

February 2006 Edition

A Pocket Guide to Adult HIV/AIDS Treatment:

Companion to *A Guide
to Primary Care of
People with HIV/AIDS*

John G. Bartlett, MD



U.S. Department of Health and Human Services
HRSA
Health Resources and Services Administration

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Companion to
**A Guide to Primary Care of
People with HIV/AIDS**

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Important Information for Users of This Pocket Guide

This document is provided as an information resource for physicians and other health care professionals to guide them in the appropriate treatment of patients with HIV/AIDS. Recommendations for care and treatment change rapidly, and opinions 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 in 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 single reference or service can take the place of medical training, education, and experience. 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 are for informational purposes only. Determination of appropriate treatment is the responsibility of the treating physician.

Abbreviations Used in This Pocket Guide

Drug Abbreviations

ABC: abacavir (<i>Ziagen</i>)	IVIG: intravenous immune globulin
APV: amprenavir (<i>Agenerase</i>)	LPV/r: lopinavir/ritonavir (<i>Kaletra</i>)
ATV: atazanavir (<i>Reyataz</i>)	NFV: nelfinavir (<i>Viracept</i>)
AZT: zidovudine (<i>Retrovir</i>)	NNRTI: non-nucleoside reverse transcriptase inhibitor
CBV: Combivir (AZT+3TC)	NRTI: nucleoside reverse transcriptase inhibitor
ddI: didanosine (<i>Videx</i>)	NVP: nevirapine (<i>Viramune</i>)
d4T: stavudine (<i>Zerit</i>)	PI: protease inhibitor
ddC: zalcitabine (<i>Hivid</i>)	RBT: rifabutin (<i>Mycobutin</i>)
DLV: delavirdine (<i>Rescriptor</i>)	RTV: ritonavir (<i>Norvir</i>)
EFV: efavirenz (<i>Sustiva</i>)	r: ritonavir in dose <400 mg/day
ENF: enfuvirtide (<i>Fuzeon</i> , T-20)	SQV: saquinavir (<i>Invirase</i> , <i>Fortovase</i>)
FTC: emtricitabine (<i>Emtriva</i>)	TPV: tipranavir (<i>Artivus</i>)
FTV: Fortovase (saquinavir, soft gel cap)	3TC: lamivudine (<i>Epivir</i>)
FPV: fosamprenavir (<i>Lexiva</i>)	T-20: enfuvirtide (<i>Fuzeon</i>)
HU: hydroxyurea	TDF: tenofovir (<i>Viread</i>)
IDV: indinavir (<i>Crixivan</i>)	TMP-SMX: trimethoprim sulfamethoxazole
INH: isoniazid	TZV: <i>Trizivir</i> (ABC+AZT+3TC)
INV: Invirase (saquinavir, hard gel cap)	VZIG: varicella zoster immune globulin
	ZDV: zidovudine (<i>Retrovir</i>)

Miscellaneous Abbreviations

ART: antiretroviral therapy	q: every
EC: enteric coated	qd: daily
HAART: highly active antiretroviral therapy	qid: four times per day
IV: intravenous	qm: monthly
IM: intramuscular	qod: every other day
VL: viral load	qw: every week
bid: twice per day	soln: solution
biw: twice per week	tid: three times per day
CNS: central nervous system	tiw: three times per week
hs: bedtime (hour of sleep)	TAMS: thymidine analogue assoc. mutations
mo: month	ULN: upper limit of normal
po: by mouth	

Drug Information

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 – italics)		
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)										
Abacavir (ABC, Ziagen)	300 mg tab (see also: Trizivir); 20 mg/mL po soln	300 mg bid	No effect	Standard			Usual	Hypersensitivity: fever, rash, GI sx, dyspnea§¶¶		
Combivir (CBV)	AZT 300 mg + 3TC 150 mg (tab)	1 bid	No effect	Fixed formulation not recommended			Usual	AZT side effects§		
Didanosine (Videx EC; ddI)††	125, 200, 250, and 400 mg EC capst††		½ hr before or 2 hr after meal Separate dosing of ATV, TPV/r	>60 kg 200 mg/d	>60 kg 125 mg/d	>60 kg 125 mg/d	Usual	Pancreatitis, peripheral neuropathy, GI intolerance §		
		EC Caps		400 mg qd	250 mg qd	<60 kg 125 mg/d			<60 kg 100 mg/d	<60 kg 75 mg/d¶¶
		with TDF		250 mg/d	200 mg/d					
Emtricitabine (Emtriva, FTC)	200 mg cap	200 mg qd	No effect	200 mg q72 h			Usual	Minimal§ HBV flare »		
Lamivudine (Epivir; 3TC)	150, 300 mg tab (see also: Combivir & Trizivir); 10 mg/mL po soln	150 mg bid or 300 mg qd		150 mg x 1 then 100 mg/d			Usual	Minimal§ HBV flare »		

Epzicom	3TC 300 mg + ABC 600 mg	1 qd	No effect	Fixed formulation not recommended in renal failure	Usual	ABC hypersensitivity, HBV flare »
Stavudine (Zérit, d4T) †	15, 20, 30, 40 mg cap 1 mg/mL po soln	Wt >60 kg: 40 mg bid Wt <60 kg: 30 mg bid	No effect	>60 kg 20 mg q 12 h >60 kg 20 mg q 24 h <60 kg 15mg q 12 h	Usual	Peripheral neuropathy, pancreatitis, lipodystrophy, ascending paresis (rare)§
Tenofovir (Viread, TDF)	300 mg tab (see also: Truvada)	300 mg qd	Take with meal	300 mg q 48 hr 300 mg 2 days/wk 300 mg q 7 days¶	Usual	Minimal. Renal toxicity (rare)§ HBV flare »
Trizivir (TZV)	AZT 300 mg + 3TC 150 mg + ABC 300 mg (tab)	1 bid	No effect	Fixed formulation not recommended in renal failure	Usual	Hypersensitivity reaction (ABC), bone marrow suppression (AZT), GI intolerance (ABC)§ HBV flare »
Truvada	TDF 300 mg + FTC 200 mg	1 qd	No effect	Fixed formulation not recommended in renal failure	Usual	Minimal. Renal toxicity, HBV flare »

Drug Table 1. Antiretroviral Agent Characteristics – continued
(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	
Zidovudine (Retrovir, AZT)	100 cap, 300 mg tab (see also: Combivir & Trizivir)						
	10 mg/mL IV soln	300 mg bid		300 mg bid	300 mg qd	100 mg tid	
	10 mg/mL po soln	200 mg bid	No effect				Peripheral neuropathy, stomatitis§
Protease Inhibitors (PIs)							
Atazanavir (Reyataz, AZT)	100, 150, and 200 mg capsules	400 mg qd; ATV 300 mg/RTV 100 mg qd. Boosting is often preferred and is required if ATV is combined with TDF or EFV	Take with food Avoid concurrent buffered ddl, antacids	Standard		CPS* 7-9: 300 mg qd CPS* > 9: Avoid	Benign increase in indirect bilirubin, GI intolerance, transaminitis, prolongation of QTc (caution with conduction defects or drugs that do this) ‡
Fosamprenavir †† (FPV, Lexiva)	700 mg tabs	1400 mg bid or 700 mg/RTV 100 mg bid or 1400 mg/RTV 200 mg qd	No effect	Standard		CPS* 5-8: 700 mg bid CPS* > 9: Avoid	Rash, GI intolerance, transaminitis, headache, hepatitis ‡

Indinavir (IDV, Crixivan)	200, 333, 400 mg caps	800 mg q 8h; separate buffered ddl $\geq$ 1 hr IDV 400 mg/RTV 400 mg bid or # IDV 800 mg/RTV 100-200 mg bid #	1 hr before or 2 hr after meal unless with RTV	Standard	600 mg q8h	GI intolerance, nephrolithiasis, transaminitis, benign increase in indirect bilirubin ††
Lopinavir/ Ritonavir (LPV/r) (Kaletra)	200/50 mg tabs; LPV 80 mg + RTV 20 mg/mL po soln††	400 mg LPV + 100 mg RTV (2 tabs) bid Soln: 5 mL bid	No effect	Standard	§§	Transaminitis, GI intolerance (esp diarrhea), asthenia ††
Nelfinavir (NFV, Viracept)	250, 625 mg tabs 50 mg/g powder	1250 mg bid or 750 mg tid	Take with high fat meal	Standard	§§	GI intolerance, diarrhea, transaminitis††
Ritonavir (RTV, Norvir)	100 mg caps 600 mg/ 7.5 mL po soln	600 mg q12h #; separate ddl $\geq$ 2 h	Food improves GI tolerance	Standard	§§	GI intolerance, paresthesia, transaminitis, taste perversion ††
Saquinavir †† (SQV, Invirase)	200 mg caps 500 mg tabs	SQV 1000 mg bid + RTV 100 bid †† SQV 2000 mg qd + RTV 100 mg qd ††	Take within 2 hours of meal	Standard	§§	GI intolerance, transaminitis ††
Tipranavir (TPV, Aptivus)	250 mg caps	500 mg bid with RTV 200 mg bid	Take TPV and RTV with food	Standard	CPS B or C: Avoid	Hepatotoxicity – monitor ALT, skin rash, GI intolerance, multiple drug interactions

Drug Table 1. Antiretroviral Agent Characteristics – continued

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

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Delavirdine (DLV, Rescriptor)	100, 200 mg tabs	400 mg tid	No effect	Standard	§§	Rash
Efavirenz ††† (EFV, Sustiva)	50, 100, 200 mg caps 600 mg tabs	600 mg hs	Avoid high fat meal	Standard	§§	CNS x 2-3 wks, rash, hepatitis, false + cannabinoid test
Nevirapine (NVP, Viramune)	200 mg tabs 50 mg/5 mL po susp	200 mg qd x 14 days, then 200 mg bid	No effect	Standard	Standard; give post dialysis Avoid	Rash, hepatitis, hepatic necrosis esp women with CD4 >250 in first 6 wks

Fusion Inhibitors

Enfuvirtide (ENF, Fuzeon, T-20)	90 mg single-use vials to be reconstituted with 1.1 mL H ₂ O	90 mg (1 mL) SQ q12h into upper arm, anterior or abdomen (rotate sites)	N/A	Standard	Usual Dose	Site reactions
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+	The combination of ddI & d4T "should be used in pregnant women only when the potential benefit clearly outweighs the potential risk." Efavirenz should be avoided in first trimester of pregnancy and used with caution in women with reproductive potential. Avoid APV liquid in pregnancy.	++	The following are no longer available: buffered ddI, lopinavir/r 133/33 mg cap, amprenavir, or Fortovase.
+	Drug change or dose change could be considered on a case-by-case basis noting the risk of resistance with underdosing.	**	Capsule is the preferred formulation due to high propylene glycol in the po solution; po soln contraindicated in pregnancy.
§	Class adverse reaction: lactic acidosis with steatosis (see Drug Table 2). Most common with d4T, ddI, and AZT.	#	See Drug Table 4 for dosing recommendations when using dual PI, PI plus NRTI, or dual PI plus NNRTI.
¶	Give post dialysis	*	CPS= Child Pugh Score
¶¶	Registry for hypersensitivity 1-800-270-0425	§§	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.
+++	Efavirenz should be avoided in first trimester of pregnancy and used with caution in women with reproductive potential. Avoid APV liquid in pregnancy.	++	Class adverse effects include lipodystrophy with hyperglycemia, fat redistribution, hyperlipidemia, and possible increased bleeding with hemophilia. ATV does not cause hyperlipidemia. All PIs may cause elevated transaminases (see Drug Table 2).
»	3TC, FTC, and TDF: Risk of flare of chronic HBV if discontinued.		

Drug Table 2.
Antiretroviral Agents, Class Adverse Reactions

Reaction	Lactic acidosis	Hepatotoxicity	Hyper-glycemia	Fat redistribution	Hyper-lipidemia	Rash
Definition	Lactic acid >2 mmol/mL usually >5 mmol/mL	Gr III = AST/ALT 5-10 X ULN Gr IV = AST/ALT > 10 x ULN	Fasting glucose >126 mg/dL	Fat accumulation Lipodystrophy	See Adult ART Table 5	DRESS* (NVP, ABC) SJS, TEN (NVP, EFV, DLV) ABC hypersensitivity
Frequency	1-3% NRTI recipients with median onset at 4 mo	NRTIs: d4T, ddI, AZT (lactic acidosis) Pls: (15-30%) NVP: 11% in first 6 wks in women with baseline CD4 >250; possible hepatic necrosis and death NNRTI: (8-15%)	3-17% with Pls	4-50%		ABC hypersensitivity: 5-8%, 90% in 1st 6 wks EFV, NVP: 8-16% most in 1st 6 wks
Agents	NRTIs: d4T +ddI > d4T > ddI > AZT; rare with 3TC, ABC, FTC or TDF	NRTI: Lactic acidosis with steatosis NVP: Hepatic necrosis Pls, NNRTIs: transaminitis	Pls	Fat accumulation: Pls Lipodystrophy: NRTIs esp d4T Also occurs without antiretrovirals	Pl: esp RTV; not noted with ATV and reduced frequency with FPV	NNRTI: NVP > EFV & DLV Pls: FPV increased risk with sulfa allergy NRTI: ABC*

Risk Factors	Prolonged use NRTI (esp d4T) Female, pregnancy, obesity, ribavirin, metformin	HCV or HBV infection, ETOH, male sex NVP: baseline CD4 >250 in female, > 400 in male	Pre-existing glucose intolerance	No clear risks defined	Risk for CVD: HBP, smoking, obesity, genes, prior MI/stroke, diabetes, age	ABC: genetic predisposition NNRTI: 1st 12 wks Female
Sx	GI (abd pain, anorexia, nausea, vomiting), wasting, dyspnea, cardiac arrhythmias	Most common: asymptomatic ↑ALT/AST due to all PIs and NNRTIs NVP: may cause lethal hepatonecrosis Note: ↑ indirect bilirubin with IDV or ATV is clinically inconsequential but may cause jaundice	Polyuria, polydipsia, polyphagia, weight loss	Fat accumulation: abd (visceral), buffalo hump, breasts, lipomas Fat atrophy: face, extremities, buttocks	Cardiovascular disease with stroke or MI/angina Triglycerides >2000 mg/dL - pancreatitis	Common: MP rash Severe: Stevens-Johnson synd, TEN#, DRESS* NVP : hepatonecrosis with fever, rash, and/or GI sx 1st 16 wks ABC hypersensitivity: ≥ 2 systems involved 1st 6 wks
Lab	Lactate >2 mmol/mL; life-threatening if >10 mmol/mL	LFIs: liver biopsy is usually not helpful.	Fasting glucose >126 mg/dL	Appearance is best "lab test", CT scan, MRI, waist and hip measurement, Bioelectric Impedence Analysis, DEXA, ultrasound	↑ triglycerides ↑ cholesterol, LDL cholesterol	Eosinophilia: variable

Drug Table 2. – continued Antiretroviral Agents, Class Adverse Reactions

Reaction	Lactic acidosis	Hepatotoxicity	Hyper-glycemia	Fat redistribution	Hyper-lipidemia	Rash
Treatment	Lactate 2-5 mmol/mL + Sx -D/C NRTI if sx severe Lactate level is 5-10 mmol/mL: D/C NRTIs. Lactate > 10 mmol/mL (medical emergency): D/C NRTIs + supportive care (ventilator, dialysis, IV HCO₃) IV thiamine or riboflavin (?) Post recovery: use low risk NRTIs (3TC, FTC, TDF) or avoid class	Hypersensitivity reactions to ABC or NVP (fever, eosinophilia, rash, systemic response usually in first 6-18 wks); D/C drug immediately and do not rechallenge Asymptomatic elevations of LFT (<10x ULN): repeat LFTs q 1-2 wks Symptomatic or elevations of LFT (> 5-10x ULN) or hyperlactatemia or hypersensitivity (ABC or NVP): D/C ART or change regimen. Some "treat through" asymptomatic ALT > 10x ULN. ALT may return to baseline or persist; liver biopsy usually not helpful	Use standard diabetes treatment with diet and exercise Preferred hypoglycemics are metformin or thiazolidinediones D/C PI only if uncontrolled hyperglycemia	D/C d4T, ddI, AZT for fat atrophy Cosmetic surgery Exercise? Change PI to ATV or NNRTI Lipodatrophy: D/C d4T	NECP guidelines (pg 29): • General ↑ • LDL cholesterol ↑ • Statins • Triglycerides ↑ • fibrates	Most rashes do not require drug discontinuation D/C drug if blisters, bullae, mucous membranes involved, fever, elevated ALT/AST Withdraw NNRTI if severe: mucous membrane involvement (SJS); blisters or bullae, epidermal necrosis (TEN), systemic reaction (fever, arthralgia, myalgias) Treatment: IV fluids, antipyretics, pain management, care in burn unit. Role of steroids not clear. Do not rechallenge NVP and ABC: rash as component of DRESS* or ABC hypersensitivity or NVP hepatonecrosis reaction: D/C drug and supportive care
Monitor During Therapy	None	LFTs at baseline and q 3-6 mo NVP: LFTs at wks 0,2,4,8,12,16 then q 3 mo	Fasting glucose baseline, at 3-6 mo, then yearly	Appearance	Fasting lipid profile at baseline, at 3-6 mo post HAART initiation, then yearly.	Appearance

*DRESS: (Drug Rash, Eosinophilia, & Systemic Symptoms) Life threatening complication that is seen with NVP and ABC - usually in the first 6 weeks of therapy

+Lifestyle changes: d/c smoking, diet, weight reduction, exercise, tx HBP and diabetes

TEN: Toxic epidermal necrolysis

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

Agent	Reaction
Abacavir	• Fatal hypersensitivity reactions: do not restart • Lactic acidosis and steatosis
Amprenavir	Oral soln contains large amounts of propylene glycol: avoid with renal failure, hepatic failure, pregnancy, & metronidazole
Atazanavir	None
Delavirdine	None
Didanosine	Fatal and nonfatal pancreatitis: do not restart Lactic acidosis with steatosis Fatal lactic acidosis when combined with stavudine in pregnancy
Efavirenz	None
Emtricitabine	Lactic acidosis with steatosis
Enfuvirtide	None
Indinavir	None
Lamivudine	Lactic acidosis with steatosis Patients with HBV infection should receive only dosage and formulations appropriate for treatment of HIV
Lopinavir	None
Nelfinavir	None
Nevirapine	Hepatotoxicity including fulminant and cholestatic hepatitis & hepatic necrosis: monitor intensively in first 18 wks of therapy Severe, life-threatening skin reaction including toxic epidermal necrolysis (TEN), Stevens-Johnsson syndrome, etc Do not restart if there is serious liver injury or serious drug reaction
Ritonavir	Potentially serious drug interactions with nonsedating antihistamines, sedative hypnotics, antiarrhythmics, or ergot alkaloids
Stavudine	Lactic acidosis with steatosis Fatal and non-fatal pancreatitis Fatal lactic acidosis when combined with didanosine in pregnancy
Tenofovir	Lactic acidosis and steatosis; discontinuation in pts with HBV co-infection may cause exacerbation of acute HBV
Tipranavir	Hepatotoxicity including clinical hepatitis and hepatic decompensation
Zalcitabine	Severe peripheral neuropathy Pancreatitis (rare) Hepatic failure in patients with HBV infection (rare) Lactic acidosis and steatosis
Zidovudine	Hematologic toxicity: anemia & leucopenia Lactic acidosis and steatosis

Drug Table 4.
Combination Antiretroviral Therapy, Dose Adjustments*

	RTV	SQV	NFV	FPV	LPV/r	ATV	NVP	EFV
IDV	IDV 400+ RTV 400 bid or IDV/r 800/ 100-200 bid	ND	IDV 1200 + NFV 1250 bid	IDV-SD APV-SD	ND	NR	NVP-SD IDV 1000 q8h	EFV-SD IDV- 1000 q8h or EFV SD/ IDV 800 bid/ RTV 200 bid
RTV	-	SQV/r 1000/100 or 400/400 bid	-	FPV/r 1400/ 200 qd or 700/ 100 bid	co-form- ulated	ATV/r 300/100 qd	NVP-SD RTV-SD	EFV-SD RTV-SD
SQV	-	-	NFV- SD + SQV 1200 bid or SQV 800 tid	ND	SQV 1000 bid + LPV/r- SD	SQV 1200 + ATV 400 qd	NVP-SD + SQV/RTV 400/400 bid or 1000/100 bid	EFV-SD + SQV/RTV 400/400 bid
NFV	-	-	-	ND	ND	ND	NVP-SD NFV-SD	EFV-SD NFV-SD
FPV	-	-	-	-	NR	ND	ND	EFV-SD FPV/r 1400/300 qd or 700/100 bid
LPV	-	-	-	-	-	ND	NVP-SD LPV/r 533/133 bid	EFV-SD LPV/r 533/133 bid
ATV	-	-	-	-	-	-	ND	EFV-SD + ATV/r 300/100 qd
TPV**								

* Doses are in mg; ND = Inadequate data; NR = Not recommended; SD = Standard dose;

**TPV must be combined with RTV and should not be combined with any other PI

Drug Table 5.
Drug Interactions: Contraindicated Combinations

Class	Contraindicated Agent	ART Agents	Alternatives
Ca++ channel blocker	Bepiridil	RTV, ATV, FPV, TPV	-
Antiarrhythmics	Flecainide, Propafenone	RTV, LPV/r, TPV	-
	Amiodarone, quinidine	RTV, IDV, TPV	
Lipid lowering	Simvastatin, Lovastatin	All PIs, DLV	Pravastatin or Fluvastatin, possibly Atorvastatin, Rosuvastatin
Antimycobacterials	Rifampin	All PIs; all NNRTIs except EFV	Use Rifabutin*
	Rifabutin	DLV, SQV (unless used with RTV)	-
	Rifapentine	All PIs, NVP, DLV, EFV	Rifampin or rifabutin
Antihistamine	Astemizole, Terfenadine	All PIs, DLV, EFV	Loratadine, Fexofenadine, Cetirizine, or Desloratidine
Antineoplastics	Irinotecan	ATV	-
GI	Cisapride	All PIs, DLV, EFV	-
	H2 blockers, proton pump inhibitors	DLV, ATV	
Neuroleptic	Clozapine	RTV	-
	Pimozide	All PIs	-
Psychotropic	Midazolam† Triazolam	All PIs, DLV, EFV	Temazepam, Lorazepam
	Alprazolam	DLV	
Ergot alkaloids	Ergotamine	All PIs, DLV, EFV	Consider Sumatriptan
Herbs	St. John's wort	All PIs & EFV, DLV, NVP	Alternative antidepressants
Miscellaneous	Fluticasone	RTV and all RTV/PI combinations	

* See Drug Table 7, pg 14 for Rifabutin and antiretroviral dose adjustments

† Midazolam may be used with caution as a single dose given for a procedure

Drug Table 6.
Drug Interactions: Nucleosides

Drug	AZT	d4T	ddl	TDF
Methadone	AZT AUC ↑ 43%; no dose change; monitor for AZT toxicity	d4T ↓ 27%; no dose change	-	No change in methadone or TDF levels
ddl	-	Magnifies toxicity Use with caution	-	ddl ↑ 44% Pt > 60 kg: 250 mg/d (ddl) Pt < 60 kg: 200 mg/d (ddl)
Ribavirin	Inhibits AZT activation; avoid if possible	No data	Magnifies ddl toxicity; avoid	No data
ATV	-	-	ddl EC: separate dosing due to food restrictions	Avoid concomitant use unless ATV combined with RTV
Cidofovir Ganciclovir Valgancyclovir	Ganciclovir + AZT ↑ marrow toxicity Monitor CBC	-	-	Combinations may decrease CrCl
LPV/r	No data	No data	No data	TDF AUC ↑ 34% Standard doses and monitor for TDF toxicity
TPV	AZT AUC ↓ 31–42% Right dose?	-	TPV Cmin ↓ 44% with ddl EC Separate by 2 hrs	

Drug Table 7.
Drug Interactions: Combinations with
PIs or NNRTIs Requiring Dose Modifications

Class	Agent	ART
Antifungal	Ketoconazole	IDV: IDV 600 mg tid
		RTV, LPV/r: Ketoconazole $\leq$ 200 mg/d, FPV $\leq$ 400 mg/d
		NVP: Not recommended
	Voriconazole	Current use with RTV ($\geq$ 400 mg/d) or EFV is contraindicated; no data for NNRTIs, NFV, ATV, TPV, FPV, LPV/r but bidirectional interaction anticipated; Monitor for toxicity; IDV is OK
	Itraconazole	IDV and TPV: itraconazole dose $\leq$ 200 mg or monitor levels
Oral contraceptives	-	Additional method of contraception recommended with: RTV, NFV, EFV, LPV/r, NVP, FPV. (IDV & ATV are OK)
		No data for SQV
Anticonvulsants	Phenobarbital, Phenytoin, Carbamazepine	Avoid carbamazepine + IDV and phenytoin + LPV; all other combinations of NNRTIs or PIs & designated anticonvulsants should be given with caution and monitoring of anticonvulsant levels or consider valproic acid
Methadone	-	NVP and EFV may decrease methadone substantially; monitor for withdrawal IDV has no interaction; other PIs may cause modest decrease in methadone levels and require monitoring for withdrawal Methadone decreases buffered ddl levels - consider ddl EC (no interaction).
Antibiotics	Clarithromycin	RTV, LPV/r, TPV, DLV: Decrease clarithromycin dose in renal failure.
		EFV, ATV: Consider alternative (e.g. azithromycin)
Erectile dysfunction	Sildenafil	PIs + DLV: $\leq$ 25 mg q48 h
	Vardenafil	PIs + DLV: $\leq$ 2.5 mg/d
	Tadalafil	PIs + DLV: $\leq$ 10 mg q72 h

Drug Table 7. – continued
Drug Interactions: Combinations with
PIs or NNRTIs Requiring Dose Modifications

Class	Agent	ART
Anti-mycobacterials	Rifabutin	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 q 8h + RBT 150 mg/d or 300 mg 3x/wk
		LPV/r 400/100 mg + RBT 150 mg qod or 3x/wk
		NFV 1000 mg tid + RBT 150 mg/d or 300 mg 3x/wk
		NVP standard + RBT standard
		RTV 600 mg bid + RBT 150 mg qod or 150mg 3x/wk
		RTV (maintain usual dose) + PI (standard dose) + RBT 150 mg qod or 3x/wk
	Rifampin	All PIs & NNRTIs contraindicated except EFV using standard doses of rifampin; consider EFV daily dose of 800 mg qd
Lipid Lowering	Lovastatin, Simvastatin	Avoid PIs and DLV; no data for EFV and NVP
	Atorvastatin	Atorvastatin levels ↑480%–SQV/RTV, 70%–NFV, 9x–TPV, 150%–FPV, 590%–LPV/r; ↓43% EFV; No data–IDV, ATV, NVP
	Pravastatin	Levels pravastatin ↑33%–LPV/r, ↓50% SQV/RTV; No data for other PIs or NNRTIs
Miscellaneous	Theophylline	RTV: Monitor theophylline levels
	Warfarin	RTV, DLV, EFV: Monitor INR closely if given with any PI or NNRTI
	Trazedone	RTV: lowest dose + monitor CNS signs
	Desipramine	RTV: Consider desipramine dose reduction
	Grapefruit juice	IDV↓, SQV↑
	Ca channel blockers	ATV, FPV, RTV: contraindicated Others: dose titration of Ca channel blockers + EKG monitoring
	Diltiazem	All PIs: Reduce diltiazem dose 50% + monitor EKG
	ABC Antacids	TPV↓ ABC levels 35–45%; ABC dose? ATV and TPV levels↓; give PI 2 hrs before or 1 hr after
	PPI	ATV: Avoid PPI

Antiretroviral Therapy

**Adult ART Table 1.
When to Start Therapy***

Clinical Category	CD4+ Count	Viral Load	Recommendation
Symptomatic (AIDS or severe symptoms)	Any value	Any value	Treat
Asymptomatic, AIDS	CD4+ < 200/mm ³	Any value	Treat
Asymptomatic	CD4+ > 200/mm ³ but < 350/mm ³	Any value	Offer treatment, but consider patient readiness, probability of adherence, potential side effects, and prognosis based on CD4 count, CD4 slope, and HIV viral load
Asymptomatic	CD4+ > 350/mm ³	> 100,000 c/mL	Consider therapy or observe (Data inconclusive for either alternative)
Asymptomatic	CD4+ > 350/mm ³	< 100,000 c/mL	Defer therapy and observe

* There are special considerations for pregnant women; consult Pregnancy Tables 1-3

**Adult ART Table 2.
Suggested Minimum Target Trough Levels**

Drug	Concentration
APV	400 mg/mL
IDV	100 mg/mL
LPV	1000 mg/mL
NFV	800 mg/mL
RTV	2100 mg/mL
SQV	100-250 mg/mL
EFV	1000 mg/mL
NVP	3400 mg/mL

Adult ART Table 3.
Starting Regimens for Antiretroviral Naïve Patients

NRTI-Based Regimens		# of pills per day
Preferred Regimens	efavirenz + (lamivudine or emtricitabine) + (zidovudine or tenofovir DF) – except for pregnant women or women with pregnancy potential	2–3
Alternative Regimens	• efavirenz + (lamivudine or emtricitabine) + (didanosine or stavudine or abacavir) - except for pregnant women or women with pregnancy potential	2–4
	• nevirapine + (lamivudine or emtricitabine) + (zidovudine or abacavir or tenofovir or stavudine* or didanosine) (Avoid in women with baseline CD4 > 250 and men with baseline CD4 > 400)	3–6
PI-Based Regimens		# of pills per day
Preferred Regimens	lopinavir/ritonavir + (lamivudine or emtricitabine) + zidovudine	6–7
Alternative Regimens	• atazanavir + (lamivudine or emtricitabine) + (zidovudine or stavudine* or abacavir or didanosine) or (tenofovir + ritonavir)	3–6
	• fosamprenavir + (lamivudine or emtricitabine) + (zidovudine or stavudine* or abacavir or tenofovir or didanosine)	5–8
	• fosamprenavir/ritonavir + (lamivudine or emtricitabine) + (zidovudine or tenofovir or didanosine or stavudine* or abacavir)	5–8
	• indinavir + ritonavir† + (lamivudine or emtricitabine) + (zidovudine or tenofovir or didanosine or stavudine* or abacavir)	7–12
	• nelfinavir + (lamivudine or emtricitabine) + (zidovudine or stavudine* or tenofovir or didanosine or abacavir)	5–8
	• saquinavir (Invirase) + ritonavir + (lamivudine or emtricitabine) + (zidovudine or stavudine* or tenofovir or didanosine or abacavir)	7–15
	• lopinavir/ritonavir + (lamivudine or emtricitabine) + (stavudine* or abacavir or tenofovir or didanosine)	5–7
Triple NRTI Regimen – As Alternative to PI- or NNRTI-based regimens		# of pills per day
Alternative Regimens	• abacavir + lamivudine + zidovudine	2

* Stavudine is associated with higher rates of lipodystrophy and mitochondrial toxicity than other NRTIs

† Low-dose (100–400 mg) ritonavir

Adult ART Table 4. Advantages and Disadvantages of Antiretroviral Regimens

	Advantages	Disadvantages
NNRTIs	Class– less lipodystrophy Save PI option Extensive experience	Low genetic barrier to resistance Class resistance / Drug interactions High rate of rash reactions
EFV	Potent Low pill burden qd Once daily dosing	CNS toxicity Teratogenic in first trimester
NVP	Extensive experience in pregnancy No food effect	ADR: hepatotoxicity + rash Contraindicated in women with baseline CD4 count >250
PI	Class– extensive experience Save NNRTI option	ADR– lipodystrophy Multiple drug interactions GI intolerance
ATV	Once daily dosing Low pill burden No hyperlipidemia	ADR: Jaundice + PR interval prolongation Drug interaction with TDF and EFV
LPV/r	Potency Coformulated with RTV	ADR: GI intolerance Reduced levels in pregnancy
FPV/r	Low pill burden No food effect Once daily dosing	ADR: skin rash
IDV/r	No food requirement bid dosing with RTV boosting	ADR: Nephrolithiasis Requirement for po fluid
NFV	Substantial experience in pregnancy	ADR: diarrhea High rate virologic failure Food requirement
SQV/r	Improved GI tolerance with Invirase	ADR: GI intolerance
NRTIs		
AZT/ 3TC/ ABC	Coformulated No food effect Preserves PI and NNRTI options	Higher rate of virologic failure if used alone ADR: ABC hypersensitivity
NRTI pairs		
AZT/ 3TC*	Extensive experience Coformulated No food effect	ADR: GI intolerance + narrow suppression (AZT) HBV flare when 3TC stopped
d4T/ 3TC*	No food effect Once daily	ADR of d4T ** HBV flare when 3TC stopped
TDF/ 3TC* or FTC	Well tolerated Once daily TDF + FTC coformulated	HBV flare when TDF, 3TC, or FTC stopped
ddI/ 3TC*	Once daily	ADR: ddI** Food effect HBV flare when 3TC stopped
ABC/ 3TC*	Once daily No food effect Coformulated	ADR: ABC hypersensitivity HBV flare when 3TC stopped

* FTC is similar to 3TC; has longer intracellular half life and has less extensive experience

** ADRs- d4T lipodystrophy, lactic acidosis, peripheral neuropathy; ddI- peripheral neuropathy, pancreatitis and lactic acidosis

Adult ART Table 5. Antiretroviral Regimens or Components That Are Not Generally Recommended

	Rationale	Exception
Antiretroviral Regimens Not Recommended		
Monotherapy	• Rapid development of resistance • Inferior antiretroviral activity when compared to combination with three or more antiretrovirals	Pregnant women with HIV-RNA <1,000 copies/mL using zidovudine monotherapy for prevention of perinatal HIV transmission
Two-agent drug combinations	• Rapid development of resistance • Inferior antiretroviral activity when compared to combination with three or more antiretrovirals	For patients currently on this treatment, it may be reasonable to continue if virologic goals are achieved
ABC + TDF + 3TC as a triple NRTI regimen	High rate of virologic failure and resistance	No exception
TDF + ddI + 3TC	High rate of virologic failure and resistance	No exception
TDF + ddI + NNRTI	High rate of virologic failure Possible reduced CD4 response	No exception
Antiretroviral Components Not Recommended As Part of Antiretroviral Regimen		
Saquinavir hard gel capsule (Invirase) as single PI	• Poor oral bioavailability (4%) • Inferior antiretroviral activity when compared to other protease inhibitors	No exception
d4T + ddI	Reports of serious, even fatal, cases of lactic acidosis with hepatic steatosis	When no other antiretroviral options are available and potential benefits outweigh the risks*
ATV + IDV	Potential for additive hyperbilirubinemia	No exception
FTC + 3TC	No potential benefit	No exception
Efavirenz in pregnancy	Teratogenic in nonhuman primate	When no other antiretroviral options are available and potential benefits outweigh the risks*

Adult ART Table 5. – continued
Antiretroviral Regimens or Components That Are
Not Generally Recommended

	Rationale	Exception
Antiretroviral Components Not Recommended As Part of Antiretroviral Regimen (continued)		
Amprenavir oral solution in: • pregnant women • children <4 yr old • patients with renal or hepatic failure • patients treated with metronidazole or disulfiram	Oral liquid contains large amount of the excipient propylene glycol, which may be toxic in the patients at risk	No exception
d4T + ZDV	Antagonistic	No exception
ddC + d4T or ddC + ddI	Additive peripheral neuropathy	No exception
ATV + IDV	Additive hyperbilirubinemia	No exception
FTC + 3TC	Similar agents; no potential benefit	No exception
Hydroxyurea	• Decreases CD4 count • Augments d4T- and ddI-associated side effects, such as pancreatitis & peripheral neuropathy • Inconsistent evidence of improved viral suppression • Contraindicated in pregnancy (Pregnancy Category D)	No exception
Not Recommended As Part of Initial Antiretroviral Regimen		
DLV	Modest antiretroviral effect	*
RTV as single PI	GI intolerance	*
d4T + ddI	Increased peripheral neuropathy, lactic acidosis, and pancreatitis	*
NFV + SQV	High pill burden of 16-22 caps/day	*
TPV	Tested and approved only for salvage	*

* Reasonable to use in unusual circumstances

Adult ART Table 6. Laboratory Monitoring

- Baseline tests, CBC, chemistry profile including liver and renal function tests, PAP smear for female patients, *Toxoplasma gondii* IgG, VDRL (or RPR), anti-HCV, anti-HBc, and PPD (if no prior positive, see TB tables)
- Confirm HIV Ab + if not documented
- Viral load at baseline (x2) and 2-8 wks after initiating therapy or new regimen, then every 3-4 months, clinical event, or significant (3x or $> 0.5 \log_{10}$ c/mL) change in VL
- CD4 count at baseline and then every 3-6 months
- Antiretroviral agent toxicity (see Drug Table 2, pg 8)
- Resistance tests

Recommended

- Virologic failure within 4 weeks of stopping ART
- Suboptimal suppression
- Acute HIV infection

Consider

- Chronic HIV infection, before therapy

Not Usually Recommended

- After discontinuation of drugs for more than 4 weeks
- Viral load $< 1,000$ c/mL

**Adult ART Table 7.
Resistance Mutations***

Drug	Major †	Minor †
Protease Inhibitors		
IDV	46 IL, 82 AFT, 84 V	10 IRV, 20 MR, 24 I, 32 I, 36 I, 54 V, 71 VI, 73 SA, 77 I, 90 M
NFV	30 N, 90 M	10 FI, 36 I, 46 IL, 71 VL, 77 I, 82 AFTS, 84 V, 88 DS
RTV	82 AFTS, 84 V	10 FIRV, 20 MR, 32 I, 33 F, 36 I, 46 IL, 50 V, 54 VL, 71 VT, 77 T, 90 M
SQV	48 V, 90 M	10 IRV, 54 VL, 71 VT, 73 S, 77 I, 82 A, 84 V
FPV	50 V, 84 V	10 FIRV, 32 I, 46 IL, 47 V, 54 LVM, 73 S, 82 AFST, 90 M
LPV/r	32 I, 47 VA, 82 AFTS	10 FIVR, 20 MR, 24 I, 31 I, 33 F, 46 IL, 50 V, 53 L, 54 VLAMTS, 63 P, 71 VT, 73 S, 90 M
ATV	50 L, 84 V, 88 S	10 IFV, 16 E, 20 RMI, 24 I, 32 I, 33 IFV, 36 ILV, 46 I, 48 V, 54 LVMT, 60 E, 62 V, 71 VITL, 73 CSTA, 82 A, 90 M, 93 L
TPV	33 I, 82 LT, 84 V	10 IV, 13 V, 20 MR, 35 G, 36 I, 43 T, 46 L, 47 V, 54 AMV, 58 E, 69 K, 74 P, 83 D, 90 M, 46 I, 54 V

* Adapted from IAS-USA Topics HIV Med 2005; 13:125. See <http://www.iasusa.org>

† **Major**: usually develop first; associated with decreased drug binding; **Minor**: also contribute 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.

**Adult ART Table 7. – continued
Resistance Mutations***

Drug	Codon Mutations
Nucleosides and Nucleotides	
AZT	41 L, 44 D, 67 N, 70 R, 118 I, 210 W, 215 YF, 219 Q
d4T	41 L, 44 D, 65 R, 67 N, 70 R, 118 I, 210 W, 215 YF, 219 QE
3TC	65 R, 184 VI
FTC	65 R, 184 VI
ddI	65 R, 74 V
ABC	65 R, 74 V, 115 F, 184 V
TDF	65 R
Multinucleoside A- Q 151 M	62 V, 75 I, 77 L, 116 Y, 151 M
Multinucleoside B 69 insertion	41 L, 67 N, 69 insert, 70 R, 210 W, 215 YF, 219 QE
Multinucleoside TAMS	41 L, 67 N, 70 R, 210 W, 215 YF, 219 QE
NNRTIs	
NVP	100 I, 103 N, 106 AM, 108 I, 181 CI, 188 CLH, 190 A
DLV	103 N, 106 M, 181 C, 188 L, 236 L
EFV	100 I, 103 N, 106 M, 108 I, 181 CI, 188 L, 190 SA, 225 H
Multi-NNRTI resistance	103 N, 106 M, 188 L
Multi-NNRTI resistance-accumulation	100 I, 106 A, 181 CI, 190 SA, 230 L

* Adapted from IAS-USA Topics HIV Med 2005; 13:125. See <http://www.iasusa.org>

Definitions

Virologic Failure:

- Failure to achieve VL < 400 c/mL by 24 wks or < 50 c/mL by 48 wks. Note: Most patients will have a decrease in VL of $\geq 1 \log_{10}$ c/mL at 1–4 weeks
- Viral suppression followed by repeated positive viral load

Immunologic Failure:

Failure to increase CD4 count 25-50 cells/mm³ during first year

Note: Mean increase is about 150 cells/mm³ in a year with HAART in treatment naïve patients

Clinical Failure:

Occurrence or recurrence of HIV-related event ≥ 3 months after start of HAART

Note: Must exclude immune reconstitution syndromes

Management of Regimen Failure

Assessment

- Adherence: Address cause and/or simplify regimen
- Tolerability
 - Change one drug within class
 - Change classes; e.g. PI-based HAART vs NNRTI-based HAART
- Pharmacokinetic Issues

Virologic Failure

Definition:

- 1) HIV RNA > 400 c/mL (VL) after 24 weeks of treatment
- 2) VL > 50 c/mL after 48 weeks of treatment
- 3) Viral load detectable after achieving undetectable (viral rebound) VL indicating failure should be confirmed; “Blips” (isolated VL values of 50–1,000 c/mL) do not constitute failure if unconfirmed

Assessment:

- Review treatment history and prior resistance tests
- Assess adherence, intolerance and pharmacokinetic issues (food/fasting requirements, drug interactions, malabsorption)
- Distinguish between limited, intermediate, and extensive prior treatment and drug resistance
- The viral load that defines an indication for therapeutic intervention is in the range of 400–5000 c/mL; The threshold of 400 may result in multiple drug exposures and limited access to resistance tests (since a threshold of 1000 c/mL is often required to do the test); a delay to a threshold of 5000 c/mL risks accumulation of multiple resistance mutations including class resistance
- Perform resistance tests while the patient is receiving the failed regimen or within 4 weeks of stopping it
- Identify 2–3 active drugs for the next regimen; two active drugs are essential for viral suppression
- If no resistance is demonstrated: consider continuation with emphasis on adherence, possibly with therapeutic drug monitoring
- With low level viremia (< 5000 c/mL) and limited drug exposure consider boosting a PI, or intensification by adding a nucleoside or change therapy
- With intermediate or extensive prior drug exposure, consider an agent with a new mechanism of action (enfuvirtide) usually combined with a PI including TPV or an experimental drug such as TMC 114
- With extensive treatment failures, multiple resistance mutations and no available regimens likely to achieve virologic goals: the goal of therapy is to preserve immune function and avoid HIV-associated complications; HIV therapy should be continued

Adult ART Table 8. Methods to Achieve Readiness to Start HAART & Maintain Adherence

Patient-related

- Negotiate a plan or regimen that the patient understands and to which she or he commits
- Take time needed, > 2 visits, to ensure readiness before 1st 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 answering 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 9.
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 ≥160 mg/dL	LDL >190 mg/dL (LDL 160-190 Drug therapy optional)
No CHD & ≥ 2 Risks*	LDL <100 mg/dL	LDL ≥130 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 < 70 mg/dL	LDL ≥100 mg/dL	LDL >130 mg/dL (100-129 mg/dL: drug optional)
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 CHD • 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 NCEP – *Circulation* 2004; 110:227.

Editors Note: This table is a basic condensation of complex guidelines. Readers are encouraged to consult and use the tools available on the NHLBI web site: <http://www.nhlbi.nih.gov/guidelines/cholesterol/>

* CHD Risk Factors: Age (men >45 years; women >55 yrs or premature menopause without estrogen replacement); hypertension, current smoking, history of cardiovascular disease in first degree relative (<55 years for male relative and <65 years 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 NHLBI website: <http://www.nhlbi.nih.gov/guidelines/cholesterol/index.htm>

Adult ART Table 10. Drug Therapy for Hyperlipidemia

(Recommendations of the ACTG [Dube MP et al, CID 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/day (max. 40 mg/day), fluvastatin 20-40 mg/day, or atorvastatin 10 mg/day. Use particular caution when giving LPV/r or NFV with Atorvastatin; also see Table 5. Drug Interactions: Contraindicated Combinations.

† Fibrate: Gemfibrozil 600 mg bid $\geq$ 30 minutes before meal or Fenofibrate tablets (e.g. Tricor) 160 mg qd Micronized fenofibrate (capsules) 67mg qd to start, max. dose 201 mg qd

Antiretroviral Therapy in Pregnancy

Continually updated recommendations:

US Department of Health and Human Services. *Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the U.S.*

November 17, 2005. Available at: <http://aidsinfo.nih.gov>.

Recommendation for antiretroviral drugs in pregnancy:

All pregnant women with HIV infection should be treated.

Goal of therapy:

VL < 1000 c/mL

Regimen:

See Pregnancy Table 1

Pregnancy Table 1. Preferred Antiretroviral Agents

NRTI Class

- Preferred: AZT/3TC
- Alternates: ddI, FTC, d4T, ABC
- Insufficient data: TDF
- Not recommended: ddC

NNRTI Class

- Preferred: NVP (if baseline CD4 is < 250/mm³)
- Not recommended: EFV and DLV

PI Class

- Recommended: NFV (1250 mg bid), SQV/r (1000/100 mg bid)
- Alternatives: IDV, LPV/r, RTV
- Insufficient data: APV, FPV, ATV, TPV

Entry Inhibitor Class

- Insufficient data: ENF

Pregnancy Table 2.

Antiretroviral Agents: Pharmacokinetic and Toxicity Data*

Agent	FDA cat.**	Experience in Pregnancy
Nucleoside/nucleotide reverse transcriptase inhibitors		
ABC	C	No studies; concern for hypersensitivity
ddl	B	Well tolerated; usual pharmacokinetics; concern for lactic acidosis; avoid ddl + d4T
FTC	B	No studies
3TC	C	Well tolerated; usual pharmacokinetics
d4T	C	Well tolerated; usual pharmacokinetics; concern for lactic acidosis; avoid ddl + d4T
TDF	B	No studies; animal studies show bone abnormalities
ddC	C	No studies; teratogenic in animals
ZDV	C	Well tolerated; preferred agent
Non-nucleoside reverse transcriptase inhibitor		
DLV	C	No studies
EFV	D	Teratogenic; 4/142 birth defects; avoid in 1st trimester
NFV	C	Well tolerated; contraindicated as initial Rx with CD4 > 250; single dose with labor causes high rates of resistance
Protease inhibitors		
APV	C	No studies; oral solution is contraindicated
ATV	B	No studies; theoretical concern for elevated indirect bilirubin
FPV	C	No studies
IDV	C	Low levels and theoretical concern for elevated indirect bilirubin
LPV/r	C	No studies
NFV	B	Well tolerated; extensive experience; use 1250 mg bid
RTV	B	No studies
SQV	B	Levels are low: use SQV: RTV 800/100 mg bid or 1000/100 mg bid
TPV	C	No studies

* June 23, 2005

** Pregnancy categories: A=Controlled studies show no risk
 B=No evidence of risk in humans
 C=Risk cannot be excluded
 D=Positive evidence of risk

Pregnancy Table 3. Antiretroviral Drugs for Delivery

A. ACTG 076 Protocol (Should be used as part of ART regimen in all pregnant women, if possible)

Antepartum: AZT 300 bid or 200 tid po, wk 14 until delivery

Intrapartum: AZT IV 2 mg/kg over first hr then 1 mg/kg/hr until delivery

Postpartum: (Infant): AZT syrup 2 mg/kg po q 6h (or 1.5 mg/kg q 6h IV) x 6 wks

B. Regimen for 2nd & 3rd Trimesters

Standard ART, but:

- Include AZT * according to 076 protocol
- Treat based upon maternal clinical/immunologic status but avoid: EFV, HU, AZT & d4T, d4T & ddI, APV solution
- Previously untreated pregnant women with VL <1000 c/mL and CD4 >350 cells/mm³ may be treated with AZT monotherapy, AZT + 3TC, or HAART

C. Choices for Untreated Women Presenting In Labor and Their Infants

NVP: 200 mg po onset labor; **Infant:** single 2 mg/kg po at 48-72 hrs

AZT: 600 mg po onset labor and 300 mg po q3h until delivery PLUS 3TC 150 mg po onset labor and 150 mg po q12h until delivery; **Infant:** AZT 4mg/kg po q12h PLUS 3TC 2mg/kg po q12h for 7 days

AZT: 2mg/kg IV bolus then 1mg/kg/hr IV infusion until delivery; **Infant:** AZT 2mg/kg po q6h for 6 wk (ACTG 076 Protocol)

NVP + AZT: NVP:200 mg po onset labor PLUS AZT 2mg/kg IV bolus then 1 mg/kg/hr IV infusion until delivery; **Infant:** NVP single 2 mg/kg po at 48-72 hrs PLUS AZT 2mg/kg po q6h for 6 wk

* Unless unacceptable side effects or toxicity or requires d4T-containing regimen

** **AZT & d4T:** pharmacologic antagonism; do not use together. **APV** oral solution (only) is contraindicated in pregnancy because it contains large quantities of propylene glycol, which cannot be metabolized in pregnancy. **d4T & ddI:** concerns about lactic acidosis; use only when other NRTIs have failed or caused unacceptable side effects/toxicity (*New Engl J Med* 1999; 340:1723). **EFV, HU:** concerns about teratogenicity or birth defects; **EFV:** avoid in pregnancy.

Drug Information

A listing of antiretroviral drugs with information pertinent to their use in pregnancy may be found in **Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States, Table 3.**

Pregnancy Table 4. Pregnancy Issues

Adverse Drug Reactions (ADR)

Generally, pregnant women are at the same risk of ADRs as non-pregnant individuals, but some ADRs may be more common because of pregnancy-related physiologic changes: anemia (iron & folate deficiency), nausea & vomiting (esp in 1st trimester), amniotransferase elevation. PIs may exacerbate pregnancy-related risk of hyperglycemia and NRTIs (especially d4T/ddI) increase risk of lactic acidosis.

Risk for Perinatal HIV Transmission

Viral load in plasma & genital tract (most significant), primary infection or late stage HIV, low CD4 count, STDs/other co-infections, pre-term delivery, increasing duration of membrane rupture, placental disruption, invasive fetal monitoring or assessment, vaginal delivery, and lack of AZT prophylaxis.

Post-Partum Risk

Breast feeding: not recommended in U.S.

Pregnancy Table 5. Clinical Scenarios and Management of Untreated Pregnant Patients Including C-Section

Scenario 1: No prior ART

- Standard lab and clinical care
- HAART for VL > 1000 c/mL
- Include the 3-part 076 protocol (see Pregnancy Table 3A)
- Consider delay initial therapy until after 1st trimester

Scenario 2: Currently receiving ART

- Continue therapy, but include AZT according to 076 protocol (see Pregnancy Table 3A)
- Option to stop in 1st trimester

Scenario 3: Woman in labor no prior therapy—options are:

- Intrapartum AZT and 6-week course for neonate
- AZT/3TC during labor and 3 weeks for neonate
- Single dose NVP intrapartum and single dose for infant
- Two-dose NVP and intrapartum AZT and 6 weeks AZT for newborn

Scenario 4: Woman has delivered

- Discuss HIV detection and implications
- Offer AZT to infant
- The mother should be evaluated for HIV management

Pregnancy Table 6. Clinical Scenarios and Management of Treated Pregnant Patients Including C-Section

Time of Presentation	Recommended Management
Early In Pregnancy (< 36 Weeks)	- Continue ART with standard monitoring, but: - May consider discontinuation during 1st trimester: all drugs should be stopped and restarted simultaneously to reduce risk of resistance - Include AZT if tolerated; see cautions for antiretrovirals, Pregnancy Table 3 footnotes
Late In Pregnancy (≥ 36 Weeks)	- Continue antiretroviral therapy including AZT without interruption during labor and delivery - VL $> 1,000$ copies/mL: Counsel that C-section is likely to reduce the risk of transmission to infant, but counsel about risks and benefits of all choices
C-Section Planned But Presents in Labor or With Ruptured Membranes	- Initiate ACTG 076 Protocol, Intrapartum in Pregnancy Table 3A - Rapid progression of labor: vaginal delivery - If long labor anticipated: consider C-section after loading dose of AZT or give pitocin to expedite delivery

Pregnancy Table 7. Delivery Procedures and Therapy

Procedure	Therapy
Cesarean Section	- Schedule for 38 wk - If on ART, IV AZT starting 3 hrs before C-section and continue all other antiretroviral drugs with the exception of d4T - Infant: Use ACTG 076 Protocol, Postpartum (infant) in Pregnancy Table 3A
Vaginal Delivery	- If on ART give IV AZT with initiation of labor and continue all other antiretroviral drugs with the exception of d4T - Avoid rupture of membranes, fetal scalp electrodes, forceps delivery, and vacuum extractor - Infant: If TREATED mother, use ACTG 076 Protocol, Postpartum (infant) in Pregnancy Table 3A If UNTREATED mother, use treatment from Pregnancy Table 3C which matches maternal regimen

Antiretroviral Pregnancy Registry: www.APRegistry.com

1011 Ashes Dr, Wilmington NC 28405

Telephone: 800-258-4263

Fax: 800-800-1052

Prevention of HIV for Providers in Three Steps

Step 1: Screen Patients for Risk Behaviors

- Behaviors and clinical factors associated with HIV, other STDs, and IV drug use (every visit)
- STD symptoms: most are asymptomatic (every visit)
- Pregnancy
- Screening tests

Patients	Test
Routine	
• All patients	• Syphilis serology: RPR or VDRL*
• All women	• Trichomonas wet mount or culture
• All women ≤ 25 years and sexually active	• Cervical specimen for <i>C. trachomatis</i>
Consider	
• All men and women not included above	• Screening for GC and <i>C. trachomatis</i> by urethral (men) or cervical (women) specimen or first catch urine for NAAT*
• Anal receptive sex	• Anal swab for GC culture and, if available, for <i>C. trachomatis</i>
• Oral receptive sex	• Pharyngeal culture for GC
• Possible pregnancy	• Pregnancy test

* Repeat RPR or VDRL annually. Consider repeating screening tests for *N. gonorrhea* and *C. trachomatis* annually or more frequently if sexually active, if screening previous 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). If sex with persons with unknown or negative serologic status, stress proper condom use.

- IDU

Stop using drugs

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>)
- 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

- Per act relative risks of HIV transmission

- Condom vs no condom: 1:20
- Compared to insertive vaginal sex: receptive vaginal sex 2:1, receptive anal sex 10:1, insertive fellatio 1:10, insertive anal sex 1.3:1, receptive fellatio 1:5 (STD 2002;29:38)

Note: Risks for condom use and acts are multiplicative; e.g, for the ratio for anal sex without a condom vs vaginal insertive sex with a condom is 100:1

- Viral load: each $\log_{10}$ reduction in viral load reduces probability of transmission 2.5 fold.
- Non-occupational postexposure prophylaxis: not endorsed by CDC due to “uncertain effectiveness.”
- HAART recipients: decreases in VL probably reduces but risk transgression in behavior eliminates this benefit; with structured treatment interruption, warn patient that viral load increases as does 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 needlesharing partners have been notified
- **Follow-ups:** Ask about new sex or needlesharing partners who have not been notified
- **Referrals:** All contacts should be referred to the Health Department; 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

Adult OI Table 1.
2001 USPHS/IDSA Guidelines for Prevention of Opportunistic Infections

Pathogen	Episode	Indication*	First Choice	Alternatives	Comment
Strongly Recommended					
<i>P. carinii</i>	1 ^o & 2 ^o	Primary CD4 < 200 or CD4 % < 14, thrush, hx AIDS defining illness or FUI Secondary Hx PCP unless immune reconstitution: see comment	TMP-SMX 1 DS/d † or TMP-SMX 1 SS/d †	Dapsone 100 mg/d or Dapsone 50 mg/d + pyrimethamine 50 mg/wk + leucovorin 25 mg/wk or Dapsone 200 mg + pyrimethamine 75 mg + leucovorin 25 mg/wk or Aerosol pentamidine 300 mg/mo or Atovaquone 1500 mg/d or TMP-SMX 1 DS† 3x /wk	Immune reconstitution recommendations: Discontinue primary & secondary prophylaxis if CD4 > 200 cells/mm³ for ≥ 3 mos Restart Prophylaxis: Restart prophylaxis if CD4 decreases to < 200 cells/mm³
Tuberculosis		See Adult OI Tables 2 and 3			

Toxoplasmosis	1 ⁰	+ anti-Toxoplasma IgG and CD4 <100 cells/mm ³	TMP- SMX 1 DS + qd	TMP- SMX 1 SST qd or Dapsone 50 mg/d + pyrimethamine 50 mg/wk + Leucovorin 25 mg/wk or Dapsone 200 mg/wk + pyrimethamine 75 mg/wk + Leucovorin 25 mg/wk or Atovaquone 1500 mg/d ± pyrimethamine 25 mg/d + Leucovorin 10 mg/d	Immune reconstitution recommendations: Discontinue if CD4 >200 cells/mm ³ for ≥ 3 mos Restart Prophylaxis: CD4 falls to <100-200 cells/mm ³
	2 ⁰	Toxo tx unless immune reconstitution: see comment	Sulfadiazine 500-1000 mg qid + Pyrimethamine 25-50 mg/d + Leucovorin 10-25 mg/d	Clindamycin 300-450 mg q 6-8 hr + Pyrimethamine 25-50 mg/d + Leucovorin 10-25 mg/d or Atovaquone 750 mg q 6-12 hr + Pyrimethamine 25 mg/d + Leucovorin 10 mg/d	Immune reconstitution recommendations: Discontinue if HAART 6-12 mos, CD4 >200 cells/mm ³ , and asymptomatic Restart Prophylaxis: CD4 falls to <200 cells/mm ³
Mycobacterium avium complex	1 ⁰	CD4 <50 cells/mm ³	Azithromycin 1200 mg/wk Clarithromycin 500mg bid	Rifabutin†300 mg/d or Azithromycin 1200 mg / wk + Rifabutin† 300 mg/d	Immune reconstitution recommendations: Discontinue if CD4 >100 cells/mm ³ for ≥ 3 mo
	2 ⁰	Hx MAC disease	Clarithromycin 500 mg bid + Ethambutol 15 mg/kg/d ± Rifabutin† § 300 mg/d	Azithromycin 500 mg/d + Ethambutol 15 mg/kg/d ± Rifabutin† 300 mg/d	Immune reconstitution recommendations: Discontinue if CD4 >100 cells/ mm ³ x >6 mo and Rx 12 mo and asymptomatic

Adult OI Table 1. – continued
2001 USPHS/IDSA Guidelines for Prevention of Opportunistic Infections

Pathogen	Episode	Indication*	First Choice	Alternatives	Comment
Varicella	1 ^o	Chickenpox /shingles exposure + susceptible (no history of disease and varicella seronegative)	VZIG 5 vials (6.25 mL) IM <96 h post exposure		Acyclovir has been removed from OI prophylaxis guidelines due to lack of documented efficacy
Cryptococcosis	2 ^o	Hx Cryptococcal meningitis	Fluconazole 200 mg po qd	Amphotericin B 0.6-1.0 mg/kg iv qw-tiw or itraconazole 200 mg capsule po qd	Immune reconstitution recommendations: Discontinue if CD4 >100 X 6 mo and completed initial Rx and asymptomatic
Cytomegalovirus	2 ^o	Prior end-organ disease	Extra ocular: ganciclovir 5 mg/kg/day IV 5-7 days/wk, valganciclovir 900 mg/d, or foscarnet 90mg/kg IV qd or cidofovir 5 mg/kg q 2 weeks For retinitis: ganciclovir sustained release implant q 6-9 months plus valganciclovir 900mg/d or ganciclovir or foscarnet (above doses)	Cidofovir 5 mg/kg IV qow with probenecid 2 grams po 3 hours before the dose followed by 1 gram po 2 hours after the dose, and 1 gram po 8 hours after the dose (total of 4 grams) or Fomivirsen 1 vial (330µg) injected into the vitreous, then repeated every 2-4 wks or Valganciclovir 900 mg po qd	Immune reconstitution recommendations: Discontinue if CD4 >100-150 X 6 mo + no active disease + negative ophthalm exam

Generally Recommended					
<i>S. pneumoniae</i>	1 ⁰	All Patients with CD4 > 200	Pneumovax	None	Immune reconstitution: Consider reimmunization if CD4 increases to >200 and initial immunization was given when CD4 <200
Hepatitis B	1 ⁰	Susceptible- (anti-HBc negative)	HBV vaccine series	None	
Influenza	1 ⁰	All patients	Influenza vaccine	Rimantidine 100 mg bid Amantadine 100 mg bid Oseltamivir 75 mg qd	
Hepatitis A	1 ⁰	Susceptible- (anti-HAV neg) and anti-HCV positive	Hepatitis A vaccine series	None	

* Indication is separately defined for:

1⁰ = Primary: No prior infection with this pathogen

2⁰ = Secondary: Prior infection with this pathogen

† SS= Single strength tablet, DS=double strength tablet

‡ Dose adjusted for concurrent PI/NNRTI

§ Rifabutin reduces levels of clarithromycin by 50% (consider azithromycin if RBT is used)

¶ Added Rx needed to protect the contralateral eye and other organ systems

Tuberculosis and HIV

Latent TB and HIV Co-infection Candidates For Testing

- All HIV-infected patients without prior positive PPD 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

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

- Positive PPD (≥ 5 mm induration) 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 weeks after last exposure to TB case; those placed on prophylaxis should be discontinued if PPD negative at 12 weeks)
- History of inadequately treated TB that healed

Patients meeting skin test positivity criteria should be evaluated to rule out active TB disease before initiating treatment

Adult OI Table 2. Recommended Drug Regimens for Treatment of Latent TB in HIV Co-infected Adults			
	Regimen	Adult Dosage (max)	Criteria for Completion
Preferred Regimens			
All patients	INH daily for 9 mos	300 mg qd + pyridoxine 50 mg qd	270 doses within 9 mos (up to 12 mos with interruptions)
	INH twice-weekly for 9 mos	900 mg + pyridoxine 100 mg 2x/wk	76 doses within 9 mos (up to 12 mos with interruptions)
Alternative Regimen			
Contacts of isoniazid-resistant, rifampin-susceptible TB	RIF daily for 4 mos†	RIF 10 mg/kg (600 mg) RBT is alternative if patient is receiving HAART*	120 doses within 6 mos
8 week regimen: PZA + RIF	No longer recommended due to excessive hepatotoxicity including 7 deaths (not in persons known to have HIV co-infection) MMWR 2003;52:735		

Abbreviations: INH = isoniazid, RIF = rifampin, RBT = rifabutin, PZA = pyrazinamide, DOT = directly observed therapy

* See Drug Table 7 for RBT & PI/NNRTI dose adjustments

† May not be used with patients taking PI/NNRTI with the exception of RTV/SQV, RTV, or EFV

Adult OI Table 3.
Monitoring of Patients on Latent TB Prophylaxis

Latent TB Regimen	Monitoring
All patients	• Initial clinical evaluation • Educate patients about side effects associated with LTBI treatment • Advise to stop treatment and promptly seek medical evaluation if these occur
INH	• Contact with patient monthly; LFTs at baseline and 3 mo* and with hepatitis sx • Include careful questioning about side effects and a brief physical examination checking for evidence of hepatitis or other side effects
Rifampin or rifabutin + PZA	• Clinic visits at 2,4,6, & 8 wks; CBC & LFTs at baseline, 2,4, & 6 wks or with symptoms† • Include careful questioning about side effects and a brief physical examination checking for evidence of hepatitis or other side effects

* INH: D/C if ALT 5X ULN or symptoms plus ALT $\geq$ 3X ULN

† Rifampin/rifabutin + PZA: D/C if ALT $\geq$ 5X ULN or if symptoms plus any abnormal LFTs

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

Special Treatment Notes

PREGNANCY: INH regimens preferred for pregnant women. Some experts would use RIF plus PZA as alternate regimen in HIV-infected pregnant women. PZA should be avoided during first trimester.

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.

ART/TB Treatment Interactions

* Rifabutin should not be used with hard-gel saquinavir (as sole PI) or delavirdine.

Rifampin/Rifabutin

See Drug Table 7

Identical for General Population Except:

- CD4 < 100/mm³: Continuation phase should be daily or 3x/week; once weekly rifapentine regimen should not be used
- Positive cultures at 2 months: "Strongly consider" 7 month continuation phase (total 9 mo)
- In absence of prior HIV therapy and CD4 < 350/mm³: delay antiretroviral drugs for 4-8 weeks
- RIF may be used with 2 NRTIs + EFV, RTV + SQV (Invirase or Fortovase) or AZT/3TC/ABC
- Rifabutin combined with other PIs and NNRTI requires dose adjustment of both; See: www.cdc.gov/nchstp/tb/ or www.medscape.com/updates/quickguide
- When starting NNRTI or PI in patient receiving RIF, substitute rifabutin 2 weeks prior to NNRTI or PI to give a 2 week washout period for RIF
- Paradoxical reaction: Frequency is 7-36%; clinical features: high fever, increased adenopathy, CNS lesions, pulmonary infiltrates and pleural effusions; treatment: symptomatic; if severe give prednisone 1 mg/kg and reduce dose at 1-2 weeks

**Adult OI Table 4.
Treatment of Drug-Susceptible TB**

Drugs	Phase 1 (8 weeks)	Phase 2*: regimen, doses, minimal duration
INH RIF PZA EMB	8 weeks • 7 d/wk for 8 wks (56 doses) or • 5 d/wk for 8 wks (40 doses)	• INH/RIF 7 d/wk for 18 weeks (126 doses) or • INH/RIF 5 d/wk for 18 weeks (90 doses) or • INH/RIF 2x/wk for 18 weeks (36 doses)
INH RIF PZA EMB	2 wk/6 week 7 d/wk, for 2 wks (14 doses), then 2x/week for 6 wks (12 doses)	INH/RIF 2x/wk for 18 weeks (36 doses)
INH RIF PZA EMB	8 weeks 3 x/week for 8 weeks (24 doses)	INH/RIF 3x/week for 18 weeks (54 doses)
INH RIF EMB	8 weeks • 7 d/week for 8 wks (56 doses) • 5 d/week for 8 wks (40 doses)	• INH/RIF 7 d/week for 31 weeks (217 doses) or • INH/RIF 5 d/wk for 31 weeks (155 doses) or • INH/RIF 2x/wk for 31 weeks (62 doses)

INH = isoniazide, RIF = rifampin, RPT = rifapentine, PZA = pyrazinamide, EMB = ethambutol

* Patients with cavitation at baseline and positive cultures at 2 months should receive 31 week continuation phase for total of 9 months

Adult OI Table 5.
Doses of Antituberculosis Drugs – First-line Drugs

Drug	Daily	1/wk	2x/wk	3x/wk
INH	5 mg/kg (300)*	15 mg/kg (900)	15 mg/kg (900)	15 mg/kg (900)
RIF	10 mg/kg (600)	-	10 mg/kg (600)	10 mg/kg (600)
RPT	-	-	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	-	2000 mg	1200 mg
56-75 kg	1200 mg	-	2800 mg	2000 mg
76-90 kg	1600 mg	-	4000 mg	2400 mg

*Dose in mg/kg and (usual dose in mg)

Adult OI Table 6. Management of Opportunistic Infections (MMWR 2004; 53 RR 15)

***Bartonella*: Treat ≥ 3 mo**

- Preferred: erythromycin 500 mg qid po or IV or doxycycline 100 mg bid po or IV x ≥ 3 mo
- Alternative: azithromycin 600 mg/d po or clarithromycin 500 mg bid po x ≥ 3 mo
- Note: If relapse: treat lifelong; CNS: Use IV or po doxycycline

***Candida* Thrush: Treat 7–14 days**

- Preferred: clotrimazole troches 10 mg po 5x/d or Nystatin susp 5 mL qid or pastilles 4–5 x/d or fluconazole 100 mg po/d; all 7–14 days
- Fluconazole–refractory: Itraconazole oral solution ≥ 200 mg/d po or amphotericin B 0.3 mg/kg/d IV
- Recurrent disease: Consider chronic fluconazole or itraconazole

***Candida* Esophagitis: Treat 14–21 days**

- Preferred: Fluconazole 100 mg/d (up to 400 mg/d) po or IV x 14–21 days
- Alternative: Itraconazole oral soln 200 mg/d, capsosungin 70 mg IV x 1, then 50 mg/d x 7 days or amphotericin B 0.3–0.7 mg/kg/d or voriconazole 200 mg/d po or IV or liposomal amphotericin 3–5 mg/kg/d

***Candida* Vaginitis: Treat 3–7 days**

- Preferred: Topical azole (clotrimazole, butoconazole, miconazole, tioconazole, terconazole) x 3–7 days or topical nystatin or fluconazole 150 mg x 1 day or itraconazole 200 mg bid x 1 day or 200 mg/d x 3 days
- Recurrent: Daily topical azole

***Cryptococcosis*: Treat lifetime unless immune reconstitution**

- Acute phase: Amphotericin B 0.7 mg/kg/d IV + flucytosine 25 mg/kg qid po x 14 days
- Consolidation phase: Fluconazole 400 mg/d po x 8 weeks
- Chronic maintenance phase: Fluconazole 200 mg/d po until CD4 > 100–200/mm³ x ≥ 6 mo
- Alternative — Acute phase: Amphotericin B 0.7 mg/kg/d x 14 days (without 5FC) or fluconazole 400–800 mg po or IV qd ± flucytosine 25 mg/kg/ qid po
- Alternative — Consolidation phase: Itraconazole 200 mg bid po
- Alternative — Chronic maintenance phase: Itraconazole 200 mg/d po until CD4 > 100–200/mm³ x ≥ 6 mo
- Note: Drain CSF if OP > 200 mL H₂O

Cryptosporidiosis

- Preferred: Symptomatic treatment + HAART
- Alternatives: Nitazoxanide 500 mg po bid or paromomycin 25–35 mg/kg/d in 2–3 doses

Adult OI Table 6. – continued
Management of Opportunistic Infections
(MMWR 2004; 53 RR 15)

Cytomegalovirus retinitis

- Immediate sight-threatening lesions: Intravitreal implant + valganciclovir 900 mg/d po
- Peripheral lesions: Valganciclovir 900 mg bid po x 14–21 days, then 900 mg/d
- Alternative: Ganciclovir 5 mg/kg q 12h IV x 14–21 days, then 5 mg/kg/d or foscarnet 60 mg/kg IV q 8 h x 14–21 days, then 90–120 mg/kg/d single dose x 14 days or cidofovir 5 mg/kg/d weekly x 2 IV or 1 hr x 2 wks, then 5 mg/kg IV every other wk; patient must be hydrated with ≥ 1 L saline prior to cidofovir and receive probenecid 2 gm 3 hrs prior to cidofovir and 1 gm at 2 and 8 hrs after or fomivirsen intravitreal infections (relapses only)
- Maintenance therapy:
 - Preferred: Valganciclovir 900 mg po qd or foscarnet 90–120 mg/kg/d IV until: inactive disease, CD4 > 100 –150 mm³ x 6 mo and consultation with ophthalmologist
 - Implant: Need replacement q 6–8 mo if CD4 < 100 –150/mm³
 - Alternative: Maintenance ganciclovir, cidofovir
- Immune reconstitution uveitis (IRU): periocular steroids or short course systemic steroids

CMV esophagitis or colitis

- Preferred: Ganciclovir or foscarnet IV x 21–28 days or until symptoms resolve; valganciclovir po is appropriate if symptoms are not severe
- Maintenance: Not necessary except if there are relapses

CMV pneumonia

- Indication to treat: Histologic evidence of disease and failure to respond to other pathogens

CMV neurologic disease

- Preferred: Ganciclovir + foscarnet IV (above doses) until improvement
- Maintenance: Lifetime

Hepatitis B

- Indication for treatment: HBV:(HbeAg pos or HBV DNA $> 10^5$ /mL) + (liver disease by histopathology or ALT > 2 x ULN)
- HBV + HAART:
 - Preferred: TDF/FTC or TDF/3TC
 - Alternative: (3TC or FTC) + adefovir or entecavir
 - Preferred eAg pos: Peginterferon x 48 weeks
- HBV without HAART: Adefovir, entecavir or peginterferon

Adult OI Table 6. – continued
Management of Opportunistic Infections
(MMWR 2004; 53 RR 15)

Hepatitis C

- Indications to treat: HCV RNA > 50 IU/mL, liver biopsy showing fibrosis or inflammation, no contraindications, stable HIV and (?) CD4 > 200/mm³
- Preferred: Peginterferon alfa2a 180ug or peginterferon alfa 2b 1.5 mg/kg, each SC q 9 weekly + ribavirin 400 mg bid po x 48 weeks

Herpes simplex: Moderate or severe mucocutaneous

- Preferred: Acyclovir 5 mg/kg q 8 h IV, then famciclovir 500 mg bid po or valacyclovir 1 gm bid po or acyclovir 400 mg tid po until lesions heal
- Acyclovir resistant: Foscarnet 120–200 mg/kg/d IV in 2–3 doses or cidofovir 5 mg/kg weekly until clinical response

Herpes zoster

- Dermatomal: Famciclovir 500 mg tid po or valciclovir 1 gm tid po x 7–10 days
- Extensive cutaneous or visceral: Acyclovir 10 mg/kg q 8 h IV until response

Microsporidiosis

- Preferred: HAART + symptomatic treatment
- *Enterocytozoon bienersi* (80% of diarrheal disease due to microsporidia): Fumagillin 60 mg/d po
- Non-*enterocytozoon bienersi* (20% of diarrheal disease): Albendazole 400 mg po bid until CD4 > 200/mm³
- Disseminated disease: Itraconazole 400 mg/d, albendazole 400 mg bid (*Brachiola* or *Trachipleistophora*)

Mycobacterium avium

- Preferred: Clarithromycin 500 mg bid po plus ethambutol 15 mg/kg/d po $\pm$ rifabutin 300 mg/d po until treatment $\geq$ 12 mo + asymptomatic + CD4 > 100/mm³ $\geq$ 6 mo
- Alternative: Azithromycin 500–600 mg/d po in place of clarithromycin
- Alternative “3rd drug”: ciprofloxacin 500–750 mg bid po or levofloxacin 500 mg/d po or amikacin 10–15 mg/kg/d IV
- Immune reconstitution: Moderately severe — NSAIDs; severe or persistent — prednisone 20–40 mg/d x 4–8 weeks

***Mycobacterium tuberculosis* (see Adult OI Tables on tuberculosis)**

Adult OI Table 6. – continued

Management of Opportunistic Infections

(MMWR 2004; 53 RR 15)

***Pneumocystis jiroveci* (also known as *Pneumocystis carinii*)**

- Preferred: TMP-SMX 15–20 mg TMP/kg/d IV in 3–4 daily doses or 2 DS tid po x 21 days
- Alternative (IV therapy): Pentamidine 3–4 mg/kg IV infused over 1 hr or dapsone 100 mg/d po + TMP 15 mg/kg/d (3 daily doses) or primaquine 15–30 mg (base)/d po + clindamycin 600–900 mg q 6–8 h IV or 300–450 mg q 6–8 po or atovaquone 750 mg bid po (with food)
- $\text{PaO}_2 < 70$ mm/Hg room air or A-a gradient: Day 1–5 40 mg bid; Day 6–10 40 mg/d; Day 11–21 20 mg/d
- Maintenance
 - Preferred: TMP-SMX 1 DS/d or 1 DS bid po
 - Alternative: Dapsone 100 mg/d po or dapsone 50 mg/d + pyrimethamine 50 mg/wk po + leucovorin 25 mg/wk po or aerosolized pentamidine 300 mg q mo or atovaquone 1500 mg/d po; All until $\text{CD4} > 200/\text{mm}^3 \times \geq 3$ mo

Toxoplasmosis

- Preferred: Pyrimethamine 200 mg/d po x 1 then 50 mg/d (< 60 kg) or 75 mg/d (> 60 kg) plus sulfadiazine 1000 mg q 6 h po (< 60 kg) or 1500 mg q 6 h po (> 60 kg) plus leucovorin 10–20 mg/d po (up to 50 mg/d) $\times \geq 6$ weeks
 - Alternative: Pyrimethamine and leucovorin (above doses) plus
 - 1) Clindamycin 600 mg q6 h IV or po or
 - 2) Atovaquone 1500 mg bid po or
 - 3) Azithromycin 900–1200 mg/d po
 - 4) TMP-SMX 5 mg/kg TMP bid IV or atovaquone 1.5 gm bid po (with meals)
 - Maintenance
 - Preferred: Sulfadiazine 500–1000 mg qid po + leucovorin 10–25 mg/d
 - Alternative:
 - 1) Clindamycin 300–400 mg q 6–8 h plus pyrimethamine 25–50 mg/d + leucovorin 10–25 mg/d
 - 2) Atovaquone 750 mg q 6–12 h $\pm$ pyrimethamine 25 mg/d + leucovorin 10 mg/d
- Continue until $\text{CD4} \geq 100/\text{mm}^3$, continue maintenance until $\text{CD4} > 200/\text{mm}^3 \times \geq 6$ months

Occupational HIV Postexposure Prophylaxis (PEP)

Considerations in Occupational Exposure to HIV

PEP Guidelines

Updated US Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Postexposure Prophylaxis. *MMWR Recommendations and Reports*. September 30, 2005; 54 (RR-9):1. Available at <http://www.cdc.gov/mmwr/>

Risk of HIV transmission

The risk of transmission continues to be related to exposure to infectious material and the source of that material. Exposure is defined as either percutaneous injury with a contaminated sharp object or exposure of mucous membranes or nonintact skin (skin that is abraded, chapped or with dermatitis) to infectious material. The current understanding of exposure contingencies is summarized in Occupational Postexposure Table 1.

The risk of HIV transmission (without prophylaxis) is 0.3 % (3/1,000) from percutaneous injury and 0.09 % (9/10,000) from mucocutaneous exposure. The following are associated with increased risk of transmission: device (needle) with visible blood, needle placed in artery or vein, deep injury, large volume, high viral load.

Efficacy of PEP

The efficacy of AZT monotherapy prophylaxis is estimated to be 80% in retrospective case control series. To date there have been only six recorded prophylaxis failures associated with occupational exposures in the US.

**Occupational Postexposure Table 1.
Exposure Contingencies**

Exposure Element	Explanation
Material	
Blood or bloody body fluid	Established risk of transmission with occupational exposure
CSF; pleural pericardial, peritoneal, amniotic and vaginal fluids; semen	Theoretical risk of transmission
Urine, stool, nasal secretions, sputum, tears, vomitus (if not bloody)	Not potentially infectious
Type of Exposure	
Percutaneous Not severe More severe	Solid needle or superficial injury, etc. Large bore hollow needle, deep injury, or visible blood on needle/device
Mucocutaneous Small volume Large volume	Few drops Major splash
Source of Infectiousness	
HIV positive Low risk High risk	HIV positive and asymptomatic, viral load < 1500 c/mL HIV positive and symptomatic, AIDS, acute retroviral syndrome, or known high viral load
Source unknown	For example, deceased source person with no samples available for HIV testing

**Occupational Postexposure Table 2.
Indications for HIV PEP**

Source	Type of Exposure			
	Percutaneous		Muscocutaneous	
	<i>Not Severe*</i>	<i>More Severe*</i>	<i>Small Volume*</i>	<i>Large Volume*</i>
HIV Positive				
Low Risk*†	2 drugs	≥ 3 drugs	2 drugs	2 drugs
High Risk*†	3 drugs	≥ 3 drugs	≥ 3 drugs	≥ 3 drugs
Source Unknown				
—	None or 2 drugs‡	None or 2 drugs‡	None or 2 drugs‡	None or 2 drugs‡

* See Occupational Postexposure Table 1 for explanation

† HIV resistance is a concern get expert consultation

‡ PEP is optional based on discussion of risk:benefit

Management of Health Care Workers (HCWs) With Potential HIV Exposure

The importance of rapid action in the event of a potential exposure cannot be over-emphasized since PEP, if warranted, needs to be initiated within hours.

Assessment

Documentation of the nature and degree of the exposure and the HIV status of the source patient need to be identified. Rapid testing of previously untested source patients is valuable in determining the need for PEP. The need for PEP and potential number of drugs may be determined by using Table 2.

Initiation of HIV PEP

Initiate PEP as soon as possible, preferably within hours after exposure, and continue for 4 weeks. From a practical point of view, PEP should be initiated if the source person is HIV-infected or thought to be infected, especially if the results of HIV serology likely to be delayed. PEP may be discontinued if the source is determined to be uninfected. The current recommended PEP regimens are listed in Table 3.

The following drugs are not recommended because of the potential for adverse events: abacavir, delavirdine, zalcitabine, didanosine with stavudine, and nevirapine. During pregnancy efavirenz should be avoided because of the risk of teratogenic effects and the combination didanosine with stavudine because of toxicity concerns. Additionally, indinavir should be avoided because of side effects in the newborn.

Health care workers taking PEP report adverse reactions at the rate of 17–47%. The most frequently reported reactions were nausea — 27%, malaise and fatigue — 23%. Of 503 HCW who prematurely (<28 days) stopped PEP, 24% did so because of adverse reactions. Regardless, the HCW should be advised on the need to complete the 4-week course of PEP.

Management of Health Care Workers (HCWs) With Potential HIV Exposure – *continued*

Expert Consultation

Consultation with an expert in HIV exposures and PEP is encouraged especially in the following instances:

- Initiation of PEP is delayed to > 24–36 hrs post-exposure
- The status of the source patient is unknown
- The HCW is currently pregnant or is breastfeeding
- The source patient is known to have a resistant HIV strain
- There are toxicity problems in the initiated regimen

Monitoring

- Re-evaluate HCW at 72 hours, especially if additional information becomes available about the status of the source
- HIV serology testing should be conducted at baseline, and then at 6 weeks, 12 weeks, and 6 months after exposure; if the HCW experiences hepatitis C seroconversion after exposure, HIV serology should be conducted 12 months after exposure
- Tests for HIV (P24 Ag or HIV PCR) in HCW are 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

- Toxicity monitoring

Laboratory: CBC, liver and renal function tests at baseline and at 2 weeks; HCWs given indinavir should also have urinalysis monitoring for crystalluria and hematuria

Self Report: HCWs should be advised to report rash, fever, back or abdominal pain, dysuria, blood in urine, and symptoms of hyperglycemia; they should also be counseled on the possibility of drug interactions and advised to report these should they occur

Prevention Warnings

HCW with exposure to HIV should be counseled on measures to prevent secondary transmission including: avoidance of blood or tissue donations; pregnancy and breastfeeding, especially in the first 6–12 weeks; and the use of condoms for sexual transmission.

Seroconversions

Report any Seroconversion to your local Health Department.

Occupational Postexposure Table 3. Recommended Regimens

2 Drug Regimen	3 Drug Regimen
Lamivudine or emtricitabine <i>plus</i> zidovudine, stavudine or tenofovir	Two nucleosides <i>plus</i> Preferred: lopinavir/ritonavir Alternates: atazanavir, fosamprenavir, ritonavir boosted indinavir, ritonavir boosted saquinavir or nelfinavir*

* Consider EFV if PI resistance in source and HCW has no pregnancy risk

Resources for Consultation

The following resources are available for consultation regarding HIV PEP:

- PELine: <http://www.ucsf.edu/hivcntr>
Telephone: 1-888-448-4911
- HIV Pregnancy registry: <http://www.apregistry.com/index.htm>
Telephone: 1-800-258-4263, email —registry@nc.crl.com
- FDA (for reporting unusual or severe toxicity to antiretroviral agents) at <http://www.fda.gov/medwatch>
Telephone: 1-800-332-1088
- Report HIV infections in HCP and failures of PEP to local Health Department.
- HIV/AIDS Treatment Information Service: <http://aidsinfo.nih.gov>

A Pocket Guide to Adult HIV/AIDS Treatment provides treatment information in table format for easy reference in clinical settings:

Drug Information Pages 2-16

Adult ART Tables Pages 17-29

Pregnancy Tables Pages 30-34

Prevention for Providers Pages 35-37

Adult OI Tables Pages 38-51

Occupational PEP Pages 52-58

Recommendations for HIV care and treatment are complex and change rapidly. In addition to the Pocket Guide and *A Guide to Primary Care of People with HIV/AIDS*, which the Pocket Guide supports, consult the following resources provided by the U.S. Department of Health and Human Services for frequently updated HIV treatment information:

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

National HIV/AIDS Clinical Consultation Center Warmline:

1-800-933-3413

(toll free in the U.S.)

