ul style="list-style-type: none"> <li>Virologic failure with VL <math>&gt; 1,000</math> c/mL</li> <li>Suboptimal viral suppression with VL <math>&gt; 1,000</math> c/mL</li> <li>Acute HIV infection</li> <li>Baseline, prior to initial therapy</li> </ul>
<b>Not Indicated</b>	<ul style="list-style-type: none"> <li>After discontinuation of antiretroviral therapy <math>&gt; 1</math> mo duration</li> <li>Viral load <math>&lt; 1,000</math> c/mL</li> </ul>

## Adult ART Table 8. Resistance Mutations [Top HIV Med 2009;17:5]

Drug	Codon Mutations
<b>Nucleosides and Nucleotides – Reverse Transcriptase Mutations</b>	
3TC	65R, 184VI
ABC	65R, 74V, 115F, 184V
AZT <sup>(1)</sup>	41L, 67N, 70R, 210W, 215YF, 219QE
d4T <sup>(1)</sup>	41L, 67N, 70R, 210W, 215YF, 219QE
ddl	65R, 74V
FTC	65R, 184VI
TDF <sup>(1)</sup>	65R, 70E
<b>Multinucleoside Q151M</b>	62V, 75I, 77L, 116Y, 151M
<b>Multinucleoside 69 insertion</b>	41L, 62V, 69 insert, 70R, 210W, 215YF, 219QE
<b>Non-Nucleoside Reverse Transcriptase Inhibitors</b>	
EFV	100I, 101P, 103N, 106M, 108I, 181CI, 188L, 190SA, 225SH
ETR <sup>(2)*</sup>	90I, 98G, 100I, 101EHP, 106I, 138A, 179DFT, 181CIV, 190SA, 230L
NVP	100I, 101P, 103N, 106AM, 108I, 181CI, 188CLH, 190A

(1) TAMs (induced by AZT or d4T) confer selection of 65R

(2) ETR: Most Resistance requires 181C plus  $\geq 3$  baseline mutations to show reduced response.

• Tibotec New Scoring System, Tibotec weighted scoring system (based on DUET studies): 3 points: 181 I/v; 2.5 points: 101P, 100I, 181C, 230L; 1.5 points: 138A, 106I, 190S, 179F; 1 point: 90I, 179D, 101E, 101H, 98G, 179T, 190A; 0-2 points: 74% response; 2.5-3.5 points: 52% response; 4+ points: 38% response

**Adult ART Table 8. Resistance Mutations [Top HIV Med 2009;17:5] (Cont'd)**

Drug	Major**	Minor
<b>Protease Inhibitors – Protease Gene Mutations</b>		
FPV/r	50V, 84V	10 FIRV, 32I, 46IL, 47V, 54LVM, 73S, 76V, 82AFST, 90M
ATV(3)	50L, 84V, 88S	10IFVC, 16E, 20RMITV, 24I, 32I, 33IFV, 34Q, 36ILV, 46IL, 48V, 53LY, 54LVMTA, 60E, 62V, 64LMV, 71VITL, 73CSTA, 82ATFI, 85V, 90M, 93LM
DRV/r†	47V, 50V, 54ML, 76V, and 84V	11I, 32I, 33F, 73S, 74P, 76V, 84V, 89V
IDV/r	46IL, 82AFT, 84V	10IRV, 20MR, 24I, 32I, 36I, 54V, 71VT, 73SA, 76V, 77I, 90M
LPV/r(4)	32I, 47VA, 82AFTS, 76V	10FIRV, 20MR, 24I, 33F, 46IL, 50V, 53L, 54VL AMTS, 63P, 71VT, 73S, 84V, 90M
NFV	30N, 90M	10FI, 36I, 46IL, 71VT, 77I, 82AFTS, 84V, 88DS
SQV/r	48V, 90M	10IRV, 24I, 54VL, 62V, 71VT, 73S, 77I, 82AFTS, 84V
TPV/r(5)	47V, 82LT, 84V	10V, 13V, 20MR, 33I, 35G, 36I, 43T, 46L, 54AMV, 58E, 69K, 74P, 83D, 90M
<b>Entry Inhibitors</b>		
T-20	gp41 envelope– 36DS, 37V, 38AME, 39R, 40H, 42T, 43D	
MVC(6)	X4 virus, dual or mixed tropic virus. Also mutations on HIV-1 gp120 V3 loop	
<b>Integrase Inhibitors – Integrase Mutations</b>		
RAL(7)	155H, 143RHC, 148HKR	

\*\* Major - usually develop first; associated with decreased drug binding; Minor - also contributes to drug resistance; may affect drug binding in vitro less than primary mutations. Use of Major and Minor designations for NRTIs and NNRTIs has been suspended.

- (3) ATV: ≥3 of the following mutations reduce viral response: 10F/I/V, 16E, 33F/I/V, 46I/L, 60E, 84V, 85V. Another report implicates ≥3 of the following 10C/V, 32I, 34Q, 46I/L, 53L, 54A/M/V, 82F/V, 184V.
- (4) LPV: ≥6 mutations required for resistance; 47A and possibly 47V and 32I in part high level resistance.
- (5) TPV: ≥2 of the following mutations correlates with reduced response: 33G, 82I/T, 84V, and 90M.
- (6) MVC: X4, mixed or dual tropic virus does not respond to MVC. Some mutations at codon 13 and 16 of the V3 loop appear important but are not well defined and testing from commercial sources is not available. Emergence of x4 virus is more important.
- (7) RAL: Two major pathways – 148H/K/R or 155H with minor mutation: For 148H/K/R these are 74M, 38A, 138K, or 140S. The most common and most potent cause of lost sensitivity is 148H plus & 140S. For 155H pathway the additional primary mutations are 74M, 92Q, 97A, 92Q & 97A, 143H, 163K/R, 151I, or 232N.

† With 0-2, 3, or >4 of these DRV mutations at baseline, the virologic response (<500/ml at 24 weeks) was 50%, 22% and 10% respectively.

## Pregnancy and HIV

**Pregnancy Table 1. Antiretroviral Drugs in Pregnancy\* [DHHS Guidelines April 29, 2009]**

Advisory	Drugs
<b>Nucleosides and Nucleotides</b>	
Recommended	AZT and 3TC (standard doses)
Alternatives	ddI, FTC, d4T and ABC (standard doses)
Not recommended	ddI/d4T combination
Insufficient Data to Recommend Use	TDF (concern for potential fetal bone effects)
<b>Non-nucleoside RT Inhibitors</b>	
Recommended	NVP (Avoid in women with baseline >250 cells/mm <sup>3</sup> who are starting ART)
Not recommended	EFV (use after second trimester can be considered); DLV
<b>Protease Inhibitors</b>	
Recommended	LPV/r 2 or 3 tabs bid in third trimester
Alternatives	SQV/r 1000/100 bid; NFV 1250 mg bid; IDV/r is alternative but optimal dose regimen is unknown
Insufficient Data to Recommend Use	FPV, ATV, TPV, DRV
<b>Entry Inhibitors</b>	
Insufficient data to recommend use	ENF, MVC
<b>Integrase Inhibitors</b>	
Insufficient data	RAL

\* Based on Table 3 in "Recommendations for Use of Antiviral drugs in pregnant HIV-infected women for maternal health and interventions to reduce perinatal HIV-1 transmission in the United States" US Public Health Services, July 8, 2008.

**Pregnancy Table 2. Antiretroviral Drugs and Specific Concerns for Pregnancy**

Agent	Human Studies in Pregnancy	Concerns
<b>Nucleosides and nucleotides</b>		
ABC*	Good pharmacokinetics	Must screen for HLA-B* 5701
d4T*	Good pharmacokinetics	Lactic acidosis, especially when combined with ddI
ddI	Good pharmacokinetics in pregnancy	Lactic acidosis rates increased, especially when combined with d4T
FTC*	Slightly lower level in 3rd trimester use standard dose	Lack of data for studies in pregnancy
3TC**	Well tolerated, good pharmacokinetics	AZT + 3TC-preferred

**Pregnancy Table 2. Antiretroviral Drugs and Specific Concerns for Pregnancy (Cont'd)**

Agent	Human Studies in Pregnancy	Concerns
<b>TDF*</b>	Limited studies in pregnancy Lower AUC, but trough OK in 3rd trimester. 1st trimester exposure birth defects 14/606 (2-3%). Comparable to baseline rates.	Primate study shows reduced fetal bone porosity; AUC reduced in third trimester
<b>AZT</b>	Extensive studies showing efficacy in reducing MTCT	No concerns
<b>Non-nucleosides</b>		
<b>EFV</b>	Teratogenic in humans and primates- FDA warning to avoid in first trimester; category D	Teratogenicity; may consider after second trimester if no other options
<b>NVP</b>	Good pharmacokinetics, safety and efficacy of single perinatal dose to prevent transmission shown in many trials	Chronic Rx: Pharmacokinetics not altered in pregnancy. Concern is use in treatment-naïve patients with baseline CD4 count >250 cells/mm <sup>3</sup>
<b>Protease Inhibitors</b>		
<b>ETR</b>	No pharmacokinetic data	Insufficient data to recommend
<b>PI Class</b>	Diabetes, GI intolerance	Increased rates of diabetes and ketoacidosis; unclear if rate is increased in pregnancy
<b>ATV*</b>	PK studies in pregnancy show standard doses are appropriate	Hyperbilirubinemia
<b>DRV/r</b>	No studies in pregnancy	Lack of data in pregnancy to recommend use
<b>FPV</b>	AUC decreased 36% in 3rd trimester	Safety in pregnancy data are insufficient to recommend use during pregnancy. With FPV/r, Trough adequate in PI-naïve patients
<b>IDV*</b>	AUC decreased 60-80% in pregnancy	Decreased AUC in pregnancy if not boosted; alternatives preferred, boost if necessary Concern for hyperbilirubinemia
<b>LPV/r*</b>	No studies with Meltrex formulation. Prior capsule formulation showed need to increase dose to 4 pills (533/133 mg) bid.	Inadequate data to make definitive recommendation for 3rd trimester dosing. It may be 2 tabs bid or 3 tabs bid (3 tabs bid in treatment-experienced patients). Once daily dosing not recommended.
<b>NFV*</b>	PACTG 353 showed doses of 1250 mg bid achieved therapeutic levels (but not 750 mg tid)	Lower potency compared to LPV/r, but can be considered as an alternative.
<b>SQV</b>	Studies with unboosted Fortovase showed reduced levels in pregnancy; data for Invirase are limited.	Limited data for Invirase formulation pharmacokinetics (Must be boosted, SQV/r 1000/100 bid).

**Pregnancy Table 2. Antiretroviral Drugs and Specific Concerns for Pregnancy (Cont'd)**

Agent	Human Studies in Pregnancy	Concerns
<b>TPV</b>	No data	Insufficient data to recommend use
<b>CCR5 Antagonist</b>		
<b>MVC</b>	No data	Insufficient data to recommend use
<b>Integrase Inhibitors</b>		
<b>RAL</b>	No data	Insufficient data to recommend use

**Pregnancy Table 3. Recommendations for the Use of Antiretroviral Agents in Pregnant Women [DHHS Guidelines, April 29, 2009]**

Class	Preferred	Alternative	Inadequate Data	
<b>NRTI</b>	AZT, 3TC	ddI, FTC, d4T, ABC	TDF	
<b>NNRTI</b>	NVP		ETR	EFV
<b>PI</b>	LPV/r	IDV/r, ATV/r, RTV, SQV/r, NFV	DRV, FPV, TPV	
<b>Entry</b>			MVC, ENF	
<b>Integrase Inhibitor</b>			RAL	

**Pregnancy Table 4. Recommendations for Clinical Scenarios**  
[DHHS Guidelines April 29, 2009]

Clinical Setting	Recommendation					
Pregnancy potential + indications for HAART	Initiate HAART per DHHS guidelines but avoid EFV unless contraception adequate. Exclude pregnancy before starting EFV					
Receiving HAART and becomes pregnant	1) Continue HAART if viral suppression but avoid EFV* 2) <b>Labor:</b> Continue HAART po and give IV AZT** 3) Schedule <b>C-Section</b> at 38 wks if VL>1000 c/mL near delivery 4) AZT for <b>infant</b> x 6 wks***					
Treatment-naïve, indications for HAART and pregnant	1a) Initiate HAART; include AZT, avoid EFV,* avoid NVP if CD4 >250/mm <sup>3</sup> 1b) Follow 2-4 above					
Treatment-naïve, CD4 >350/mm <sup>3</sup> and pregnant	1a) Initiate HAART to prevent perinatal transmission, avoid EFV* and avoid NVP if CD4 >250/mm <sup>3</sup> , include AZT 1b) Consider AZT monotherapy if VL <1000 c/mL 1c) Follow 2-4 above 1d) Evaluate need to continue HAART post-partum. If plan is to discontinue NNRTI-based HAART: Continue 2 NRTIs 7 d after stopping NNRTI					
Prior HAART, now off treatment and pregnant	1a) Initiate HAART based on history and resistance test results, avoid EFV,* and use AZT 1b) Follow 2-4 above					
Treatment-naïve and presents in labor	Options					
	<table border="1"> <thead> <tr> <th>Mother</th> <th>Infant</th> </tr> </thead> <tbody> <tr> <td>1. AZT IV during labor</td> <td>AZT x 6 wks</td> </tr> <tr> <td>2. AZT IV during labor + NVP 200 mg po x 1 + AZT/3TC x 7 d po post-partum Evaluate need for HAART</td> <td>AZT x 6 wks*** ± additional drugs NVP****</td> </tr> </tbody> </table>	Mother	Infant	1. AZT IV during labor	AZT x 6 wks	2. AZT IV during labor + NVP 200 mg po x 1 + AZT/3TC x 7 d po post-partum Evaluate need for HAART
Mother	Infant					
1. AZT IV during labor	AZT x 6 wks					
2. AZT IV during labor + NVP 200 mg po x 1 + AZT/3TC x 7 d po post-partum Evaluate need for HAART	AZT x 6 wks*** ± additional drugs NVP****					
Untreated HIV positive mother with newborn infant	Infant: AZT x 6 wks Mother: Evaluate need for HAART					

\* Contraindicated drugs include EFV, ddI/d4T and NVP when CD4 in >250/mm<sup>3</sup>

\*\* AZT intrapartum: 2 mg/kg/h x 1 h, then 1 mg/kg/h until delivery

\*\*\* AZT for infant <35 wks gestation: 1.5 mg/kg IV q12h or 2 mg/kg po q12h, increasing to q8h at 2 wks if >30 wks gestation at birth or at 4 wks if <30 wks gestation at birth

\*\*\*\* NVP 2 mg/kg x 1 given at 2-3 d if mother received intrapartum dose or given at birth if mother did not receive NVP.

**Pregnancy Table 5. Mode of Delivery**  
[DHHS Guidelines, April 29, 2009]

Clinical Setting	Recommendation
HIV infected presents, no current Rx >36 wks labs pending	1) Start ART per Table 4 2) Recommend C-section at 38 wks 3) IV AZT starting 3 h pre-op and single dose to infant 4) Use prophylactic antibacterials 5) Evaluate for HAART post-partum
HIV treated, pregnant and VL >1000 c/mL at 36 wks gestation	1) Continue ART if VL decreasing or change if poor virologic response 2) Schedule for C-section if VL likely to be >1000 c/mL at 38 wks 3) Continue antivirals through surgical period 4) Prophylactic antibacterials for the C-section 5) Continue ART 6) Infant should receive AZT as above
Mother receiving HAART with virologic control	Risk of perinatal transmission is <2%; relative risk of C-section is not known
Mother has scheduled C-section but presents in labor	1) Give IV AZT to mother 2) Relative risks of C-section vs vaginal delivery is unclear 3) Give postpartum AZT to infant

**Pregnancy Table 6. Drugs for Opportunistic Infections in Pregnancy**  
[DHHS Updated Prevention and Treatment of Opportunistic Infections, June 20, 2008]

Agent	Class*	Recommendation
<b>Acyclovir</b>	B	Treatment reserved for severe herpes or varicella; well tolerated and no consequences with >700 exposures
<b>Albendazole</b>	C	Teratogenic in rodents; reserve for severe microsporidiosis in 2 <sup>nd</sup> and 3 <sup>rd</sup> trimester
<b>Amoxicillin</b>	B	Standard indications
<b>Amphotericin</b>	B	Standard indications
<b>Atovaquone</b>	C	Standard indications; limited experience
<b>Azithromycin</b>	B	Standard indications
<b>Caspofungin</b>	C	Embryotoxic in rodents. No human experience
<b>Cidofovir</b>	C	Teratogenic in animals; risk in women unknown
<b>Ciprofloxacin</b>	C	Arthropathy in beagle dogs; not recommended in pregnancy but >400 cases of use with no arthropathy or birth defects
<b>Clarithromycin</b>	C	Teratogenic in animals and increased rate of abortions in women—azithromycin preferred for MAC
<b>Clindamycin</b>	B	Standard indications
<b>Clotrimazole troches</b>	C	No complications expected with oral or vaginal use

**Pregnancy Table 6. Drugs for Opportunistic Infections in Pregnancy (Cont'd)**  
**[DHHS Updated Prevention and Treatment of Opportunistic Infections, June 20, 2008]**

Agent	Class*	Recommendation
Dapsone	C	Limited experience; may increase risk of kernicterus
Doxycycline	D	Risk to infant teeth; avoid
Entecavir	C	Not teratogenic in rodents; no human data
Erythromycin	B	Standard indications
Ethambutol	B	Appears safe in humans
Famciclovir	B	Limited data in humans; reserve for severe herpes
Fluconazole	C	Bone defects in animals; reserve for severe & established fungal infections. Ampho B often preferred
Flucytosine	C	Bone defects in animals; use only after first trimester
Foscarnet	C	Teratogenic in animals and no data in humans; use for disseminated CMV
Ganciclovir	C	Teratogenic in animals; limited but favorable experience in humans
Interferon	C	Delay treatment until after pregnancy
INH	C	Standard indications + pyridoxine
Itraconazole	C	Teratogenic in animals and concern for azoles in pregnancy; use for systemic mycosis– ampho B often preferred
Mefloquine	C	May increase risk of stillbirths
Metronidazole	B	Extensive favorable experience in pregnant women standard indications
Paromomycin	C	Not absorbed; fetal toxicity unlikely
Pentamidine	C	Embryocidal in animals; limited experience in women
Primaquine	C	Limited experience; theoretical risk of hemolytic anemia with G6PD deficiency
Posaconazole	C	Teratogenic in animals; risk in women unknown
Pyrazinamide	C	Not teratogenic in rodents. Limited experience in people
Pyrimethamine	C	Teratogenic in rodents. Limited human experience suggests risk of birth defect. If used-add leukovorin
Ribavirin	X	Teratogenic in animals; not indicated in pregnancy
Rifabutin	B	Not teratogenic in animals
Rifampin	C	Teratogenic in animals; indicated for TB; vitamin K at birth
Sulfadiazine	B	Possible kernicterus if used near delivery
Sulfadiazine	B	Possible kernicterus if used near delivery
Telbivudine	B	Not teratogenic in rodents. Limited data in people
Valacyclovir	B	Prodrug of acyclovir
Voriconazole	D	Teratogenic in rodents; ampho B preferred

**Pregnancy Table 7. Drugs to Avoid During Pregnancy**

Agent	Class*	Recommendation
ACE Inhibitors and AR blockers	D	Consider labetalol for hypertension
Warfarin	X	Consider LMWH or heparin.
Anticonvulsants-carbamazepine, valproic acid, phenytoin, and phenobarbital	D	Can be continued if indicated. Consider alternate anticonvulsants.
HMG-CoA reductase inhibitor	D	Consider alternative (eg fibrinic acid, niacin)
Paroxetine	D	Consider alternative antidepressant
Miscellaneous: ergotamine, thalidomide, retinoids, Raloxifene, benzodiazepines, and misoprostol	X	Contraindicated

\* Classes:

- A - controlled studies show no risk
- B - no evidence of risk in humans
- C - risk not ruled out
- D - positive evidence of risk
- X - contraindicated in pregnancy

## Opportunistic Infections

This section presents information about the prevention and treatment of opportunistic infections with special emphasis on tuberculosis. Additional information may be obtained from current guidelines (see References on page 5).

Adult OI Table 1. 2008 NIH/CDC/IDSA Guidelines for Prevention of Opportunistic

Infections (June 20, 2008)

Pathogen	Indication	First Choice	Alternatives	Comment
<b>Strongly Recommended</b>				
<i>P. jirovecii</i>	<ul style="list-style-type: none"> <li>• CD4 &lt;200 cells/mm<sup>3</sup> <b>or</b></li> <li>• CD4 % &lt;14, thrush, hx AIDS defining illness or FUIO</li> </ul>	TMP-SMX 1 DS/d* <b>or</b> TMP-SMX 1 SS/d*	<ul style="list-style-type: none"> <li>• Dapsone 100 mg/d <b>or</b> 50 mg bid <b>or</b></li> <li>• Dapsone 50 mg/d + pyrimethamine 50 mg/wk + leucovorin 25 mg/wk <b>or</b></li> <li>• Aerosol pentamidine 300 mg/mo by Respigard II nebulizer <b>or</b></li> <li>• Atovaquone 1500 mg + pyrimethamine 25 mg + leucovorin 10 mg/d <b>or</b></li> <li>• Atovaquone 1500 mg/d <b>or</b></li> <li>• TMP-SMX 1 DS* 3x/wk</li> </ul>	<ul style="list-style-type: none"> <li>• Discontinue primary &amp; secondary prophylaxis if CD4 &gt;200 cells/mm<sup>3</sup> for ≥3 mos</li> <li>• Restart prophylaxis if CD4 decreases to &lt;200 cells/mm<sup>3</sup></li> <li>• Pyrimethamine regimens for toxoplasmosis prophylaxis also</li> <li>• TMP-SMX provides toxoplasmosis prophylaxis</li> </ul>
<b>Tuberculosis</b>	See Adult OI Table 4. Latent TB			
<b>Toxoplasmosis</b>	+ anti-Toxoplasma IgG and CD4 <100 cells/mm <sup>3</sup>	TMP-SMX 1 DS* qd	<ul style="list-style-type: none"> <li>• TMP-SMX 1 SS* qd <b>or</b></li> <li>• Dapsone 50 mg/d + pyrimethamine 50 mg/wk + Leucovorin 25 mg/wk <b>or</b></li> <li>• Dapsone 200 mg/wk + pyrimethamine 75 mg/wk + Leucovorin 25 mg/wk <b>or</b></li> <li>• Atovaquone 1500 mg/d ± pyrimethamine 25 mg/d + Leucovorin 10 mg/d</li> </ul>	<ul style="list-style-type: none"> <li>• Discontinue prophylaxis if CD4 &gt;200 cells/mm<sup>3</sup> for ≥3 mos</li> <li>• Restart Prophylaxis if CD4 decreases to &lt;100-200 cells/mm<sup>3</sup></li> <li>• Repeat toxoseroLOGY if baseline serology was negative and CD4 count subsequently &lt;100 cells/mm<sup>3</sup></li> </ul>
<i>Mycobacterium avium complex</i>	CD4 <50 cells/mm <sup>3</sup>	<ul style="list-style-type: none"> <li>• Azithromycin 1200 mg/wk <b>or</b> 600 mg po 2x/wk <b>or</b></li> <li>• Clarithromycin 500 mg bid</li> </ul>	Rifabutin† 300 mg/d (adjust dose for concurrent HAART)	<ul style="list-style-type: none"> <li>• Discontinue prophylaxis if CD4 &gt;100 cells/mm<sup>3</sup> for ≥3 mos</li> <li>• Restart Prophylaxis if CD4 decreases to &lt;100 cells/mm<sup>3</sup></li> <li>• Rule out active MAC before giving prophylaxis</li> </ul>
<b>Varicella</b>	<ul style="list-style-type: none"> <li>• <b>Post-exposure</b> Chickenpox/shingles exposure and susceptible (no history of disease and varicella seronegative)</li> </ul>	<ul style="list-style-type: none"> <li>• VZIG 5 vials (6.25 mL) 125 IU/10 kg (max 625 IU) IM</li> <li>• &lt;96 h post exposure</li> <li>• Treatment IND 1-800-843-7477</li> </ul>		<ul style="list-style-type: none"> <li>• Acyclovir has been removed from OI prophylaxis guidelines due to lack of documented efficacy</li> </ul>
	<ul style="list-style-type: none"> <li>• <b>Pre-exposure</b> No history of chickenpox, shingles, vaccine or positive serology and CD4 count &gt;200 cells/mm<sup>3</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Primary varicella vaccine (Varivax) (0.5 mL SQ) 2 doses 3 mos apart</li> </ul>		<ul style="list-style-type: none"> <li>• Routine serology not recommended</li> <li>• If vaccine causes disease treat with acyclovir</li> </ul>

\* SS= Single strength tablet, DS=Double Strength Tablet

† Dose adjusted for concurrent PI/NNRTI

Adult OI Table 1. 2008 NIH/CDC/IDSA Guidelines for Prevention of Opportunistic

Infections (June 20, 2008) (Cont'd)

Pathogen	Indication	First Choice	Alternatives	Comment
<b>Generally Recommended</b>				
<b>S. pneumoniae</b>	<ul style="list-style-type: none"> <li>All Patients with CD4 &gt;200 cells/mm<sup>3</sup> and no pneumococcal vaccine in 5 yrs with CD4 &gt;200 cells/mm<sup>3</sup></li> <li>Consider if CD4 &lt;200 cells/mm<sup>3</sup></li> </ul>	23 valent pneumococcal vaccine 0.5 mL x 1	None	<ul style="list-style-type: none"> <li>Consider reimmunization if CD4 increases to &gt;200 cells/mm<sup>3</sup> and initial immunization was given when CD4 &lt;200 cells/mm<sup>3</sup>.</li> <li>Consider revaccination in 5 years.</li> </ul>
<b>Hepatitis B</b>	Susceptible- (anti-HBc or Anti HBs negative) and HBsAg negative	HBV vaccine IM ( <i>Engerix-B</i> ) 20 mcg/mL or <i>Recombivax</i> 10 mcg/mL at 0, 1, and 6 mos	None	Measure anti-HBsAg at one month after 3 <sup>rd</sup> dose and if <10 IU/mL: revaccinate or delay until CD4 count higher
<b>Influenza</b>	All Patients (seasonal)	Influenza vaccine (.5 mL IM)	Oseltamivir 75 mg qd	
<b>Hepatitis A</b>	Susceptible- (anti-HAV negative) and risk (IDU, MSM, travel) or chronic liver disease	<ul style="list-style-type: none"> <li>Hepatitis A vaccine series: 1.0 mL x 2 separated by 6 mos</li> <li>Some delay until CD4 count is &gt;200 cells/mm<sup>3</sup></li> </ul>	None	Determine antibody response at 1 mo post vaccination. If negative, revaccinate.
<b>Histoplasma capsulatum</b>	CD4 count <150 cells/mm <sup>3</sup> + risk (occupational exposure or live in community with >10 cases/100 patient-years)	Itraconazole 200 mg/d		
<b>Coccidioidomycosis</b>	Positive IgM or IgG serology in patient in endemic area with CD4 <250 cells/mm <sup>3</sup>	<ul style="list-style-type: none"> <li>Fluconazole 400 mg qd or</li> <li>Itraconazole 200 mg bid</li> </ul>		
<b>Human papilloma virus</b>	Women age 15-26 yrs	HPV quadravalent vaccine 0.5 mL IM at 0, 2, & 6 mos		

Adult OI Table 2. Treatment of Opportunistic Infections [NIH/CDC/IDSA Updated

Infection/Organism	Treatment
<b>Bartonella</b>	<b>Bacillary angiomatosis, peliosis hepatitis, bacteremia, and osteomyelitis:</b> Erythromycin 500 mg qid po or IV x >3 mos <b>or</b> Doxycycline 100 mg bid po or IV x >3 mos <b>Alternative:</b> Azithromycin 500 mg po/d x >3 mos <b>or</b> Clarithromycin 500 mg bid po x 3 mos <b>CNS or severe infections:</b> Doxycycline 100 mg po or IV q12h +/- rifampin 300 mg po or IV x 4 mos
<b>Candida–Thrush</b>	<b>Initial episode:</b> Fluconazole 100 mg po x 7-14 d <b>or</b> topical clotrimazole troches 10 mg po 5x/d <b>or</b> nystatin as susp 4-6 mL qid <b>or</b> as 1-2 flavored pastilles 4-5x/d x 7-14 d <b>Fluconazole refractory:</b> Itraconazole soln 200 mg/d po, posaconazole soln 400 mg bidpo, amphotericin 0.3 mg/kg/d IV, anidulafungin 100 mg IV than 50 mg/d, casofungin 50 mg/d IV, micafungin 150 mg/d IV <b>or</b> ampho B susp 100 mg/mL 1 mL qid
<b>Candida–Esophagitis</b>	<b>Preferred:</b> Fluconazole 200 mg (up to 800 mg/d) po or IV x 14-21 d <b>Fluconazole refractory:</b> posaconazole soln 400 mg bid po x 28 d, ampho B 0.3-0.7 mg/kg/d IV <b>or</b> lipid ampho B 3-5 mg/kg/d, anidulafungin 100 mg IV then 50 mg/d IV, micafungin 150 mg/d IV, caspofungin 50 mg IV/d <b>or</b> voriconazole 200 mg bid po or IV
<b>Candida–Vaginitis</b>	<b>Preferred:</b> Fluconazole 150 mg po x 1 <b>or</b> topical azole x 3-7 d <b>Recurrent or complicated:</b> Fluconazole 150 mg po q72h x 2-3 <b>or</b> topical azole >7 d
<b>Cryptosporidiosis</b>	<b>Preferred:</b> HAART <b>Alternative:</b> Nitazoxanide 0.5-1.0 gm po bid with food x 2 wks
<b>Cryptococcosis–Meningitis</b>	<b>Preferred:</b> Induction with Amphotericin B 0.7 mg/kg qd <b>or</b> Liposomal amphotericin 4 mg/kg IV <b>plus</b> flucytosine 25 mg/kg qid po ≥ 2 wks then consolidation therapy with fluconazole 400 mg qd ≥ 6 wks, then maintenance therapy 200 mg/d until CD4 count is >200 cells/mm <sup>3</sup> for 6 mos <b>Alternative induction:</b> • Liposomal amphotericin 4-6 mg/kg/d IV or Amphotericin B (alone) x 4-6 wks • Fluconazole 1200 mg/d po or IV + flucytosine 100 mg/kg/d po x 6 wks <b>Alternative-consolidation:</b> Itraconazole 200 mg po bid x 8 wks (less effective) <b>Alternative-maintenance:</b> Itraconazole 200 mg/d
<b>Cytomegalovirus–Retinitis</b>	<b>Preferred for vision threatening lesion:</b> Intravitreal ganciclovir implant + valganciclovir 900 mg bid po x 14-21 d, then 900 mg qd <b>Preferred for peripheral lesions:</b> Oral valganciclovir 900 mg bid po x 14-21 d, then 900 mg qd <b>Alternatives:</b> • Ganciclovir 5 mg/kg bid IV x 14 d, then 5 mg/kg/d IV, or • Foscarnet 60 mg/kg q8h IV or 90 mg/kg q12h IV x 14 d, then 90-120 mg/kg IV qd, or • Cidofovir 5 mg/kg q7d IV x 2 then 5 mg/kg q14d IV

Opportunistic Infections Guidelines, June 20, 2008]

	Comment
	<ul style="list-style-type: none"> <li>• May need long-term suppression with doxycycline or macrolide if relapse until CD4&gt;200 cells/mm<sup>3</sup></li> <li>• May have severe Jarisch-Herxheimer reaction in first 48 h</li> </ul>
	<p><b>Alternative Initial Therapy:</b> Itraconazole soln 200 mg/d po x 7-14 days. <b>Suppressive Therapy:</b> Indicated for severe or frequent recurrences– fluconazole 100 mg/d or itraconazole soln 200 mg/d</p>
	<p><b>Alternative Initial Therapy:</b> Treat 14-21 d with itraconazole, voriconazole, posaconazole, caspofungin, micafungin, anidulafungin (prior designated doses) or ampho B 0.6 mg/kg/d IV <b>Suppressive Therapy:</b> Indicated for severe or frequent recurrences– fluconazole 100-200 mg po or posaconazole 400 mg bid po <b>Note:</b> Fluconazole refractory cases that responded to echinocandins should receive voriconazole or posaconazole prophylaxis</p>
	<p><b>Alternative Initial Therapy:</b> Itraconazole soln 200 mg/d po x 3-7 d <b>Maintenance:</b> Fluconazole 150 mg po q wk or daily topical azole</p>
	<b>Antimotility agents:</b> Loperamide or tincture of opium
	<ul style="list-style-type: none"> <li>• <b>High opening pressure:</b> LP to drain CSF until 50% OP. Repeat daily until OP &lt;200 mm Hg (this is critical).</li> <li>• Patients given 5FC should have blood levels measured to assure 2 h post dose level is 30-80 mg/ml (after 3-5 days). Adjust dose for renal failure.</li> <li>• Lipid amphotericin is preferred in patients with renal toxicity due to ampho B or have high likelihood of renal failure</li> <li>• Addition of flucytosine to ampho B increases rate of CSF clearance of cryptococcus.</li> <li>• &gt; 2 weeks induction recommended if PT has not clinically improved, with persistent ↑IC<sub>3</sub>, and has positive CSF anetmnes at 2 weeks</li> </ul>
	<p><b>Duration:</b> Implant– change q6-8mos <b>Systemic:</b> continue until inactive disease + CD4 &gt;100 cells/mm<sup>3</sup> x 3-6 mos (ophthalmology F/U required) <b>Immune recovery uveitis:</b> Periocular steroids or short course oral prednisone. • Intravitreal ganciclovir may be given until implant inserted • HAART critical component of treatment</p>

Adult OI Table 2. Treatment of Opportunistic Infections [NIH/CDC/IDSA Updated

Infection/Organism	Treatment
<b>Cytomegalovirus–Colitis, Esophagitis, Pneumonia</b>	<b>Preferred:</b> Valganciclovir (oral), ganciclovir (IV), foscarnet (IV) above doses for CMV retinitis x 21-28 d <b>Maintenance:</b> Role is unclear; consider after relapse
<b>Cytomegalovirus–Neurologic Disease</b>	<b>Preferred:</b> Ganciclovir + foscarnet above doses for CMV retinitis <b>Maintenance:</b> IV foscarnet + po valganciclovir for life
<b>Hepatitis B Virus (HBsAg positive x ≥6 mos)</b>	<b>Treatment for HIV:</b> At least 2 agents active versus both viruses usually TDF/FTC <ul style="list-style-type: none"> <li>• 3TC/FTC naive: 3TC 300 mg/d or FTC 200 mg/d + TDF 300 mg/d + additional agent for HIV</li> <li>• 3TC/FTC experienced + detectable HBV DNA (assume 3TC/FTC resistance): Add TDF 300 mg qd + (3TC or FTC) or adefovir 10 mg/d po + (3TC or FTC) or (if HIV suppression) entecavir 1 mg/d</li> </ul> <b>Duration:</b> Both treated indefinitely <b>Treat HBV and not HIV:</b> <ul style="list-style-type: none"> <li>• Usually treat both even with CD4 &gt;500 c/mL</li> <li>• HBsAg neg + HBV DNA &lt;2,000 IU/mL: Adefovir 10 mg/d po</li> <li>• HBsAg pos + HBV DNA &gt;20,000 IU/mL + ↑ALT: Peg interferon</li> </ul>
<b>Hepatitis C Virus</b>	<b>All patients:</b> 1) Discontinue or limit alcohol, 2) drug rehabilitation when appropriate, 3) HBV plus HAV vaccine if susceptible, and 4) prophylactic antibiotics if history of SBP <b>Indications and contraindications:</b> See comment <b>Genotype 1, 4, 5, or 6:</b> pegIFN alfa 2a (180 mcg) or pegIFN alfa 2b (1.5 mcg/kg) SC weekly plus ribavirin: >75 kg (165 lbs) 600 mg bid or <75 kg 600 mg q AM and 400 mg q PM (1000 mg/d) x <b>48 wks</b> <b>Genotype 2 or 3:</b> pegIFN (above doses plus ribavirin 400 mg bid) x <b>48 wks</b> <b>Monitoring:</b> Failure to achieve EVR by 12 wks indicates probability of a sustained viral response (SVR) <3%: most would stop due to futility

Opportunistic Infections Guidelines, June 20, 2008] (Cont'd)

	Comment
	<b>Maintenance:</b> Consider after relapse or severe disease <b>CMV pneumonia:</b> Indications are CMV by histology plus lack of response to other pathogens <b>HAART:</b> Critical component of treatment
	HAART is critical. Prognosis pre-HAART was poor.
	<b>Indications to treat HBV:</b> Chronic HBV and 1) Treatment of HIV or 2) Standard recommendations for treating HBV: abnormal ALT + HBsAg + HBV DNA >20,000 IU/mL or abnormal ALT + HBV DNA >2,000 IU/mL with HBsAg neg <b>HBV treatment agents to avoid with HIV co-infection without HAART:</b> 3TC, FTC, TDF and entecavir <b>HIV/HCV/HBV co-infection:</b> Treat HIV first; if not treating HIV, consider peg-interferon + Ribavirin <b>Change HIV agents:</b> Maintain agents active vs HBV <b>Stop anti-HBV agents:</b> May cause life-threatening flare- restart <b>FTC/3TC:</b> Assume cross resistance
	<b>Indications to treat:</b> 1) HCV RNA >50 IU/ml, 2) high risk of cirrhosis based on biopsy, fibroscan or laboratory for mucas, 3) stable HIV infection and 4) no contraindications (cirrhosis, depression, pregnancy, unlikely compliance) <b>Contraindications:</b> 1) Pregnancy or pregnancy potential; 2) Advanced HIV with low CD4 count (<200/mm <sup>3</sup> ); 3) Hepatic decompensation; 4) Severe active depression; 5) Marrow suppression with Hgb <10.5 g/dL, ANC <1,000/uL or platelet count <50,000/mL or creatinine >1.5; 6) Sarcoidosis or active uncontrolled autoimmune disease

Adult OI Table 2. Treatment of Opportunistic Infections [NIH/CDC/IDSA Updated

Opportunistic Infections Guidelines, June 20, 2008] (Cont'd)

Infection/Organism	Treatment	Comment
<b>Herpes Simplex Virus – Mucocutaneous</b>	<b>Orolabial:</b> Treat 5-10 d <b>Genital:</b> Treat 5-14 d <b>Agents:</b> Valacyclovir 1 gm po bid, acyclovir 400 mg po tid, famciclovir 500 mg po bid <b>Severe:</b> Acyclovir 5 mg/kg IV q8h, then oral agent for total of ≥21 d	<b>Acyclovir-resistant HSV:</b> Foscarnet 80-120 mg/kg/d IV in 2-3 daily doses <b>Alternative:</b> Topical trifluridine, topical cidofovir or topical imiquimod x 21-28 days
<b>Herpes Simplex – Keratitis</b>	<b>Preferred:</b> Trifluridine 1% ophthalmic soln 1 drop q2h up to 9 drops/d ≤21d	
<b>Herpes Simplex – Encephalitis</b>	<b>Preferred:</b> Acyclovir 10 mg/kg q8h IV x 14-21 d	
<b>Microsporidia</b>	<b>Preferred:</b> HAART <b><i>E. bieneusi</i> (20% of cases):</b> Fumagillin 20 mg po tid (not available in US) <b>Alternative:</b> Nitazoxanide 1 gm po bid with food x 60 d	<b>Enterocytozoon bieneusi:</b> Fumagillin 60 mg qd po <b>Microsporidia other than <i>E. bieneusi</i>:</b> Albendazole 400 mg bid po until CD4 >200 cells/mm <sup>3</sup> <b>Disseminated disease:</b> Itraconazole 400 mg qd po + albendazole with Trachipleistophora or Brachiola
<b><i>Mycobacterium avium</i></b>	<b>Preferred:</b> Clarithromycin 500 mg bid po + ethambutol 15 mg/kg qd po ± Rifabutin 300 mg qd po for severe disease.*  <b>Alternative to Clarithromycin:</b> Azithromycin 500-600 mg qd po + ethambutol 15 mg/kg po qd ± rifabutin* <b>Third/fourth drug:</b> ciprofloxacin 500-750 mg bid po, levofloxacin 500 mg qd po, or moxifloxacin 400 mg qd po or Amikacin 10-15 mg/kg qd IV or streptomycin 1 gm IV or IM/d	<b>Duration:</b> Until MAC treatment >12 mos, asymptomatic and CD4 count >100/mm <sup>3</sup> x 3-6 mos • Test susceptibility to clarithromycin and azithromycin • If ART-naïve, delay HAART until MAC treated 2 wks • NSAIDS for symptoms attributed to IRIS, use 20-40 mg prednisone if IRIS symptoms persist
<b><i>Mycobacterium tuberculosis</i></b>	See Adult OI Table 5-7 (pgs 82 & 83)	

\* Rifabutin reduces levels of clarithromycin by 50% (consider azithromycin if rifabutin is used). Rifabutin may need dose adjustment based on HAART regimen."

Adult OI Table 2. Treatment of Opportunistic Infections [NIH/CDC/IDSA Updated

Opportunistic Infections Guidelines, June 20, 2008] (Cont'd)

Infection/Organism	Treatment	Comment
<i>Pneumocystis jirovecii</i>	<p><b>Preferred:</b></p> <ul style="list-style-type: none"> <li>TMP-SMX (15-20 mg TMP and 75-100 mg SMX/kg/d) administered q6-8h IV; switch to po when clinically improved <b>or</b></li> <li>TMP-SMX 2 DS tid (TMP 5 mg/kg/tid) x 21 d</li> </ul> <p><b>Alternative-Severe disease:</b> Pentamidine 3-4 mg/kg/d IV infused over &gt;60 min                      Primaquine 15-30 mg po/d + clindamycin 600-900 mg IV q6-8h or 300-450 mg po q6-8h</p> <p><b>Alternative-moderate or mild disease:</b></p> <ul style="list-style-type: none"> <li>Dapsone 100 mg qd + TMP 5 mg/kg tid x 21 d; <b>or</b></li> <li>Primaquine 15-30 mg base qd + clindamycin 300-450 mg po q6h x 21 d, <b>or</b></li> <li>Atovaquone 750 mg bid po with food x 21 d</li> </ul>	<p><b>Hypoxia (PaO<sub>2</sub> &lt;70 mm Hg or A-a O<sub>2</sub> gradient &gt;35 mm Hg):</b></p> <ul style="list-style-type: none"> <li>Prednisone: 40 mg bid days 1-5, 40 mg qd days 6-10, then 20 mg qd days 11-21, <b>or</b></li> <li>IV methylprednisolone as 75% prednisone dose.</li> </ul> <p><b>Failure to respond:</b></p> <ul style="list-style-type: none"> <li>Use alternative regimen but note that response is usually slow, eg &gt;5 d</li> </ul>
Salmonella	<p><b>Preferred:</b> Ciprofloxacin 500-750 mg bid po (or moxifloxacin or levofloxacin)</p> <p><b>Alternative (if susceptible):</b> moxifloxacin or levofloxacin</p> <ul style="list-style-type: none"> <li>TMP-SMX po or IV, <b>or</b></li> <li>Ceftriaxone, <b>or</b></li> <li>Cefotaxime</li> </ul>	<p><b>NOTE:</b></p> <p><b>Mild gastroenteritis only and CD4 &gt;200 cells/mm<sup>3</sup>:</b> Treat 7-14 d; if CD4 count &lt;200 cells/mm<sup>3</sup>: Treat 2-6 wks</p> <p><b>Relapse:</b> Treat ≥6 mos or until immune reconstitution</p>
Toxoplasmosis	<p><b>Preferred-Acute (treat for at least 6 wks):</b>                      Pyrimethamine 200 mg x 1 po, then 50 mg (&lt;60 kg) or 75 mg (&gt;60 kg) qd po + sulfadiazine 1 g (&lt;60 kg) or 1.5 g (&gt;60 kg) qid po + leucovorin 10-25 mg qd po x ≥6 wks.</p> <p><b>Alternative-Acute:</b></p> <ul style="list-style-type: none"> <li>Pyrimethamine + leucovorin (as above) + one of the following:                             <ul style="list-style-type: none"> <li>Clindamycin 600 mg q6h po or IV, <b>or</b></li> <li>Atovaquone 1500 mg bid po with food <b>or</b></li> <li>Azithromycin 900-1200 qd po</li> </ul> </li> <li>TMP-SMX 5 mg/kg bid IV or po, <b>or</b></li> <li>Atovaquone 1.5 g bid po with food ± sulfadiazine 1-1.5 g q6h po</li> </ul> <p><b>Preferred-Maintenance (after ≥6 wk initial treatment):</b></p> <ul style="list-style-type: none"> <li>Pyrimethamine 25-50 mg/d po + sulfadiazine 2-4 gm po/d in 2-4 doses + leucovorin 10-25 mg/d</li> </ul> <p><b>Alternative-maintenance:</b></p> <ul style="list-style-type: none"> <li>Pyrimethamine 25-50 mg/d + leucovorin 10-25 mg po/d + clindamycin 600 mg q8h po</li> <li>Atovaquone 750 mg po q6-12h ± pyrimethamine 25 mg po qd + leucovorin 10 mg po/d or sulfadiazine 2-4 gm /d</li> </ul>	<p>Adjunctive dexamethasone given only if mass effect</p> <p>Anticonvulsants if history of seizures</p>

### Adult OI Table 3. Immune Reconstitution Syndrome

(Adapted from: Hirsch HH, et al. *Clin Infect Dis* 2004;38:1159)

#### Common Features

- MAC and TB account for 30% of reported cases; also reported with cryptococcal meningitis and CMV retinitis.
- Usually occurs at 1-8 wks post HAART initiation.
- Baseline CD4 count is usually <50 cells/mm<sup>3</sup> and increases 2-4 fold in ≤12 mos
- Rapid reduction in viral load.
- May occur while treating OI, at time of OI clinical stability or as newly detected OI.
- Usual treatment is to continue ART, antimicrobial therapy agents for the OI, and give NSAIDS and/or steroids if severe IRIS.

Agent	Clinical Features	Treatment
<i>M. avium</i>	Adenitis, pulmonary infiltrates, liver granuloma, mediastinitis, osteomyelitis, cerebritis, skin	ART, antibiotics, ± NSAIDS or steroids.
<i>M. tuberculosis</i>	Pneumonia, ARDS, adenitis, hepatitis, CNS TB, renal failure, epididymitis	ART, anti-TB meds, NSAIDS ± steroids.
<i>M. leprae</i>	Cutaneous	ART, dapsone.
<i>Cryptococcus</i>	Meningitis, palsy, hearing loss, abscess, mediastinitis, adenitis	Prednisone 0.5-1mg/kg/d. x 2-6 weeks. Delay initiation of HAART until the end of crypto meningitis induction (2-10 weeks)
<i>P jirovecii</i>	Pneumonia	ART, anti-PCP meds, steroids.
HBV and HCV	Hepatitis flare	ART, ? d/c interferon or anti-HBV agents.
JC virus	CNS lesions-inflammation (MRI)	ART, steroids.
HSV	Chronic erosive ulcers, encephalitis	ART, antivirals, steroids.
Varicella	Zoster flare	ART, antivirals.
CMV	Vitritis, cytoid macular edema, uveitis, vitromacular traction	ART, steroids, vitrectomy, IVIG.
KS	Tracheal mucosal edema, obstruction	d/c ART, steroids.
HPV	Inflamed warts	Steroids, surgery.

### Adult OI Table 4. Latent TB and HIV Co-Infection

#### Candidates For Tuberculosis Skin Test (TST) or interferon gamma release assay (IGRA):

- All HIV-infected patients without prior positive test upon entry into HIV care.
- Repeat testing annually for HIV-infected patients at risk of acquiring TB who have no prior positive tests.
- All HIV-infected patients with prior negative skin test who are discovered to be contacts of pulmonary cases.
- Some authorities are reluctant to use IGRA tests due to lack of data in immunosuppressed patients including AIDS. This is most likely to be useful with a CD4 count >200/mm<sup>3</sup> and recent BCG.

#### Indications For Treatment of Latent Tuberculosis Infection [MMWR 2000;49(RR-6)]

- Positive PPD (≥5 mm induration) or positive IGRA plus no prior completed prophylaxis or treatment for TB disease.
- Recent contact with TB case (Recent contacts who are initially TST negative should have TST repeated 12 wks after last exposure to TB case. Those placed on prophylaxis should be discontinued if PPD negative at 12 wks.)
- History of inadequately treated TB that healed

#### Treatment of Latent TB

- Rule out active TB based on symptoms and chest x-ray
- **Preferred Regimens:**
  - INH 300 mg + pyridoxine 50 mg qd for 9 mos (270 doses in ≤12 mos); or
  - INH 900 mg + pyridoxine 100 mg 2 x/wk by directly observed therapy for 9 mos (76 doses in ≤12 mos)
- **Alternative:** Rifampin 10 mg/kg (600 mg max) x 4 mos or Rifabutin with adjusted dose x 4 mos
- **MDR-TB Exposure:** Expert consultation is recommended for persons who are likely to be infected with INH and RIF (multidrug) resistant-TB and at high risk of reactivation.

#### Monitoring Therapy

- Contact monthly to review symptoms suggesting hepatitis.
- LFTs (ALT and bilirubin) at baseline, 1 mo, 3 mos, and with symptoms of hepatitis. D/C INH if asymptomatic and ALT increases to ≥5 x ULN or if symptomatic and ALT increases to ≥3 x ULN.

## Treatment of Tuberculosis Disease

[American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America: Treatment of Tuberculosis *Am J Respir Crit Care Med* 2003;167(4):603 and NIH/CDC/IDSA Updated Opportunistic Infections Guidelines, June 20, 2008]

Adult OI Table 5. Treatment of Drug-Susceptible Active Tuberculosis†

Phase 1 (8 wks)	Phase 2 (4-7 mos)*: Regimen, Doses, Minimal Duration
<b>INH, RIF, PZA, EMB 8 wks</b> • 7 d/wk for 8 wks (56 doses); or • 5 d/wk for 8 wks (40 doses)	• INH/RIF 7 d/wk for 18 wks (126 doses); or • INH/RIF 5 d/wk for 18 wks (90 doses); or • INH/RIF 2x/wk for 18 wks (36 doses).
<b>INH, RIF, PZA, EMB 2 wks/6 wks</b> 7 d/wk, for 2 wks (14 doses), then 2 x/wk for 6 wks (12 doses).	INH/RIF 2x/wk for 18 wks (36 doses)
<b>INH, RIF, PZA, EMB 8 wks</b> 3 x/wk for 8 wks (24 doses)	INH/RIF 3x/wk for 18 wks (54 doses)
<b>INH, RIF, EMB 8 wks</b> • 7 d/wk for 8 wks (56 doses) or • 5 d/wk for 8 wks (40 doses)	• INH/RIF 7 d/wk for 31 wks (217 doses); or • INH/RIF 5 d/wk for 31 wks (155 doses); or • INH/RIF 2 x/wk for 31 wks (62 doses).

INH = Isoniazide, RIF = Rifampin, PZA = Pyrazinamide, EMB = Ethambutol

\* Patients with cavitation at baseline or positive cultures at 2 mos should receive 31 wks continuation phase for total of 9 mos

† Directly observed therapy recommended. Note that total doses is considered more important than total duration.

Adult OI Table 6. Special Considerations for TB Treatment with HIV Co-Infection

Special issues for TB/HIV co-infection:
<ul style="list-style-type: none"> <li>All patients with HIV should be evaluated for TB and all TB patients should be evaluated for HIV.</li> <li><b>Risk of active TB</b> increases with decline in CD4 count, but the increase risk is noted early in HIV disease with the CD4 count is &gt;500/mm<sup>3</sup></li> <li><b>Always treat TB first</b> and <u>do not start</u> concurrent therapy due to pill burden and overlapping toxicity (rash, hepatitis, GI intolerance) <ul style="list-style-type: none"> <li><b>With CD4 count &lt;100/mm<sup>3</sup>:</b> Delay HAART ≥2 wks</li> <li><b>With CD4 count 100-200/mm<sup>3</sup>:</b> Delay HAART ≥8 wks</li> <li><b>With CD4 count &gt;200/mm<sup>3</sup>:</b> Delay HAART until the maintenance phase of TB treatment</li> <li><b>With CD4 count &gt;350/mm<sup>3</sup>:</b> Delay until TB treatment is completed</li> </ul> </li> </ul> <p>Note: 2009 WHO recommendation is to start HAART “as soon as possible”</p> <ul style="list-style-type: none"> <li><b>IRIS</b> is common and is most frequent with a baseline CD4 &lt;100/mm<sup>3</sup> and with treatment initiated in first 2 mos. Clinical features include high fevers, decreasing</li> </ul>

Adult OI Table 6. Special Considerations for TB Treatment with HIV Co-Infection (Cont'd)

respiratory function, adenopathy, CNS lesions, and pleural effusions. Treatment is symptomatic with non-steroids. For severe reactions: prednisone 1 mg/kg/d with dose taper over 1-2 wks.

• Rifampin is the only TB drug that has major interactions with agents used for HAART. EFV or NVP-based HAART can be given using standard regimens; PI-based HAART requires use of rifabutin with modified doses of the PI.

### Duration of treatment:

• Acute phase: 2 mos–INH/RIF or RBT/EMB/PZA with discontinuation of EMB if strain is pan-sensitive

• Continuation phase: INH/RIF or RBT tiw or (if CD4 >100/mm<sup>3</sup>) biw x 4-10 mos

• Total duration:

**Pulmonary TB without cavity and neg sputum** at 2 mo: 6 mo

**Pulmonary TB + cavity or positive sputum** at 2 mo: 9 mo

**Extrapulmonary TB with CNS, bone or joint involvement:** 9-12 mos

**Extrapulmonary TB at other sites:** 6-9 mos

Adult OI Table 7. Doses of Antituberculosis Drugs– First Line Drugs

Drug	7 or 5 d/wk	2 x/wk	3 x/wk
INH*	5 mg/kg (300)*†	15 mg/kg (900)*†	15 mg/kg (900)*†
RIF**	10 mg/kg (600)*	10 mg/kg (600)*	10 mg/kg (600)*
PZA (wt)			
40-55 kg	1 gm	2.0 gm	1.5 gm
56-75 kg	1.5 gm	3.0 gm	2.5 gm
76-90 kg	2.0 gm	4.0 gm	3.0 gm
EMB (wt)			
40-55 kg	800 mg	2,000 mg	1,200 mg
56-75 kg	1,200 mg	2,800 mg	2,000 mg
76-90 kg	1,600 mg	4,000 mg	2,400 mg

\* Usual dose in mg in parentheses.

† INH should be given with pyridoxine. Dose at 25 mg on for each day INH is given.

**Adult OI Table 8. Treatment of Hepatitis C [Recommendations of the American Association for Study of Liver Disease, *Hepatology* 2004;39:1147]**

**Indications for Screening: HIV Infection**

**Background:** Experience with HIV/HCV co-infection shows optimal response with pegylated interferon plus ribavirin but reduced rates of sustained viral response (undetectable HCV RNA at 24 wks post treatment) with genotype 1 of 14-29% [Chun RT, *N Engl J Med* 2004;351:451; Torrani FJ *N Engl J Med* 2004;351:438] compared to rates of 45-50% in absence of HIV [Fried MW, *N Engl J Med* 2002;347:973]. Rate of sustained viral response (SVR), the goal of therapy ranges 60-75% with treatment for 48 wks with non-1 genotypes.

**Pretreatment Evaluation**

- Counsel patient on risks and benefits – if there is a contraindication to therapy or the patient refuses therapy most of the work-up is unnecessary
- Lab tests: CBC, ALT, AST, and creatinine
- HIV status: CD4 count, viral load, OI (nearly all published experience is with stable HIV and CD4 >200 cells/mm<sup>3</sup> and mean CD4 >500 cells/mm<sup>3</sup>)
- HCV status: HCV genotype, HCV viral load, liver biopsy (if unavailable, contraindicated, or refused may elect to treat without)
- Patient status: assess co-morbidities including psychiatric disease, substance abuse, cardiopulmonary disease, renal disease

**Indications to Treat**

1. HCV RNA >50 IU/mL,
2. Liver biopsy showing fibrosis score ≥2,
3. No contraindication to interferon or ribavirin, and
4. Stable HIV infection, preferably with CD4 >200 cells/mm<sup>3</sup>.

**Contraindications:** Active substance abuse, decompensated liver disease, severe psychiatric disease, pregnancy or pregnancy potential, or unstable HIV infection

**Regimen**

- All genotypes treated with pegylated interferon and ribavirin x 48 wks
- **Peginterferon alfa 2a** (Pegasys) 180 mcg or **alfa 2b** (*Peg-Intron*) – 1.5 mcg/kg SC qw x 48 wks
- **Ribavirin:** 800-1200 mg qd in divided doses x 48 wks (1200 mg/d if >75 kg; 1000 mg/d if <75 kg; 800 mg/d if <40 kg)

**Follow-up**

- **Reinforce birth control** during 6 mos treatment
- **Lab Tests:** CBC + ALT at wks 2 & 4, then at 4-8 wk intervals
- **HCV:** Quantitative HCV RNA at 12 wks-continue if undetectable or decreased by 2 log<sub>10</sub> IU/mL. Retest at end of treatment and 6 mos post treatment (wk 72) to determine SVR.\*
- **Neuropsychiatric evaluation monthly** ± SSRI & consultation.
- **Thyroid:** TSH at 3 + 6 mos intervals.
- **HIV:** CD4 count and viral load every 3-4 mos

\* Failure to achieve no detectable HCV or a 2 log<sub>10</sub> IU/mL decrease at 12 wks indicates failure.

**Guidelines for Sexually Transmitted Disease Co-Morbidity**

CDC Guidelines for the Treatment of Sexually Transmitted Diseases  
Available on the CDC web site at: <http://www.cdc.gov/std/>

The following are additional sources of information and guidance:

- State or Local Health Department Case consultations, disease reporting, and may be able to provide hardcopy of STD Treatment Guidelines.
- STD/HIV Prevention Training Centers  
Check the web site: <http://depts.washington.edu/nnptc/> for a list of the PTCs

STD/HIV Table 1. Sexually Transmitted Disease Identification and Treatment\*

Condition	Identification/Screening	Diagnosis	Treatment
Urethritis	<ul style="list-style-type: none"> <li>• Patient self-report sx</li> <li>• Review of hx at follow-up visits, including contact with known other case</li> </ul>	Confirm Urethritis and test for Gonorrhea and Chlamydia	For non-gonococcal urethritis, treat for Chlamydia
Gonorrhea	<ul style="list-style-type: none"> <li>• Patient self-report sx</li> <li>• Review of hx at follow-up visits, including contact with known other case</li> <li>• Many infections are asymptomatic in men and women: consider urinary NAAT for GC &amp; CT in sexually active men and women</li> </ul>	Gram stain and/or culture (or other specific test) of urethral or cervical swabs. Urine NAAT or PCR tests are valid for urethral infections are most sensitive and usually more acceptable to patients	<p><b>Urethral, endocervical, rectal:</b> Ceftriaxone 125 mg IM x 1 (also for <b>pharyngeal</b>) or cefixime 400 mg po x 1, <b>PLUS</b> treatment for <i>C. trachomatis</i> if it is not ruled out: azithromycin 1 gm po x 1 or doxycycline‡ 100 mg po bid x 7 d  <b>Alternative:</b> Spectinomycin 2.0 gm IM x 1</p> <p><b>Disseminated GC:</b></p> <ul style="list-style-type: none"> <li>• Patients with disseminated GC infections are most appropriately treated in the hospital. Consult full-text of the guidelines for treatment recommendations.</li> <li>• Ceftriaxone 1 gm/d IM or IV until improved for 24-48 h, then ≥1 wk treatment with oral cefixime 400 mg qd, ciprofloxacin 500 mg bid, ofloxacin 400 mg bid, or levofloxacin 500 mg qd. High rates of fluoroquinolone resistance reported nationally; check local resistance pattern</li> </ul>
Chlamydia	<ul style="list-style-type: none"> <li>• Patient self-report sx</li> <li>• Review of hx at follow-up visits, including contacts</li> <li>• Most infections are asymptomatic</li> <li>• Routine cervical tests for sexually active women &lt;25 yrs. Consider routine NAAT urine test for GC &amp; CT in sexually active women &gt;25 yrs and men</li> <li>• Consider repeat test annually or more often with high risk</li> </ul>	Culture is infrequently available. Alternatives are DFA, EIA, and NAAT on urethral and cervical specimens. Urine NAAT or PCR tests are sensitive and often preferred.	<p>azithromycin 1 gm po x 1  <b>or</b>  doxycycline* 100 mg po bid x 7 d  <b>Alternatives:</b> erythromycin base 500 mg po qid x 7 d; erythromycin ethylsuccinate 800 mg po qid x 7 d; ofloxacin 300 mg po bid x 7 d, or levofloxacin 500 mg po qd x 7 d  <b>Pregnancy:</b> Azithromycin 1 gm po x 1; Alternatives: Amoxicillin 500 mg tid x 7 d or erythromycin regimen (above doses)</p>
Syphilis	<ul style="list-style-type: none"> <li>• Patient self-report sx</li> <li>• Contact to case</li> <li>• Screen at initial visit</li> <li>• Repeat screen annually</li> </ul>	<ul style="list-style-type: none"> <li>• RPR, VDRL or treponemal EIA <b>PLUS</b> FTA-ABS if positive</li> <li>• Darkfield exam or DFA of lesion material or exudates (primary syphilis)</li> </ul>	See STD/HIV Table 2 (pgs 90-91). Management of Syphilis Co-Infection: Summary

\* CDC STD treatment guidelines updated by authors to reflect latest research data.

† Screening interval depends upon community prevalence, outcome of previous tests, and risk.

‡ Tetracycline, fluoroquinolones contraindicated in pregnancy.

STD/HIV Table 1. Sexually Transmitted Disease Identification and Treatment\*

Condition	Identification/Screening	Diagnosis
Herpes Simplex	<ul style="list-style-type: none"> <li>• Patient self-report sx</li> <li>• Review of hx at follow-up visits</li> <li>• Most common cause of genital ulcer disease in the US and the world</li> <li>• Many infections are asymptomatic unless history is targeted</li> </ul>	<ul style="list-style-type: none"> <li>• Patients with lesions suspected to be herpes should be evaluated to establish HSV and rule out syphilis.</li> <li>• Virologic Tests: Culture, PCR (more sensitive than culture)</li> <li>• Serology for HSV-2: most sensitive test for HSV</li> </ul>
Trichomonas	Malodorous yellow-green discharge	Wet mount or culture
Pelvic inflammatory disease	Endometritis, salpingitis	Uterine, adenexal, or cervical motion tenderness

\* CDC STD treatment guidelines updated by authors to reflect latest research data.

(Cont'd)

Treatment			
	Acyclovir	Famciclovir	Valacyclovir
<b>HSV and No HIV</b>			
<b>Initial Episode</b>	400 mg tid x 7-10 d	250 mg tid x 7-10 d	1 gm bid x 7-10 d
<b>Episodic</b>	400 mg tid or 800 mg bid x 5 d or 800 mg tid x 2 d x 5-10 d	125 mg bid x 5 d or 1000 mg bid x 1 d	500 mg bid x 3 d or 1 gm qd x 5 d
<b>Suppression</b>	400-800 mg bid	250 mg bid	500 mg or 1 gm qd
<b>HSV and HIV</b>			
<b>Episodic</b>	400 mg bid or tid x 5-10 d	500 mg bid x 5-10 d	1 gm bid x 5-10 d
<b>Suppression</b>	400-800 mg bid or tid	500 mg bid	500 mg bid
Metronidazole 2 gm x 1 <b>Alternative:</b> Metronidazole 500 mg bid x 7 d			
<b>Parenteral:</b> cefoxitin 2 gm IV q6h <b>PLUS</b> doxycycline 100 mg po or IV q12h until improved, <b>THEN</b> doxycycline 100 mg bid po to complete 14 d. <b>Parenteral alternative:</b> clindamycin 900 mg IV q8h <b>PLUS</b> gentamicin (2 mg/kg IV or IM loading dose, then 1.5 mg/kg q8h) until improved, <b>THEN</b> doxycycline 100 mg bid po or clindamycin 450 mg qid po to complete 14 d course. <b>Oral regimen:</b> doxycycline 100 mg bid x 14 d <b>PLUS:</b> either ceftriaxone 250 mg IM X 1 or cefoxitin** 2 gm IM x 1 with probenecid 1 gm po x 1; with or without metronidazole 500 mg bid po x 14 d			

\*\* CDC STD treatment guidelines updated by authors to reflect latest research data.

**STD/HIV Table 2. Management of Syphilis Co-Infection: Summary\***

Form	Treatment	LP†	Follow-up VDRL/RPR	Expectation VDRL/RPR	Indications to Re-treat
Primary and Secondary syphilis	<p>Initial:</p> <ul style="list-style-type: none"> <li>• Benzathine penicillin G 2.4 mil units IM x 1</li> <li>• <b>Penicillin allergy:</b> doxycycline 100 mg po bid x 14 d or ceftriaxone 1 gm qd IV or IM x 8-10 d or azithromycin 2 gm po x 1</li> <li>• <b>Re-treatment:</b> Benzathine penicillin G 2.4 mil units IM x 3 (weekly)</li> </ul>	<ul style="list-style-type: none"> <li>• Neuro sx</li> <li>• Titer increases 4-fold</li> <li>• Symptoms persist or recur</li> </ul>	3, 6, 9, 12 & 24 mos	Four-fold decrease by 6-12 mos	<ul style="list-style-type: none"> <li>• Titer increases four-fold</li> <li>• Titer fails to decrease four-fold at 6-12 mos</li> <li>• Symptoms persist or recur</li> </ul>
Early latent (<1 yr)	<p>Initial:</p> <ul style="list-style-type: none"> <li>• Benzathine penicillin G 2.4 mil units IM x 1</li> <li>• <b>Penicillin allergy:</b> doxycycline 100 mg po bid x 14 d or ceftriaxone 1 gm qd IV or IM x 8-10 d or azithromycin 2 gm po x 1</li> <li>• <b>Re-treatment:</b> Benzathine penicillin G 2.4 mil units IM x 3 (weekly)</li> </ul>	<ul style="list-style-type: none"> <li>• Neuro symptoms</li> <li>• Symptoms persist or recur</li> </ul>	3, 6, 12, 18, & 24 mos	Four-fold decrease at 12 to 24 mos	<ul style="list-style-type: none"> <li>• Titer increases four-fold</li> <li>• Titer of &gt;1:32 fails to decrease four-fold at 12-24 mos</li> <li>• Develops signs or sx of syphilis</li> </ul>
Late latent (>1 yr or unknown duration)	<ul style="list-style-type: none"> <li>• Benzathine penicillin, 2.4 mil units IM weekly for 3 wk</li> <li>• <b>Penicillin allergy:</b> doxycycline 100 mg po bid x 28 d‡</li> </ul>	All HIV-infected patients	3, 6, 12, 18, & 24 mos	Four-fold decrease in titer at 6-12 mos (lower initial titers may remain unchanged)	<ul style="list-style-type: none"> <li>• Titer fails to decrease four-fold at 12-24 mos</li> <li>• Increase titer by four-fold at any time after 3 mos</li> </ul>
Late syphilis (tertiary, not neurosyphilis)	<ul style="list-style-type: none"> <li>• Benzathine penicillin, 2.4 mil units IM weekly for 3 wk</li> <li>• <b>Penicillin allergy:</b> doxycycline 100 mg po bid x 28 d‡</li> </ul>	All patients	6 & 12 mos	<ul style="list-style-type: none"> <li>• As above</li> <li>• Granulomatous lesions should heal</li> </ul>	<ul style="list-style-type: none"> <li>• As above</li> <li>• Documentation of T. pallidum or other histologic feature of late syphilis</li> </ul>
Neurosyphilis (or ocular syphilis)	<ul style="list-style-type: none"> <li>• Aq penicillin G, 18-24 mil units/d x 10-14 d administered as 3-4 million units IV q4h or Procaine penicillin 2.4 million units IM qd + probenecid 500 mg po qid x 10-14 d</li> <li>• Some recommend benzathine penicillin, 2.4 million units IM weekly x 3 wks after completion of IV course.</li> <li>• <b>Penicillin allergy:</b> ceftriaxone 2 gm qd IV or IM x 10-14 d or desensitize and treat with penicillin (preferred).</li> </ul>	Required	Every 6 mos until CSF normal	CSF WBC decrease at 6 mos and CSF normal at 2 yr	<ul style="list-style-type: none"> <li>• CSF WBC fails to decrease at 6 mos or if CSF VDRL is still positive</li> <li>• Persisting signs and symptoms</li> </ul>

\* CDC STD treatment guidelines updated by authors to reflect latest research data.

† Some experts recommend CSF examinations of all syphilis-HIV co-infected patients before treatment, regardless of stage, and modification of treatment accordingly. Consultation with an expert may be appropriate.

‡ Alternatives to penicillin have not been sufficiently evaluated in HIV infected persons and cannot be considered first-line therapy. If required, there needs to be close clinical monitoring. If adherence cannot be assured, desensitization and tx with penicillin is recommended.

## Occupational Post-Exposure Prophylaxis (PEP)

Source	Type of Exposure			
	Percutaneous		Mucocutaneous	
	Not Severe <sup>1</sup>	More Severe <sup>2</sup>	Small Volume <sup>3</sup>	Large Volume <sup>4</sup>
<b>HIV Positive</b>				
Low risk <sup>5</sup>	2 drugs	≥3 drugs	2 drugs	2 Drugs
High risk <sup>6</sup>	3 drugs	≥3 drugs	≥3 Drugs	≥3 drugs
<b>Source unknown</b>				
–	None or 2 drugs <sup>7</sup>	None or 2 drugs <sup>7</sup>	None or 2 drugs <sup>7</sup>	None or 2 drugs <sup>7</sup>

<sup>1</sup> Solid needle or superficial injury etc

<sup>2</sup> Large bore hollow needle, deep injury or visible blood on needle/device

<sup>3</sup> Few drops

<sup>4</sup> Major splash

<sup>5</sup> HIV positive, asymptomatic, and VL <1500 c/mL

<sup>6</sup> HIV positive and symptomatic, AIDS, acute retroviral syndrome or known high viral load; if HIV resistance is a concern – get expert consultation

<sup>7</sup> PEP is optional based on discussion of risk: benefit

### Risk for HIV Transmission

Exposure: Percutaneous injury with sharp object or exposure to mucous membranes or nonintact skin (skin that is abraded, chapped or with dermatitis).

#### Source:

- Percutaneous injury: 0.3% (3/1000)
- Mucocutaneous exposure: 0.09% (9/10,000)
- Increased risk: Device (needle) with visible blood, needle placed in artery or vein, deep injury, large volume, high viral load

#### Relative risk (without prophylaxis)

- Established risk with occupational exposure: Blood or bloody body fluid
- Theoretical risk: CSF; pleural pericardial, peritoneal, amniotic and vaginal fluids; semen
- Not infectious: Urine, stool, nasal secretions, sputum, tears, vomitus (if not bloody)

### Efficacy of PEP

- Efficacy of AZT monotherapy prophylaxis estimated at 80% in retrospective case control series
- Recorded prophylaxis failures with occupational exposure (US): 6

**Timing:** Should start PEP as soon as possible. Studies in primates show starting 36 hours post exposure is more effective than 72 hrs. Standard duration of PEP is 28 days.

**Regimens:** The 2004 CDC guidelines recommended a combination of AZT/3TC ± LPV/r. In contemporary practice, most authorities prefer TDF/FTC plus RAL or PI/r (primarily DRV/r or ATV/r) (NEJM 2010; 361:1768)

- Recommended drugs:

2 Drug Regimen	3 Drug Regimen
3TC or FTC <i>plus</i> AZT, d4T or TDF	Two nucleosides <i>plus</i> RAL or LPV/r, ATV/r or DRV/r

- Not recommended: ABC, and NVP due to potential for serious toxicity

#### Adverse reactions

- Reported frequency: 17-47%
- Most frequent: Nausea– 27%, malaise and fatigue– 23%

**Pregnancy:** Recommended regimens are considered safe (more clinical data with AZT/3TC/LPV/r)

**Expert consultation** is sometimes recommended, especially for:

- Delayed PEP to >24-36 h
- Unknown source
- Pregnancy or breastfeeding
- Resistant HIV strain in source
- Toxicity management

#### Monitoring

- **Source** – rapid HIV test preferred if serostatus is unknown
- **Re-evaluate** HCW at 72 h
- **HCW serology testing for HIV:** Baseline, 6 wks, 12 wks and 6 mos; if HCV seroconversion add a 12 mos serologic test for HIV. HIV PCR in HCW is not routinely recommended due to high rates of false positives; these tests should be done if there are symptoms compatible with the acute retroviral syndrome
- **Report any seroconversion** to CDC at 1-800-893-0485
- **Toxicity monitoring** Adapted from *NEJM* 2010;361:1768

Test	Baseline	Sx*	Wk 4-6	Wk 12	Wk 24
HIV EIA or rapid test	+	+	+	+	+
CBC, LFTs & Creatinine	+	+	-	-	-
HIV viral load	-	+	-	-	-
HbsAb	+	-	-	-	-
HBsAg	+	-	-	-	-
HCV Ab**	+	-	-	+	+

\* Symptoms of drug toxicity or seroconversion syndrome

\*\* Data on source and HbsAb status of host determines risk

#### Resources for PEP

- **PEPLine:**  
[http://www.nccc.ucsf.edu/about\\_nccc/pepline/](http://www.nccc.ucsf.edu/about_nccc/pepline/)  
 Telephone: 1-888-448-4911
- **HIV Pregnancy registry:**  
<http://www.apregistry.com/index.htm>  
 Telephone: 1-800-258-4263  
 Email: [registry@nc.crf.com](mailto:registry@nc.crf.com)
- **CDC (HCW serconversions):**  
 Telephone: 1-800-893-0485
- **HIV/AIDS Treatment Information Service:**  
<http://aidsinfo.nih.gov/>

## **NOTES**

## **The Johns Hopkins AIDS Service**

- **The Moore Clinic**  
**+1-410-955-1725**
- **The Garey Lambert Research Center**
- **AIDS Clinical Trials Unit**
- **HIV Guide**  
*<http://hopkins-hivguide.org>*
- **The Medical Management of HIV Infection**  
*<http://hopkins-hivguide.org>*
- **Center for Clinical Global Health Education**  
*<http://www.ccghe.jhmi.edu>*