

Pocket Guide to Adult HIV/AIDS Treatment

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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 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 is for informational purposes only. Determination of appropriate treatment is the responsibility of the treating physician.

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Abbreviations Used in this Pocket Guide to HIV/AIDS Treatment

Drug Abbreviations	
ABC: Abacavir (<i>Ziagen</i>)	INV: Invirase (saquinavir, HGC)
APV: Amprenavir (<i>Agenerase</i>)	IVIG: Intravenous immune globulin
ATV: Atazanavir (<i>Reyataz</i>)	LPV/r: Lopinavir/Ritonavir (<i>Kaletra</i>)
AZT: Zidovudine (<i>Retrovir</i>)	NFV: Nelfinavir (<i>Viracept</i>)
ddl: Didanosine (<i>Videx</i>)	NNRTI: Non-nucleoside Rev Trans. Inhib.
d4T: Stavudine (<i>Zerit</i>)	NRTI: Nucleoside Rev. Trans. Inhib.
ddC: Zalcitabine (<i>Hivid</i>)	NVP: Nevirapine (<i>Viramune</i>)
DLV: Delavirdine (<i>Rescriptor</i>)	PI: Protease Inhibitor
EFV: Efavirenz (<i>Sustiva</i>)	/r: Ritonavir <400 mg/d.
FTC: Emtricitabine (<i>Emtriva</i>)	RBT: Rifabutin (<i>Mycobutin</i>)
ENF: Enfuvirtide (<i>Fuzeon, T-20</i>)	RTV: Ritonavir (<i>Norvir</i>)
FTV: Fortovase (saquinavir, SGC)	SQV: Saquinavir (<i>Invirase, Fortovase</i>)
FPV: Fosamprenavir (<i>Lexiva</i>)	3TC: Lamivudine (<i>Epivir</i>)
HU: Hydroxyurea	TDF: Tenofovir (<i>Viread</i>)
IDV: Indinavir (<i>Crixivan</i>)	TMP-SMX: Trimethoprim sulfamethoxazole
INH: Isoniazid	VZIG: Varicella zoster immune globulin
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
hs: bedtime (hour of sleep)	tiw: three times per week
mo: month	TAMS: thymidine analogue assoc. mutations
po: by mouth	ULN: upper limit of normal

Baseline Evaluation

Baseline Evaluation Table 1. Laboratory Tests

Test	Comment
HIV Serology	<ul style="list-style-type: none"> • Sensitivity and specificity standard serology is > 99% - False positives: Human error - False negatives: Usually "window period" • Acute HIV: HIV RNA level >10,000 c/mL; confirm seroconversion • Rapid tests: Confirm positives
CD4	<ul style="list-style-type: none"> • Reproducibility: 95% CI = 30% • False high levels – splenectomy (use CD4%) concurrent HTLV-1 • Repeat every 3-6 months • % - CD4 > 500 = > 29%, 200-500 = 14-28%, < 200 = < 14%
HIV Viral Load	<ul style="list-style-type: none"> • Reproducibility: 95% CI = 0.3 log₁₀ c/ml or 50% • Repeat every 3-4 months
CBC	<ul style="list-style-type: none"> • Repeat every 3-6 months; more frequently as indicated • Macrocytosis with AZT and d4T
Chemical Profile	<ul style="list-style-type: none"> • Include LFT and renal function • Repeat LFT with all PIs and NNRTIs, ETOH and hepatitis • Repeat renal function with IDV & TDF
Hepatitis Screen	<ul style="list-style-type: none"> • Anti-HCV, anti-HAV, anti-HbsAg (if prior vaccine) or anti-HBcAg • Abnormal LFT: get anti-HCV & HBsAg • Positive anti-HCV: get quantitative HCV • Neg anti-HBs: Vaccinate for HBV • Pos HBsAg or anti-HCV: get LFTs • Neg anti-HAV: HAV vaccine routine
Fasting Lipid Profile and Glucose	<ul style="list-style-type: none"> • Patient at risk • Baseline for HAART; repeat at 3-4 mo and then yearly
Toxoplasma IgG	<ul style="list-style-type: none"> • 10-15% positive in U.S.
PPD	<ul style="list-style-type: none"> • Indicated if no history of TB or prior pos. PPD • Induration > 5 mm is indication for INH x 9 mo
PAP smear	<ul style="list-style-type: none"> • Baseline, at 6 months and then annual; if "inadequate" – repeat; if atypia – refer to gynecologist
Chest x-ray	<ul style="list-style-type: none"> • Indicated with pulmonary sx, positive PPD or history of chest disease; some do baseline X-ray routinely.
Urinary NAAT for Gonorrhea & Chlamydia	<ul style="list-style-type: none"> • "Consider" in sexually active patients (see STD/HIV Table 1) • Repeat at 6-12 month intervals depending on risk
VDRL	<ul style="list-style-type: none"> • Baseline and repeat annually in sexually active patients • Confirm positives with FTA-ABS
Renal Screen	<ul style="list-style-type: none"> • Urinalysis and creatinine • If ≥1+ proteinuria or elevated creatinine: quantify urine protein and do renal ultrasound.

Baseline Evaluation Table 2. Prevention of HIV for HIV Providers

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 at every visit)
- Pregnancy test (if indicated)
- 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, 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 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) (with precautions to prevent superinfection). Also stress reduced efficacy of oral contraceptives with PIs and NNRTIs. Stress proper condom use.

- IDU

- Encourage to 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 - risk in 20X greater without condoms.

- Relative risk of HIV transmission (*Sex Transm Dis* 2002;29:38):

- insertive fellatio.....1 (referent)

- receptive fellatio.....2

- insertive vaginal sex....10

- insertive anal sex.....13

- receptive vaginal sex...20

- receptive anal sex.....100

Note: Risks for condom use and acts are multiplicative; e.g, for the risk ratio for transmission by receptive anal sex without a condom vs vaginal insertive sex with a condom is 200:1

- Viral load: each log₁₀ reduction in viral load reduces probability of transmission 2.5 fold.

- Early stage disease: risk is increased about 10X during acute HIV infection (prior to sero-conversion).

- HAART recipients: decreases in VL probably reduces risk but transgression in behavior (such as not using condoms) eliminates this benefit. If treatment is discontinued for any reason, 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 needle sharing 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 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 Information

This section contains information about antiretroviral drug characteristics, interactions with other drugs and adverse effects. Additional detailed information is contained in Bartlett JB and Gallant JG *Medical Management of HIV Infection*, 2004, Johns Hopkins Medicine Health Publishing Business Group. Additional sources of information are the National Institute of Health's AIDSInfo web site: <http://www.aidsinfo.nih.gov/> as well as the drug "package inserts" which are usually available on the manufacturers' web sites as "full prescribing information."

Drug Table 1. Antiretroviral Agent Characteristics

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

Drug Name	Form	Usual Adult Dose		
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)				
Abacavir (ABC, <i>Ziagen</i>)	300 mg tab; (see also: Trizivir and Epzicom) 20 mg/ml po soln.	300 mg bid or 600 mg qd		
Combivir (CBV)	AZT 300 mg + 3TC 150 mg (tab)	1 bid		
Didanosine (<i>Videx; Videx EC; ddl</i>)†	Buffered tabs: 25, 50, 100, 150, 200 mg Buffered powder: 100, 167, 250 mg bid EC caps: 125, 200, 250, and 400 mg		>60 kg	<60 kg
		Tabs	400 mg qd or 200 mg bid	250 mg qd or 125 mg bid
		Powder	250 mg bid	167 mg bid
		EC Caps	400 mg qd	250 mg qd (pref.)
		With TDF: ≤250 mg/day		
Emtricitabine (<i>Emtriva, FTC</i>)	200 mg cap	200 mg q.d.		
Epzicom	ABC 600 mg + 3TC 300 mg	1 tablet qd		
Lamivudine (<i>Epivir; 3TC</i>)	150, 300 mg tab (see also: Combivir, Trizivir, & Epzicom) 10 mg/ml po soln.	150 mg bid or 300 mg qd		
Stavudine (<i>Zerit; d4T</i>) †	15, 20, 30, 40 mg cap; 75, 100 mg XR cap (not available as of 12/04) 1 mg/mL po soln.	Wt >60 kg: 40 mg bid or 100XR qd Wt <60 kg: 30 mg bid or 75XR qd		
Tenofovir (<i>Viread, TDF</i>)	300 mg tab (see also: Truvada)	300 mg qd		
Trizivir	AZT 300 mg + 3TC 150 mg + ABC 300 mg (tab)	1 bid		
Truvada	TDF 300 mg + FTC 200 mg	1 tablet qd		

† The comb. of ddl & d4T should be avoided, especially in pregnant women. EFV-avoid in 1st trimester of preg. and use with caution in women with preg. potential. Avoid APV liquid in preg.

‡ Drug change or dose change could be considered on a case-by-case basis noting the risk of resistance with underdosing.

Food Effects	Renal Failure Dosing			Liver Failure Dosing	Toxicity (main toxicity – italics)
	CrCl 30-59 ml/min	CrCl 10-29 ml/min	CrCl <10 or dialysis		
No effect	Standard			Usual	<i>Hypersensitivity</i> - fever, rash, GI sx, dyspnea§¶¶¶
No effect	Fixed Formulation not recommended			Usual	AZT side effects§ HBV flare##
Take 1/2 hr before or 2 hr after meal Separate dosing of IDV, RTV, DLV, ATV	>60 kg 200 mg/d <60 kg 125 mg/d	>60 kg 125 mg/d <60 kg 100 mg/d	>60 kg 125 mg/d <60 kg 75 mg/d¶¶	Usual	<i>Pancreatitis, peripheral neuropathy, GI intolerance</i> §
No effect	200 mg q48h	200 mg q72 h	200 mg q96 hrs ¶	Usual	Minimal§ HBV flare##
No effect	Not recommended in renal failure			Usual	ABC hypersensitivity ¶¶¶ HBV flare ***
No effect	150 mg qd	150 mg x 1 then 100 mg/d	150 mg x 1 then 25-50 mg/d ¶	Usual	Minimal§
No effect	>60 kg-20 mg q 12 h <60 kg-15 mg q12 h	>60 kg- 20 mg q 24 h <60 kg-20 mg 24 h	>60kg- 20 mg q24 h <60 kg-15mg q 24 h ¶	Usual	<i>Peripheral neuropathy, Pancreatitis, hyperlipidemia, lipoatrophy, ascending paresis (rare)</i> §
No effect	300 mg q 48 hr	300 mg 2 days/wk	300 mg q 7 days ¶	Usual	Fanconi syndrome (rare)§, HBV flare##
No effect	Fixed formulation not recommended in renal or hepatic failure			Usual	<i>Hypersensitivity reaction (ABC), bone marrow suppression (AZT), GI Intolerance (AZT)</i> §
No effect	1 tab q48h	Not recommended		Usual	TDF renal toxicity (rare) HBV flare ***

§ Class adverse reaction - lactic acidosis with steatosis. (see pg 19).

¶ Give post dialysis

¶¶¶ Registry for hypersensitivity reactions 800-270-0425

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

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

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

Drug Name	Form	Usual Adult Dose
Nucleoside Reverse Transcriptase Inhibitors (NRTIs) (Cont'd.)		
Zalcitabine (<i>Hivid</i> ; ddC)	0.375, 0.75 mg tab	0.75 mg tid
Zidovudine (<i>Retrovir</i> , AZT)	100 cap, 300 mg tab; (see also: Combivir & Trizivir) 10 mg/ mL IV soln. 10 mg/ mL po soln.	300 mg bid 200 mg tid
Protease Inhibitors (PIs) Doses with/without RTV Boosting (see Drug Table 13)		
Amprenavir (APV, <i>Agenerase</i>) - SG caps will be discontinued in 2005	50, 150 mg caps 15 mg/ml po soln **	>50 kg: 1200 mg bid (caps) or 1400 mg bid (po soln.) or APV 600 mg/RTV 100 mg bid# or 1200 mg/RTV 200 mg qd
Atazanavir (<i>Reyataz</i> , ATV)	100, 150, and 200 mg capsules	400 mg qd; ATV 300 mg/RTV 100 mg qd. RTV boosting is required if ATV is combined with TDF or EFV and often preferred.*
Fosamprenavir (FPV, <i>Lexiva</i>)	700 mg tabs	1400 mg bid or 700 mg/RTV 100 mg bid or 1400 mg/RTV 200 mg qd (treatment naïve only)
Indinavir (IDV, <i>Crixivan</i>)	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
Lopinavir/ Ritonavir (LPV/r, <i>Kaletra</i>)	LPV 133.3 mg + RTV 33.3 mg (cap); LPV 80 mg + RTV 20 mg/ mL po soln (42% alcohol)	400 mg LPV + 100 mg RTV (3 caps) bid Soln: 5 mL bid

* Childs-Pugh score

†† Inivrase taken with ritonavir. Inivrase not recommended as sole PI.

** APV caps and solution NOT interchangeable on mg per mg basis. Capsule is the preferred formulation due to high propylene glycol in the po solution; po soln contraindicated in pregnancy.

See Drug Tables 12 & 13 for dosing recommendations when using dual PI or PI plus NNRTI.

Food Effects	Renal Failure Dosing			Liver Failure Dosing	Toxicity (main toxicity – italics)
	CrCl 30-59 ml/min	CrCl 10-29 ml/min	CrCl <10 or dialysis		
No effect	Standard	0.75 mg bid	0.75 mg qd	Usual	<i>Peripheral neuropathy, Stomatitis</i> §
No effect	300 mg bid	300 mg qd or 300 mg bid	300 mg qd	200 mg bid	<i>Anemia, neutropenia, headache, asthenia, GI intolerance</i> §
Avoid high fat meal	Standard		No data	CPS* 5-8: 450 mg bid CPS* 9-12: 300 mg bid	GI intolerance, rash, oral paresthesias, hepatitis ††
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, prolongation of QTc; caution with conduction defects or drugs that do this. ††
No effect	Standard			CPS* 5-8: 700 mg bid CPS* >9: Avoid	<i>Rash, GI intolerance, headache, hepatitis</i> ††
1 hr before or 2 hr after meal unless with RTV	Standard			600 mg q8h	GI intolerance Nephrolithiasis, benign increase in indirect bilirubin ††
Take with food	Standard			§§	GI Intolerance (esp. diarrhea), asthenia ††

§§ 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.

All PIs may cause hepatitis (see Drug Table 3).

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

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

Drug Name	Form	Usual Adult Dose
Protease Inhibitors (PIs) (Cont'd) Doses with/without RTV Boosting (see Drug Table 13)		
Nelfinavir (NFV, <i>Viracept</i>)	250, 625 mg tabs 50 mg/g powder	1250 mg bid or 750 mg tid
Ritonavir (RTV, <i>Norvir</i>)	100 mg caps 600 mg/ 7.5 mL po soln	600 mg q12h #; separate ddl \geq 2 h
Saquinavir (SQV) <i>Fortovase</i> (FTV) <i>Invirase</i> (INV)††	200 mg caps INV - 200, 500 mg caps (2005) FTV - 200 mg caps	FTV 1200 mg tid or with RTV SQV 400 mg + RTV 400 mg bid or SQV 1000 mg + RTV 100 mg bid or SQV 1600 mg + RTV 100 mg qd or INV 2000 mg + RTV 100 mg qd
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)		
Delavirdine (DLV, <i>Rescriptor</i>)	100, 200 mg tabs	400 mg tid Separate buffered ddl or antacid \geq 1 h
Efavirenz † (EFV, <i>Sustiva</i>)	50, 100, 200 mg caps, 600 mg tabs	600 mg hs
Nevirapine\$ (NVP, <i>Viramune</i>)	200 mg tabs 50 mg/5 ml po susp.	200 mg qd x14 days, then 200 mg bid
Fusion Inhibitors		
Enfuvirtide (ENF, <i>Fuzeon</i> , T-20)	108 mg single-use vials to be reconstituted with 1.1 mL H ₂ O	90 mg (1 mL) SQ q12h into upper arm, anterior thigh or abdomen (Rotate sites).

† Efavirenz should be avoided in first trimester of pregnancy and used with caution in women with reproductive potential. Avoid APV liquid in pregnancy.

†† Invirase taken with ritonavir. Invirase not recommended as sole PI.

\$ Nevirapine should be avoided in women with a baseline CD4 count $>$ 250 cells/mm³ due to high rate of symptomatic hepatitis (11%).

Food Effects	Renal Failure Dosing			Liver Failure Dosing	Toxicity (main toxicity – italics)
	CrCl 30-59 ml/min	CrCl 10-29 ml/min	CrCl <10 or dialysis		
Take with meal.	Standard			§§	Diarrhea ‡‡
Food improves GI tolerance	Standard				GI intolerance, paresthesia, hepatitis, taste perversion ‡‡
(FTV): Take with meal	Standard			§§	GI intolerance, hepatitis ‡‡
No effect	Standard			§§	Rash, hepatitis
Avoid high fat meal	Standard			§§	CNS x 2-3 wk, Rash, hepatitis, false + cannibinoid test
No effect	Standard		Standard; give post dialysis	Avoid	Rash, hepatitis; hepatic necrosis, esp. in females with a baseline CD4 >250 cells/mm ³ §
N/A	Standard	Usual dose likely		Usual dose	Site reactions, bacterial pneumonia

§§ 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.

*** Patients with chronic HBV (HbsAg) may have HBV flare if TDF, 3TC, or FTC are discontinued or if HBV becomes resistant.

Drug Table 2. Antiretroviral Agents, Target Serum Levels and CSF: Plasma Ratios

Drug	Target Serum Concentration*	CSF:Plasma Ratio†
Protease Inhibitors		
APV/FPV	400 ng/mL	<0.05
IDV	100 ng/mL	0.02–.06
LPV	1,000 ng/mL	<0.05
NFV	800 ng/mL	<0.05
RTV	2,100 ng/mL	<0.05
SQV	100–250 ng/mL	<0.05
Non-Nucleoside Reverse Transcriptase Inhibitors		
EFV	1,000 ng/mL	0.01
NVP	3,400 ng/mL	0.28–0.45
Nucleoside Reverse Transcriptase Inhibitors		
3TC	—	0.1
ABC	—	0.3–0.4
AZT	—	0.3–1.35
d4T	—	0.16–0.97
ddI	—	0.16–0.19
TDF	—	Unknown

* From DHHS Guidelines

† From McArthur JC et al. *J Neurovirol* 2003;9:205

Drug Table 3. Adverse Reactions to Antiretroviral Agents

LIFE THREATENING REACTIONS	
Hepatic necrosis	
Agent	NVP
ADR Features	GI symptoms, fever, rash (50%), eosinophilia and hepatic necrosis usually in first 6-18 weeks of NVP.
Frequency	1-2% of all NVP recipients. Rate of symptomatic hepatitis is 11% in treatment-naïve women with baseline CD4 count >250 cells/mm ³ and 6% in men with baseline CD4 count > 400 cells/mm ³ .
Monitor	Clinical warning. ALT: Baseline and at 4, 8, 16 weeks then q 3-6 months.
Intervention	Contraindicates future NNRTI. Supportive care (steroids, antihistamines appear useless).
Cutaneous: Steven-Johnson Syndrome and Toxic Epidermal Necrolysis	
Agent	NVP, less common is EFV (reported with FPV, ABC, ddI, and IDV).
ADR Features	Fever, myalgia, skin rash with blistering ± mucous membrane involvement.
Frequency	NVP 0.5-1%, EFV 0.1%.
Monitor	Patient warning.
Intervention	Intensive care of wounds including pain meds and antibiotics; may treat in burn center.
Lactic acidosis	
Agent	d4T + ddI > ddI > d4T > AZT (Rare with ABC, TDF, 3TC, and FTC).
ADR Features	GI symptoms, wasting, fatigue, ± multiorgan failure, pancreatitis, respiratory failure.
Frequency	1-10 per 1,000 patient-years for d4T, ddI or AZT.
Monitor	Clinical symptoms. No routine lactate levels, but obtain this if clinically indicated. Surrogate for lactic acid levels: High CPK and ALT; low HCO ₃ ⁻ ; anion gap
Intervention	Support; ART without NRTI or use ABC, 3TC, FTC, and/or TDF.

Drug Table 3. Adverse Reactions to Antiretroviral Agents (Cont'd.)

LIFE THREATENING REACTIONS (CONT'D.)	
Hypersensitivity	
Agent	ABC.
ADR Features	Fever, rash, fatigue, GI symptoms, usually in 1st 6 weeks of ABC therapy.
Frequency	5% of ABC recipients.
Monitor	Patient warning (in questionable cases may want to administer next dose under observation – this reaction always progresses with next dose).
Intervention	D/C ABC. Never re-challenge (if dx is probable). Supportive care (steroids and antihistamines are not useful).
SERIOUS REACTIONS	
Pancreatitis	
Agent	ddl + d4T > ddl > d4T (3TC in children).
ADR Features	Abdominal pain with elevated amylase and/or lipase.
Frequency	ddl 1-7%. (Appears to be less frequent in HAART era.)
Monitor	Patient warning. Amylase with clinical symptoms.
Intervention	Supportive care, pain meds and bowel rest (NPO).
Nephrotoxicity – Fanconi syndrome	
Agent	TDF.
ADR Features	Renal failure ± Fanconi syndrome
Frequency	Occurs primarily in patients who have inadequate dose adjustment of TDF with baseline renal dysfunction.
Monitor	Urinalysis and creatinine or BUN at 3-6 month intervals (?) (Note: This reaction may be more common in African-American males).
Intervention	Supportive care. D/C TDF.

SERIOUS REACTIONS (CONT'D.)

Renal calculi	
Agent	IDV
ADR Features	Renal colic, abdominal pain, hematuria.
Frequency	IDV 10-20%/year; higher with IDV/r 800/100-200 bid regimen.
Monitor	Urinalysis ± creatinine or BUN q 3-6 month with IDV. Clinical warning. (Note-this may be more common in Africa due to dehydration).
Intervention	Prevention is hydration with ≥ 1.5 L/d. Manage as nephrolithiasis. IDV should be stopped, given at lower dose or given with better hydration (Most use alternative PI or NNRTI).
Marrow suppression	
Agent	ZDV.
ADR Features	Neutropenia and/or anemia.
Frequency	Anemia 1-4%, neutropenia 2-8%.
Monitor	CBC at baseline and q 3 months for ZDV recipients.
Intervention	Transfusion or EPO for serious anemia if needed. D/C ZDV.
Transaminasemia	
Agent	All PIs and NNRTIs.
ADR Features	Elevated ALT that is otherwise not explained (ETOH, hepatitis B, hepatitis C etc.).
Frequency	8-15% for most PIs and NNRTIs.
Monitor	ALT q 3-6 months.
Intervention	Must distinguish ALT elevations due to other drugs (lactic acidosis with steatosis due to d4T, ddI or ZDV, hypersensitivity due to ABC, or NVP hepatic necrosis) and due to other causes (hepatitis viruses, ETOH, etc.). Many D/C the PI or NNRTI if the ALT is > 5x ULN although this often resolves with drug continuation.

Drug Table 3. Adverse Reactions to Antiretroviral Agents (Cont'd.)

MISCELLANEOUS REACTIONS	
GI intolerance	
Agent	All PIs, ZDV, and ddI.
ADR Features	Nausea, vomiting, diarrhea, anorexia.
Frequency	Common.
Monitor	Patient warning.
Intervention	Symptomatic – may improve with food (except ddI and IDV without RTV); NFV and LPV/r-associated diarrhea is usually managed with Imodium; many improve with continuation of treatment.
Peripheral neuropathy	
Agent	ddI, d4T, and ddC.
ADR Features	Paresthesias and pain of lower extremities .
Frequency	10-30% (or more) based on duration.
Monitor	Patient warning; symptoms and ankle jerk reflexes.
Intervention	D/C implicated agent. Symptomatic treatment – pain meds, foot bridge, etc.
Rash	
Agent	NNRTIs (NVP & EFV), APV, FPV, and ABC.
ADR Features	Maculopapular ± pruritus.
Frequency	NVP & EFV – 15%, FPV – 20%, APV – 20%, and ABC – 5%.
Monitor	Patient warning.
Intervention	R/O NNRTI associated Stevens-Johnson syndrome or TEN and ABC hypersensitivity. Also R/O rash due to HIV-associated dermatologic complications and drug rashes due to other meds especially TMP-SMX, dapsone etc. Most “treat through” maculopapular rashes.
CNS Toxicity	
Agent	EFV.
ADR Features	“Disconnected syndrome” with bad dreams, somnolence, impaired concentration reduced attention etc.
Frequency	>50% with EFV.
Monitor	Patient warning.
Intervention	Usually resolves in 2-3 weeks.

MISCELLANEOUS REACTIONS (CONT'D.)

Insulin resistance	
Agent	PIs especially IDV.
ADR Features	Elevated FBS and symptoms of diabetes.
Frequency	3-5%.
Monitor	FBS at baseline and q 3-6 months.
Intervention	Diet and exercise, metformin or glitazone if indicated. May switch to NNRTI regimen.
Hyperlipidemia	
Agent	PIs (except ATV) and d4T.
ADR Features	Increase total and LDL cholesterol and triglycerides.
Frequency	Variable.
Monitor	Fasting lipid profile at baseline and at 3-6 months.
Intervention	Based on National Cholesterol Education Program (<i>JAMA</i> 2001;285:2486) See pages 26-27, Drug Tables 6 & 7
Fat atrophy	
Agent	d4T (primarily).
ADR Features	Thinning of buccal fat in face; extremities and buttocks.
Frequency	Common with long term use.
Monitor	Self image is most important.
Intervention	D/C d4T early if possible – changes are either slow to reverse or are irreversible.
Fat accumulation	
Agent	PIs.
ADR Features	Increase abdominal girth, breast size, buffalo hump.
Frequency	20-80% of those receiving HAART.
Monitor	Self image is most important.
Intervention	May change to NNRTI based regimen for cosmetic reasons; restorative surgery.

Drug Table 4. Antiretroviral Agents, “Black Box” warnings

Agent	Reaction
Abacavir	<ul style="list-style-type: none"> • Fatal hypersensitivity reactions: Do not restart • Lactic acidosis and steatosis
Amprenavir	<ul style="list-style-type: none"> • Oral soln. contains large amounts of propylene glycol - avoid with renal failure, hepatic failure, pregnancy, & with metronidazole
Atazanavir	None
Delavirdine	None
Didanosine	<ul style="list-style-type: none"> • Fatal and nonfatal pancreatitis: Do not restart • Lactic acidosis with steatosis • Fatal lactic acidosis when combined with stavudine in pregnancy
Efavirenz	None
Emtricitabine	<ul style="list-style-type: none"> • Lactic acidosis w/ steatosis • Flare of hepatitis B (HbsAg) when antiretroviral is stopped
Enfuvirtide	None
Indinavir	None
Lamivudine	<ul style="list-style-type: none"> • Lactic acidosis with steatosis. Patients with HIV infection should receive only dosage and formulations appropriate for treatment of HIV. • Flare of hepatitis B (HbsAg) when antiretroviral is stopped
Lopinavir	None
Nelfinavir	None
Nevirapine	<ul style="list-style-type: none"> • Hepatotoxicity including fulminant and cholestatic hepatitis & hepatic necrosis, especially in females with baseline CD4 count >250 cells/mm³; monitor intensively in first 18 wks of therapy. • Severe, life-threatening skin reaction including toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome, etc. • Do not restart if there is serious liver injury or serious drug reaction.
Ritonavir	<ul style="list-style-type: none"> • Potentially serious drug interactions with nonsedating antihistamines, sedative hypnotics, antiarrhythmics, or ergot alkaloids.
Stavudine	<ul style="list-style-type: none"> • Lactic acidosis with steatosis • Fatal and non-fatal pancreatitis • Fatal lactic acidosis when combined with Didanosine in pregnancy
Tenofovir	<ul style="list-style-type: none"> • Lactic acidosis and steatosis • Flare of hepatitis B (HbsAg) when antiretroviral is stopped
Zalcitabine	<ul style="list-style-type: none"> • Severe peripheral neuropathy • Pancreatitis (rare) • Hepatic failure in patients with HBV infection (rare) • Lactic acidosis and steatosis
Zidovudine	<ul style="list-style-type: none"> • Hematologic toxicity - anemia & leukopenia • Lactic acidosis and steatosis

Drug Table 5. Recommendations for Monitoring Adverse Reactions By Drug

Agent	ADR	Clinical	Laboratory
Nucleosides and nucleotide RT inhibitors			
ZDV	Anemia	Fatigue	CBC baseline
	Neutropenia	—	CBC baseline, q 3 mo & prn
	GI intolerance	—	—
d4T & ddI	Lactic acidosis	Symptoms	Symptoms-lactic acid level or CPK, ALT, HCO
	Peripheral neuropathy	Symptoms DTRs	(PE and symptoms)
	Fat atrophy	Symptoms	(Appearance)
	Pancreatitis	Symptoms	Symptoms-amylase and/or lipase
ABC	Hypersensitivity	Symptoms	CPK, LFTs, & CBC.
TDF	Fanconi syndrome	—	U/A & BUN or creatinine at baseline, 3-4 mo, and annual or more frequently if reduced baseline renal function, low body weight, or long duration of TDF therapy.
3TC & FTC	—	—	—
Non-nucleoside RT inhibitors			
NVP	Hepatic necrosis	Symptoms	ALT-baseline wk 4,8, 16 & q 3-6 months. If symptoms: LFTs & CBC (eosinophilia).
	Rash	Symptoms	—
	Transaminitis	Asymptomatic	ALT as above
EFV	CNS toxicity	Symptoms	—
	Rash	Symptoms	—
	Transaminitis		ALT-baseline and q 3-6 months
Protease inhibitors			
IDV	Nephrolithiasis	Symptoms	U/A & creatinine or BUN baseline and q 3-6 months
FPV, APV	Hypersensitivity Rash	Symptoms	
All PIs	Insulin resistance	Symptoms	FBS baseline, 3-4 months, and then annual or more frequent PRN
	Hyperlipidemia	Asymptomatic	Lipid profile baseline and q 6 months

Drug Table 6. 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 \geq 130 mg/dL	LDL >190 mg/dL (LDL 160-190 Drug therapy optional)
No CHD & \geq 2 Risks*	LDL <130 mg/dL	LDL \geq 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 \geq 70 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 - 499mg/dl reduction of non-HDL cholesterol becomes a secondary goal after reaching LDL goal.			

Adapted from: *JAMA* 2001; 285:2486-2497. Updated - *Circulation* 2004;110:207.

Editors Note: This table is a basic condensation of complex guidelines. Readers are encourage 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, hx 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 Cardio Vascular 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 7. 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 8**.

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.

Drug Table 8. Drug Interactions: Contraindicated Combinations

Class	Contraindicated Agent	ART Agents	Alternatives
Ca++ channel blocker	Bepidil	RTV, APV, ATV, FPV	-----
Antiarrhythmics	Flecainide, Propafenone	RTV, LPV/r	-----
	Amiodarone, quinidine	RTV, IDV	
Lipid lowering	Simvastatin, Lovastatin	All PIs, DLV	Pravastatin or Fluvastatin, possibly Atorvastatin Rosuvastatin
Antimycobacterials	Rifampin	IDV, NFV, APV, FPV, LPV/r, SQV (unless given with RTV), DLV, ATV, & NVP	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	Reglan
	H2 blockers, proton pump Inhibitors	DLV, ATV	
Neuroleptic	Pimozide	All PIs	-----
Psychotropic	Midazolam†, Triazolam	All PIs, DLV, EFV	Temazepam, Lorazepam, or Oxazepam††
	Alprazolam	DLV	
Ergot alkaloids	Ergotamine	All PIs, DLV, EFV	Consider sumatriptan
Herbs	St. John's wort	All PIs & EFV, DLV	Alternative antidepressants

* See Table 9 for Rifabutin and antiretroviral dose adjustments

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

†† Reviewer opinion

Drug Table 9. Drug Interactions: Combinations with PIs or NNRTIs Requiring Dose Modifications

Class	Agent	ART
Antifungal	Itraconazole	IDV - Monitor for Itraconazole toxicity and consider IDV dose of 600 mg tid (unless boosted); itraconazole dose ≤ 200 mg bid
	Ketoconazole	IDV– IDV 600 mg tid
		RTV, LPV/r–Ketoconazole ≤ 200 mg/d, FPV ≤ 400 mg/d
		NVP– Not recommended
Voriconazole	RTV (>400 mg/d), LPV/r, EFV,SQV: potential for bi-directional inhibition with voriconazole-monitor for toxicities. No data for low dose RTV boosting, NVP, DLV, NFV, ATV, APV, and FPV. IDV is OK	
Oral contraceptives	-----	Additional method of contraception recommended with: RTV, NFV, APV, EFV, LPV/r, NVP, FPV. (IDV & ATV are OK)
		No data – SQV
Anticonvulsants	Phenobarbital, Phenytoin, Carbamazepine	Avoid carbamazepine + IDV and phenytoin + LPV; all other combinations of NNRTIs or PIs & designated anti-convulsants should be given with caution and monitoring of anticonvulsant and PI levels or consider valproic acid)
Methadone	-----	NVP and EFV may decrease methadone substantially; monitor for withdrawal. IDV has no interaction; other PIs may decrease methadone levels and require monitoring for withdrawal. Methadone decreases buffered ddl levels - consider ddl EC (no interaction).
Antibiotics	Clarithromycin	RTV, LPV/r, DLV – Decrease clarithromycin dose in renal failure.
		EFV, ATV – Consider alternative to Clarithromycin (e.g. Azithromycin)
Erectile Dysfunction Agents	Sildenafil	PIs & DLV: ≤ 25 mg q 48 hr. and monitor
	Vardenafil	PIs & DLV: ≤ 2.5 mg q 72 hr
	Tadalafil	PIs & DLV: start with 5 mg and do not exceed 10 mg q 72 hr.

Drug Table 9. Drug Interactions: Combinations with PIs or NNRTIs Requiring Dose Modifications (Cont'd.)

Class	Agent	ART
Anti-Mycobacterials	Rifabutin	All PIs with RTV boosting: standard dose PI/r + RBT 150 mg qod or 150 mg 3x/wk
		APV 1200 mg bid + RBT 150 mg/d or 300 mg 3x/wk
		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 bid + RBT 150 mg qod or 150 mg 3x/wk
		NFV 1000 mg tid + RBT 150 mg/d or 300 mg 3x/wk
		NVP standard + RBT standard (no adjustment)
		RTV 600 mg bid + RBT 150 mg qod or 150mg 3x/wk
	RTV 400 mg + SQV 400 mg bid + RBT 150 mg 3x/wk	
	Rifampin	All PIs & NNRTIs contraindicated except RTV+SQV (400/400 mg bid), or EFV (800 mg/day) using standard doses of rifampin. NVP - if necessary, use with caution and monitor LFTRs
Lipid Lowering	Lovastatin, Simvastatin	Avoid PIs and DLV; no data for EFV and NVP. Caution with LPV/r, FPV, SQV/r.
	Atorvastatin	PI - Use with caution starting with lowest possible dose and monitor. FPV-consider alternative agent.
	Pravastatin	No dose change - RTV, SQV, LPV/r. No data-IDV, NFV, APV, FPV, ATV, and NNRTIs

Drug Table 9. Drug Interactions: Combinations with PIs or NNRTIs Requiring Dose Modifications (Cont'd.)

Class	Agent	ART
Miscellaneous	Antacids	APV, ATV, ddC, DLV, TPV/r-separate dosing by 1-2 hr to avoid reduced ARV bioavailability.
	Ca++ channel blockers Bepridil	APV, ATV, FPV, RTV-contraindicated. All other ARVs-drug dependent; may require dose titration and close monitoring
	All Others	All ARVs-drug dependent; may require dose titration and close monitoring
	Desipramine	RTV- Consider desipramine dose reduction
	Diltiazem	All PIs-start diltiazem with 50% dose & monitor EKG.
	Grapefruit juice	IDV ↓, SQV ↑
	H2 Blockers	ATV-separate medications by 12 hrs
	Ribavirin	ddl toxicity potentiated by ribavirin-avoid use
	Theophylline	RTV – Monitor theophylline levels
	Trazedone	RTV – lowest dose & monitor CNS
	Warfarin	RTV, DLV, EFV – Monitor INR closely if given with any PI or NNRTI

Drug Table 10. Drug Interactions: Nucleosides

Drug	AZT	d4T	ddl	TDF
Methadone	AZT AUC ↑ 40%; no dose change	d4T ↓ 27%; no dose change	Buffered ddl ↓ 61% consider ↑ ddl dose or use ddl EC	No data
ddl	–	Increased toxicity: pancreatitis, periph- eral neuropathy and lactic acidosis. Avoid if possible.	–	ddl ↑ 44% consider ddl 250 mg bid or ddl EC.
Ribavirin	Inhibits AZT activation. Avoid if possible	No data	Magnifies ddl toxicity; avoid.	No data
ATV	–	–	Buffered ddl - take ATV 2 hr before or 1 hr after ddl. Or use ddl EC - separate dosing due to food restrictions.	Avoid concomi- tant use unless ATV combined with RTV (ATV/r).
IDV	–	–	Buffered ddl - take 1 hr apart	–
Cidofovir, Gancyclovir, Valgancyclovir	–	–	–	Combination may increase levels of antiviral - monitor for toxicity

General:

- Patients should be advised to avoid all recreational drugs.
- Recreational drugs are known to interfere with adherence to prescribed regimens.

Drug Table 11. Drug Interactions: Recreational Drug Interactions*

Recreational Drug	Possible Effect of Mixing Recreational Drug with an Antiretroviral
Alcohol	Alcohol increases risk of pancreatitis with ddI. Alcohol increases ABC levels by 41% (Clinical significance unknown); augments progression of chronic HCV & HBV.
Amphetamines	RTV (low and high dose) and DLV may increase amphetamine serum levels by 2-3-fold.
Amyl Nitrate	Unknown
Barbiturates	IDV may increase serum levels of phenobarbital. May reduce levels of PIs and NNRTIs.
Cocaine	(Interaction unlikely)
Ecstasy (MDMA)	Increase in MDMA serum level and increased likelihood of overdose with PI's and NRTIs. Death has been reported with Ritonavir.
GHB (liquid X)	RTV may cause increased serum level of GHB.
Ketamine	RTV in combination with Ketamine may cause chemical hepatitis.
LSD	Unknown
Marijuana	PIs may increase THC levels (EFV may cause false positive screening test). Reduces IDV and NFV AUC by 20%; significance is unknown
Sedatives	PIs, DLV and EFV increases the serum levels of Halcion (triazolam), Valium (diazepam), Ambien (zolpidem) and Versed (midazolam) resulting in prolonged sedation. PIs, DLV and EFV may increase the levels of other benzodiazepines except lorazepam, oxazepam, and temazepam.

* The exact interaction of recreational drugs and antiretrovirals is not known. These effects are derived largely from the pharmacology/metabolism of both the prescribed and recreational drug and the theorized effects of both being taken simultaneously.

Sources of Information:

- The PWA Health Group Newsletter, Winter 1998-99 Issue 38
- Postulated Interactions with Recreational Drugs, The Immunodeficiency Clinic of Toronto's University Health Network
- The AIDS Reader 2003, 13:433.

Drug Table 12. Coadministration of PIs and NNRTIs - Dose Adjustments

	DLV	EFV	NVP
APV	Not recommended	APV 1200 bid + RTV 200 bid + EFV SD	ID
ATV	ID	ATV 300 mg + RTV 100 mg + EFV SD	ID
FPV	Avoid	<ul style="list-style-type: none"> • FPV 1400 mg qd + RTV 300 mg qd + EFV SD • FPV 700 mg bid + RTV 100 mg bid + EFV SD 	ID
IDV	DLV SD + IDV 600 q8h	<ul style="list-style-type: none"> • IDV 1000 q8h + EFV SD or consider • IDV 800 q12h + RTV 200 mg bid + EFV STD 	IDV 1000 q8h + NVP SD
LPV/r	ID	LPV/r 533/133 mg bid + EFV SD	LPV/r 533/133 mg bid + NVP SD
NFV	ID	NFV SD + EFV SD	NVP SD + NFV SD
RTV	ID	RTV SD + EFV SD	RTV SD + NVP SD
SQV	FTV 800 tid + DLV SD	SQV 400 mg bid + RTV 400 mg bid + EFV SD	<ul style="list-style-type: none"> • SQV 400 mg bid + RTV 400 mg bid + NVP SD • SQV 1000 mg bid + RTV 100 mg bid + NVP SD

All Doses in mg

Abbreviations: ID= Inadequate Data, SD= Standard Dose

Drug Table 13. Co-administration of PIs: Dose Adjustments

Drug	FPV	IDV	LPV/r	NFV	RTV	SQV
ATV	ID	Contra- indicated	ID	ID	ATV 300 qd + RTV 100 mg qd	ATV 400 qd + SQV 1200 mg qd
FPV		ID	Not recommended	ID	• FPV 700 bid + RTV 100 bid or • FPV 1400 qd* + RTV 200 qd	ID
IDV			IDV 600 bid +LPV/r SD	IDV 1200 bid + NFV 1250 bid	• IDV 400 bid + RTV 400 bid or • IDV 800 bid + RTV 100- 200 bid	ID
LPV/r				ID		LPV/r SD + SQV 1000 bid
NFV					NFV 500-750 bid + RTV 400 bid	NFV 1200 bid + FTV 800 tid
RTV						• RTV 400 bid + SQV 400 bid or • RTV 100 bid + SQV 1000 bid • RTV 100 qd + SQV 1600 qd • RTV 100 qd + SQV 2000 qd†

All Doses in mg

Abbreviations: ID= Inadequate Data, SD= Standard Dose

* Use bid regimen for treatment experienced patients

† Invirase dose using 500 mg tablets

Antiretroviral Therapy

Adult ART Table 1A. Indications for ART: DHHS Guidelines – 2004*

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 especially if VL is >20,000 c/mL, but controversial †
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**

† Patient readiness, probability of adherence, and prognosis based on CD4 count and HIV load need to be considered

Adult ART Table 1B. Indications for ART: IAS-USA Guidelines – 2004

Clinical Category	CD4+ Count	Viral Load
Symptomatic (AIDS or severe symptoms)	Treat*	—
CD4+ <200 cells/mm ³	Treat†	—
CD4+ 200–350 cells/mm ³	Consider†	Especially if CD4 count is closer to 200, VL is >50,000-100,000 c/mL, or CD4 decline is >100 cells/mm ³ /yr
CD4+ 350–500 cells/mm ³	Monitor†	Consider if VL is >100,000 c/mL or CD4 decline is >100 cells/mm ³ /yr
CD4+ >500 cells/mm ³	Monitor†	—

* Evidence from published prospective clinical trials

† Evidence from cohort studies

Adult ART Table 2A. Starting Regimens for Antiretroviral Naïve Patients: DHHS Guidelines – 2004

Regimens	# of pills per day
Preferred Regimens NNRTI-Based	
efavirenz + (lamivudine or emtricitabine) + (zidovudine or tenofovir DF) – except for pregnant women or women with pregnancy potential	2-3
Preferred Regimens PI-Based	
lopinavir/ritonavir + (lamivudine or emtricitabine) + zidovudine	8-9
Alternative Regimens NNRTI-Based	
• efavirenz + (lamivudine or emtricitabine) + (didanosine, stavudine, or abacavir) - except for pregnant women or women with pregnancy potential	3-4
• nevirapine + (lamivudine or emtricitabine) + (zidovudine, stavudine*, tenofovir or didanosine) -except with baseline CD4 count >250 cells/mm ³ in women or >400 cells/mm ³ in men	5
Alternative Regimens PI-Based	
• atazanavir + (lamivudine or emtricitabine) + (zidovudine, didanosine, abacavir, or stavudine*) or (tenofovir + ritonavir)	4-6
• fosamprenavir+ (lamivudine or emtricitabine) + (zidovudine, stavudine*, tenofovir, didanosine, or abacavir)	5-8
• fosamprenavir/ritonavir† + (lamivudine or emtricitabine) + (zidovudine, stavudine*, tenofovir, didanosine, or abacavir)	5-8
• indinavir + ritonavir† + (lamivudine or emtricitabine) + (zidovudine, stavudine*, tenofovir, didanosine, or abacavir)	7-12
• nelfinavir + (lamivudine or emtricitabine) + (zidovudine, stavudine*, tenofovir, didanosine, or abacavir)	5-8
• saquinavir (sgc or hcg)† + ritonavir + (lamivudine or emtricitabine) + (zidovudine, stavudine*, tenofovir, didanosine, or abacavir)	13-16
• lopinavir/ritonavir + (lamivudine or emtricitabine) + (stavudine*, tenofovir, didanosine, or abacavir)	7-10
Triple NRTI Regimen – As Alternative to PI- or NNRTI-based regimens	
• abacavir + lamivudine + (zidovudine or stavudine*)	2 pills/day

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

† Low-dose (100-400 mg) ritonavir

Adult ART Table 2B. Starting Regimens for Antiretroviral Naïve Patients: IAS-USA Guidelines – 2004

PREFERRED	
NNRTI Component	<ul style="list-style-type: none"> • Efavirenz • Nevirapine for selected patients
PI component	<ul style="list-style-type: none"> • Atazanavir/ritonavir • Saquinavir/ritonavir • Lopinavir/ritonavir • Indinavir/ritonavir
NRTI Component	<ul style="list-style-type: none"> • (Zidovudine or tenofovir) plus (lamivudine or emtricitabine) • Didanosine plus emtricitabine
ALTERNATIVES	
PI Component	<ul style="list-style-type: none"> • Fosamprenavir/ritonavir • Atazanavir • Nelfinavir
NRTI component	<ul style="list-style-type: none"> • Abacavir + lamivudine • Didanosine + lamivudine • Zidovudine + abacavir • Stavudine + lamivudine
Special Circumstances Only	Zidovudine, lamivudine and abacavir

Adult ART Table 2C. W.H.O. Starting Regimens for Resource Limited Countries, 2004

Criteria	Regimen			
	NVP/d4T/3TC	NVP/AZT/3TC	EFV/3TC/d4T	EFV/AZT/3TC
Use in pregnancy or pregnancy potential	Yes	Yes	No	No
Use in TB coinfection	Alternative	Alternative	Yes	Yes
Availability in fixed combination	Yes	Yes	No	No
Lab monitoring requirements	None	Hct	None	Hct
Cost per month	\$281-387	\$383-418	\$297-1,080	\$611-986

Adult ART Table 3. Advantages and Disadvantages of Antiretroviral Regimens

Drugs	Advantages	Disadvantages
Non-Nucleoside Reverse Transcriptase Inhibitors		
Class	Extensive experience Less lipodystrophy Saves PI option	Low genetic barrier to resistance Class resistance Drug interactions
EFV	Potent Low pill burden, once daily dosing, no food effect	CNS toxicity Teratogenic
NVP	Extensive experience with single dose in pregnancy	ADR-rash and hepatotoxicity including hepatic necrosis Contraindicated in women with baseline CD4 >250 cells/mm ³
Protease Inhibitors		
Class	Class-extensive experience Saves NNRTI option	ADR – metabolic complications Multiple drug interactions
ATV	Once daily dosing Low pill burden No hyperlipidemia	ADR-Jaundice & PR interval prolongation Drug interaction with TDF and EFV (can be overcome by ATV/RTV)
LPV/r	Potency Coformulated with RTV	ADR-GI intolerance Food requirement Minimal experience with and 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 boosting	ADR-Nephrolithiasis Requirement for po fluid
NFV	Substantial and favorable experience in pregnancy	ADR-diarrhea High rate virologic failure Food requirement
SQV/r	Reduced pill burden with Invirase 500 mg tab. Once daily option.	ADR-GI intolerance (sgc worse than hgc) High pill burden (until 500 mg tab INV available)

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

Drugs	Advantages	Disadvantages
Nucleoside Reverse Transcriptase Inhibitors		
AZT/3TC/ABC	Co-formulated Minimal drug interactions No food effect Preserves PI and NNRTI options	Higher rate of virologic failure ADR-ABC hypersensitivity HBV flare when 3TC stopped
Nucleoside Reverse Transcriptase Inhibitor Pairs		
AZT/3TC	Extensive experience Co-formulated No food effect	ADR-GI intolerance and marrow suppression (AZT) HBV flare when 3TC stopped
d4T/3TC or FTC	No food effect Once daily	ADR of d4T† HBV flare when 3TC or FTC stopped
TDF/FTC*	Well tolerated Co-formulated Once daily	HBV flare when TDF or FTC stopped
ddl/3TC or FTC	Once daily	ADR-ddl† HBV flare when 3TC or FTC stopped Food effect
ABC/3TC*	Co-formulated Once daily No food effect	ADR-ABC hypersensitivity HBV flare when 3TC stopped

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

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

Adult ART Table 4. Antiretroviral Regimens or Components That Are Not Generally Recommended

	Rationale	Exception
Antiretroviral Regimens Not Recommended		
Monotherapy	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Rapid development of resistance • Inferior antiretroviral activity when compared to combination with three or more antiretrovirals 	For patients currently on this treatment, it is reasonable to continue if virologic goals are achieved
ABC + TDF + 3TC as a triple NRTI regimen	High rate of virologic failure and resistance	High rate of virologic failure and resistance
TDF + ddI + 3TC	High rate of virologic failure and resistance	No exception
Antiretroviral Components Not Recommended As Part of Antiretroviral Regimen		
Amprenavir oral solution in: <ul style="list-style-type: none"> • pregnant women; • children <4 yr old; • patients with renal or hepatic failure; and • 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
ATV + IDV	Potential for additive hyperbilirubinemia	No exception
d4T + ddI in pregnancy	Reports of serious, even fatal, cases of lactic acidosis with hepatic steatosis with or without pancreatitis in pregnant women	When no other antiretroviral options are available and potential benefits outweigh the risks*
d4T + ZDV	Antagonistic	No exception
ddC + d4T or ddC + ddI	Additive peripheral neuropathy	No exception
Efavirenz in pregnancy	Teratogenic in nonhuman primate and humans.	When no other antiretroviral options are available and potential benefits outweigh the risks*

Adult ART Table 4. Antiretroviral Regimens or Components That Are Not Generally Recommended (Cont'd.)

	Rationale	Exception
Hydroxyurea	<ul style="list-style-type: none"> • 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
Saquinavir hard gel capsule (Invirase) as single PI	<ul style="list-style-type: none"> • Poor oral bioavailability (4%) • Inferior antiretroviral activity when compared to other protease inhibitors 	No exception
FTC + 3TC	No potential benefit	No exception
Not Recommended As Part of Initial Antiretroviral Regimen		
APV as single PI	Pill burden of 16 caps/day.	*
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.	*
AZT + ddC	Modest antiretroviral effect.	*

* Reasonable to use in unusual circumstances.

Adult ART Table 5. Interactions of Antiretrovirals (IAS-USA 2004 Guidelines)

Drug	Drug 2	Result	Recommendation
3TC	FTC	Similar drug	Avoid
APV	DLV	↑ APV, ↓ DLV	Avoid
APV	EFV	↓ APV	Use APV/r
APV or FPV	LPV/r	↓ APV & ↓ LPV	Avoid
ATV	TDF	↓ ATV	Use ATV/r
ATV	EFV	↓ ATV	Use ATV/r
ATV	IDV	↑ bilirubin	Avoid
AZT	d4T	Antagonism	Avoid
d4T	ddl	↑ toxicity	Avoid esp. with pregnancy
EFV	IDV	↓ IDV	↑ IDV dose
EFV	LPV/r	↓ LPV	↑ LPV dose (2x/day)
EFV	RTV	↑ EFV, ↑ RTV	↓ RTV dose
EFV	SQV	↓ SQV	Use SQV/r
NFV	SQV	↑ NFV	↓ SQV dose
NVP	LPV/r	↓ LPV	↑ LPV/r (2x/day)
NVP	IDV	↓ IDV	↑ IDV dose or IDV/r
NVP	SQV	↓ SQV	Use SQV/r
TDF	ddl	Enteric coated ddl- ↑ ddl level	ddl dose: >60 kg - 250 mg <60 kg - 200 mg

Adult ART Table 6. Methods to Achieve Readiness to Start HAART& Maintain Adherence

Patient-related:

- Negotiate a plan or regimen that the patient understands and to which s/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 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 7. Therapeutic Failure - Definitions

Virologic Failure	<ul style="list-style-type: none">• 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 ≥ 1 log₁₀ c/mL at 1-4 weeks.• Viral suppression followed by repeated positive viral load
Immunologic Failure	Failure to increase CD4 count 25-50 cells/mm ³ during first year. Note: Mean increase is about 150 cells/mm ³ in first 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.

Adult ART Table 8. Strategies for Managing Therapeutic Failure

Management of Drug Intolerance

Change single drug within class, change of classes (PI → NNRTI or NNRTI → PI) or symptomatic treatment (anti-emetic, anti-diarrheal agent, etc.)

Management of Virologic Failure

Virologic failure indicates: 1) failure of drug to reach target site due to inadequate adherence or pharmacokinetic issues (food/fasting effects, drug interactions, etc.) or 2) HIV resistance.

- Address adherence and pharmacokinetic issues
- Resistance testing – preferably while taking the failing regimen or within 4 weeks after discontinuation

Options for managing virologic failure after adherence and pharmacokinetic issues have been addressed

- Distinguish between limited, intermediate and extensive drug resistance taking into account the treatment history and prior resistance tests
- "Blips" are defined as isolated VL tests showing 50-1000 c/ml that are not sustained; these do not constitute virologic failure.
- There is no consensus about treatment changes based on VL— aggressive response is a change when two consecutive VL measurements are >400 c/ml after suppression to <400 c/ml; some delay until VL >1,000 c/ml to permit resistance tests, but this permits ongoing viral replication and selection of additional resistance mutations.
- Resistance tests should be done while the patient is taking the failing regimen or within 4 weeks of discontinuation; if there is a longer interval off therapy consider re-initiation of the regimen followed by resistance tests at 2-4 weeks.
- With limited prior treatment experience consider early change to minimize continued selection of resistance mutations and change at least two drugs; single drug substitutions based on resistance tests can be considered but is unproven.
- Treatment failure with no resistance mutations: Consider non-adherence or pharmacokinetic issues.
- Intermediate prior treatment and drug resistance: Goal is resuppression with change of at least 2 drugs.
- Extensive prior treatment and drug resistance: Goal is to preserve immune function and prevent clinical progression. Discontinuation of treatment, even failing therapy, may lead to rapid clinical deterioration.
- Specific tactics in failing regimens with multiple resistance mutations: 1) enfuvirtide (T-20), preferably combined with ≥two active agents; 2) use of new drugs through a treatment IND or clinical trial; 3) strategies may differ based on severity of immunodeficiency so that with a CD4 <100 cells/mm³ addition of a single drug to achieve even modest viral suppression may prevent clinical progression but with higher CD4 counts continuation of the failing regimen may be more appropriate.

Adult ART Table 9. Indications for Resistance Testing

Indicated	Virologic failure with VL >1,000 c/mL Suboptimal viral suppression with VL >1,000 c/mL Acute HIV infection
Consider Testing	Chronic HIV infection before initiating therapy
Not Indicated	After discontinuation of antiretroviral therapy >1 month duration Viral load >1,000 c/mL

Adult ART Table 10. Resistance Mutations

Drug	Codon Mutations
Nucleosides and Nucleotides	
3TC	44D, 65R, 118I, 184VI
ABC	65R, 74V, 115F, 184V
AZT	41L, 44D, 67N, 70R, 118I, 210W, 215YF, 219Q
d4T	41L, 44D, 65R, 67N, 70R, 118I, 210W, 215YF, 219QE
ddC	65R, 69D, 74V, 184V
ddI	65R, 74V
FTC	65R, 184 V/I
TDF	65R
Multinucleoside Q151M	62V, 75I, 77L, 116Y, 151M
Multinucleoside 69 insertion	41L, 62V, 67N, 69 insert, 70R, 210W, 215YF, 219QE
Multinucleoside TAMS	41L, 44D, 67N, 70R, 118I, 210W, 215YF, 219QE
Non-Nucleoside Reverse Transcriptase Inhibitors	
DLV	103N, 106M, 181C, 188L, 236L
EFV	100I, 103N, 106M, 108I, 181CT, 188L, 190SA, 225H
NVP	100I, 103N, 106AM, 108I, 181CI, 188 CLH, 190A
Multi-NNRTI resistance	103N, 106M, 188L
Multi-NNRTI resistance-accumulation	100I, 106A, 181CI, 190SA, 230L

Adult ART Table 10. Resistance Mutations (Cont'd.)

Drug	Major	Minor
Protease inhibitors		
APV, FPV	50V, 84V	10 FIRV, 32I, 46I, 47V, 54LVM, 73S, 90M
ATV	50L, 84V	10IFV, 20RMI, 24T, 32I, 33IFV, 36ILV, 46I, 48V, 54V, 71V, 73CSTA, 82A, 88S, 90M
IDV	46IL, 82AFT, 84V	10IRV, 20MR, 24I, 32I, 36I, 54V, 71VT, 73SA, 77I, 90M
LPV/r		10 FIRV,, 20MR, 24I, 32I, 33F, 46IL, 47VA, 50V, 53L, 54VL AMTS, 63P, 71VT, 73S, 82 AFTS, 84V, 90M
NFV	30N, 90M	10FI, 36I, 46IL, 71V, 77I, 82AFTS, 84V, 88I
RTV	82AFTS, 84V	10FIRV, 20MR, 32I, 33F, 36I, 46IL, 54VI, 71VT, 77I, 90M
SQV	48V, 90M	10IRV, 54VL, 71VT, 73S, 77I, 82A, 84V
TPV	33IF, 82AFLT, 84V	10IV, 20MLT, 46I, 54V
Multi PI resistance	46IL, 82AFTS, 84VAC, 90M	10 FIRV, 32I, 54VML
Entry Inhibitors		
T-20	Gp41 envelope - 36DS, 37V, 38AM, 39R, 42T, 43D	

* Adapted from IAS-USA *Topics HIV Med* 2004;12:119.

† 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.

Pregnancy and HIV

Pregnancy Table 1. Antiretroviral Drugs in Pregnancy – DHHS Guidelines*

Advisory	Drugs
Nucleosides and Nucleotides	
Recommended	AZT and 3TC
Alternatives	ddl, FTC, d4T and ABC
Not recommended	ddC
Insufficient Data to Recommend Use	TDF (concern for potential fetal bone effects)
Non-nucleoside RT Inhibitors	
Recommended	NVP (Use with caution or avoid in women with CD4 >250/mm ³ who are starting ART)
Not recommended	EFV (use in second trimester can be considered); DLV
Insufficient Data to Recommend Use	DLV
Protease Inhibitors	
Recommended	NFV and SQV/r (Fortovase)
Alternatives	IDV, LPV/r, RTV
Insufficient Data to Recommend Use	APV, FPV, ATV
Fusion Inhibitors	
Insufficient data to recommend use	All

* 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, June 23, 2004.

Pregnancy Table 2: Antiretroviral Drugs and Specific Concerns for Pregnancy

Agent	Human studies in pregnancy	Concerns
Nucleosides and nucleotides		
ABC	No studies	Hypersensitivity reaction
ddl	PACTG 249-well tolerated and good pharmacokinetics	Lactic acidosis rates increased, esp. when combined with d4T
3TC	Well tolerated, good pharmacokinetics	AZT + 3TC-preferred
TDF	No studies	Primate study shows neonatal bone toxicity in 25%
ddC	No studies	Rarely used and toxic
AZT	Extensive studies showing efficacy in reducing MTCT	Possible mitochondriod toxicity reported from France; not supported in US studies
Non-nucleosides		
DLV	No studies; anecdotal cases: 3/7 ectopic pregnancies	Concerns for potency and tid regimen
EFV	Teratogenic in humans and primates-FDA warning to avoid in 1st trimester	Teratogenicity
NFV	Good pharmacokinetics shown in PACTG 250 safety and efficacy of single perinatal dose to prevent transmission shown in many trials	Chronic Rx: High rate of serious adverse reactions-hepatic necrosis with baseline CD4 >250 cells/mm ³ and severe rash reactions
Protease inhibitors		
APV	No studies	Avoid oral solution (propylene glycol) Concern for pharmacokinetics
ATV	No studies	Hyperbilirubinemia Concern for pharmacokinetics
FPV	No studies	Concern for pharmacokinetics
IDV	AUC decreased 60-80% in pregnancy	Decreased AUC in pregnancy Concern for hyperbilirubinemia
LPV/r	No studies – PACTG 354 pending	Concern for pharmacokinetics
NFV	PACTG 353 showed doses of 1250 mg bid achieved therapeutic levels (but not 750 mg tid)	Concerns for potency of NFV
SQV	PACTG 386 showed SQV/r 800/100 mg bid produced adequate levels (but not SQV 1200 mg tid)	A preferred PI-based regimen

Pregnancy Table 3. Antiretroviral Regimens in Pregnant Women

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 with d4T, d4T with 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:** pharm. 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 and HU** are teratogenic.

Pregnancy Table 4. Management of UNTREATED Pregnant Patients Including C-Section

Time Of Presentation	Recommended Management
<p>Early In Pregnancy (<36 Weeks)</p>	<ul style="list-style-type: none"> • Standard clinical, immunologic and virologic evaluation and resistance testing (same as other pts). • If VL >1,000 or CD4 <350, HAART with AZT (076 Protocol); but consider delaying ART until after 10-12 wks gestation due to concerns for antiretroviral agents at the time of organogenesis. This risk is not established with the possible exception of EFV. See also, Pregnancy Tables 1 & 2. • VL <1,000 and CD4 >350, consider AZT monotherapy (076 Protocol), AZT +3TC, or HAART after the first trimester for prevention of perinatal transmission; [<i>J Infect Dis 2001</i>; 183:539] • Monitor VL and CD4+ to plan for delivery
<p>Late In Pregnancy (≥36 Weeks)</p>	<ul style="list-style-type: none"> • Standard clinical, immunologic and virologic evaluation and resistance testing. • If VL >1,000 or CD4 <350, HAART with AZT (076 Protocol); see cautions, Pregnancy Tables 1 & 2. • VL <1,000 and CD4 >350, consider AZT monotherapy (076 Protocol), AZT +3TC, or HAART for prevention of perinatal transmission; [<i>J Infect Dis 2001</i>; 183:539] • 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.
<p>Labor</p>	<ul style="list-style-type: none"> • Initiate therapy (See Pregnancy Table 3.C., above for Untreated Women Presenting In Labor) • Postpartum immunologic and virologic evaluation of mother for ART. • Infant should undergo diagnostic testing for HIV to determine need for ongoing ART.
<p>Postpartum</p>	<ul style="list-style-type: none"> • Initiate the 6 wk neonatal AZT protocol preferably within 6-12 hours of delivery. • Infant should undergo diagnostic testing to determine need for ART. • The mother should undergo evaluation to determine indications for ongoing ART.

Pregnancy Table 5. Management of TREATED Pregnant Patients Including C-Section

Time Of Presentation	Recommended Management
Early In Pregnancy (<36 Weeks)	<ul style="list-style-type: none"> • Continue ART with standard monitoring, but: <ul style="list-style-type: none"> o May consider discontinuation during 1st trimester: all drugs should be stopped and restarted simultaneously to reduce risk of resistance. o Include AZT if tolerated; see cautions for antiretrovirals, Pregnancy Tables 1 & 2.
Late In Pregnancy (≥36 Weeks)	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Initiate ACTG 076 Protocol, Intrapartum in Table 3, Above; • 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 6. Delivery Procedures and Therapy

Procedure	Therapy
Cesarean Section	<ul style="list-style-type: none"> • Schedule for 38 wk. • If on ARV, 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 Table 3, Above.
Vaginal Delivery	<ul style="list-style-type: none"> • If on ARV 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 <i>TREATED</i> mother, use ACTG 076 Protocol, Postpartum (infant) in Table 3.A., above. If <i>UNTREATED</i> mother use treatment from Table 3.C., above which matches maternal regimen.

Antiretroviral Pregnancy Registry (www.APRegistry.com): This is an observational database on women who have exposure to antiretroviral drugs during pregnancy. The main goal is to determine teratogenicity. No names or other identifiers are collected.

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Pregnancy Table 7: Drugs for Opportunistic Infections in Pregnancy

Agent	Class*	Recommendation
Acyclovir	B	Treatment reserved for severe herpes or varicella; well tolerated and no consequences with >700 exposures
Albendazole	C	Teratogenic in rodents; reserve for severe microsporidiosis in 2nd and 3rd trimester
Amphotericin	B	Standard indications
Atovaquone	C	Standard indications; limited experience
Azithromycin	B	Standard indications
Cidofovir	C	Teratogenic in animals; risk in women unknown
Ciprofloxacin	C	Arthropathy in beagle dogs; not recommended in pregnancy
Clarithromycin	C	Teratogenic in animals and increased rate of abortions in women – azithromycin preferred for MAC
Clindamycin	B	Standard indications
Dapsone	C	Limited experience; may increase risk of kernicterus
Doxycycline	D	Risk to infant teeth; avoid
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 + pyridoxime
Itraconazole	C	Teratogenic in animals and concern for azoles in pregnancy; use for systemic mycosis-ampho B often preferred
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

Adult ART Table 7: Drugs for Opportunistic Infections in Pregnancy (Cont'd.)

Agent	Class*	Recommendation
Primaquine	C	Limited experience; theoretical risk of hemolytic anemia with G6PD deficiency
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
TMP-SMX	C	Teratogenic in rodents; avoid use in first trimester if possible
Valacyclovir	B	Prodrug of acyclovir
Voriconazole	D	Teratogenic in rodents; amphotericin B preferred

* 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

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

Pathogen	Indication	First Choice
Strongly Recommended		
<i>P. carinii</i>	CD4 < 200 or CD4 % <14, thrush, hx AIDS defining illness or FUO	TMP-SMX 1 DS/d* or TMP-SMX 1 SS/d*
Tuberculosis	See Adult OI Table 4. Latent TB	
Toxoplasmosis	+ anti-Toxoplasma IgG and CD4 <100 cells/mm ³	TMP- SMX 1 DS* qd
<i>Mycobacterium avium complex</i>	CD4 <50 cells/mm ³	Azithromycin 1200 mg/wk Clarithromycin 500 mg bid
Varicella	Chickenpox /shingles exposure + susceptible (no history of disease and varicella seronegative)	VZIG 5 vials (6.25 ml) IM <96 h post exposure

* 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)

Alternatives	Comment
<p>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</p>	<p><u>Immune reconstitution recommendations:</u> Discontinue primary & secondary prophylaxis if CD4 >200 cells/mm³ for ≥3 mos.</p> <p><u>Restart Prophylaxis:</u> Restart prophylaxis if CD4 decreases to <200 cells/mm³</p>
<p>TMP- SMX 1 SS* 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</p>	<p><u>Immune reconstitution recommendations:</u> Discontinue if CD4 >200 cells/mm³ for ≥3 mos</p> <p><u>Restart Prophylaxis:</u> CD4 decreases to <100-200 cells/mm³</p>
<p>Rifabutin†300 mg/d or Azithromycin 1200 mg / wk + Rifabutin† 300 mg/d</p>	<p><u>Immune reconstitution recommendations:</u> Discontinue if CD4 >100 cells/mm³ for ≥3 mo</p> <p><u>Restart prophylaxis</u> CD4 decreases to 400 cells/mm³</p>
	<p>Acyclovir has been removed from OI prophylaxis guidelines due to lack of documented efficacy</p>

Adult OI Table 1. 2001 USPHS/IDSA Guidelines for Prevention of Opportunistic Infections (Cont'd.)

Pathogen	Indication *	First Choice
Generally Recommended		
<i>S. pneumoniae</i>	All Patients with CD4 > 200	Pneumovax
Hepatitis B	Susceptible- (anti-HBc or Anti HBs negative)	HBV vaccine series
Influenza	All Patients	Influenza vaccine
Hepatitis A	Susceptible- (anti-HAV neg) and risk: MSM, IDV, chronic liver disease inducing chronic HBV or HCV	Hepatitis A vaccine series

Alternatives	Comment
None	<u>Immune reconstitution:</u> Consider reimmunization if CD4 increases to >200 and initial immunization was given when CD4 <200.
None	
Rimantidine 100 mg bid Amantadine 100 mg bid Oseltamivir 75 mg qd	
None	

Adult OI Table 2. Treatment of Opportunistic Infections

Infection/Organism	Treatment
Bartonella	<p>Preferred:</p> <ul style="list-style-type: none"> • Erythromycin 500 mg qid po or IV, or • Doxycycline 100 mg bid po or IV. <p>Alternative:</p> <ul style="list-style-type: none"> • Azithromycin 600 mg qd po or • Clarithromycin 500 mg bid po
Candida – Thrush	<p>Preferred:</p> <ul style="list-style-type: none"> • Clotrimazole troches 10 mg po 5x/d, or • Nystatin susp 5 ml qid or pastilles 4-5x/d, or • Fluconazole 100 mg qd po, or • Itraconazole oral susp 200 mg qd
Candida – Esophagitis	<p>Preferred:</p> <ul style="list-style-type: none"> • Fluconazole 100 mg qd (up to 400 mg) qd po or IV x 14-21d, or • Itraconazole oral soln 200 mg qd po.
Candida – Vaginitis	<p>Preferred:</p> <ul style="list-style-type: none"> • Topical azole x 7d, or • Topical naftifine x 7-14d, or • Topical boric acid x 14d, or • Itraconazole 200 mg bid x 1d or 3d, or • Fluconazole 150 mg x 1 po
Cryptosporidiosis	HAART
Cryptococcosis – Meningitis	<p>Preferred:</p> <p>Amphotericin B 0.7 mg/kg qd IV plus flucytosine 25 mg/kg qid po x 2 weeks</p>
Cytomegalovirus - Retinitis	<p>Preferred:</p> <ul style="list-style-type: none"> • Intraocular ganciclovir implant + valganciclovir 900 mg qd po (preferred for immediate vision threatening lesion), or • Ganciclovir 5 mg/kg bid IV x 14-21 d, then 5 mg/kg/d IV, or • Valganciclovir 900 mg bid po x 14-21 d, then 900 mg qd po, or • Foscarnet 60 mg/kg q8h IV or 90 mg/kg q 12h IV x 14-21 d; then 90-120 mg/kg IV qd, or • Cidofovir 5 mg/kg q 7d IV x 2 then 5 mg/kg q 14d IV.

Comment
<p>Duration: ≥ 3 months; lifelong if relapse</p>
<p>Fluconazole refractory:</p> <ul style="list-style-type: none"> • Itraconazole oral soln 200 mg qd po, or • Ampho B 0.3 mg/kg/d IV <p>Relapsing disease: Chronic fluconazole only if recurrences are frequent or disabling</p>
<p>Duration: Continue azole with disabling or recurrent infection</p> <p>Fluconazole-refractory:</p> <ul style="list-style-type: none"> • Caspofungin 70 mg x 1, then 50 mg qd IV x 7 d, or • Ampho B 0.3-0.7 mg/kg qd IV
<p>High opening pressure: Lumbar drainage</p> <p>Renal failure or Ampho B intolerance: Lipid formulation amphotericin 4 mg/kg IV qd + flucytosine 25 mg/kg qid po x 2 weeks</p> <p>Consolidation therapy: Fluconazole 400 mg po qd x 8 weeks or until CSF cultures are sterile</p> <p>Alternative-consolidation: Itraconazole 200 mg bid po</p> <p>Maintenance therapy: Fluconazole 200 mg qd po</p> <p>Alternative-maintenance:</p> <ul style="list-style-type: none"> • Ampho B 1 mg/kg/wk IV (if multiple relapses on azole or intolerance to azoles) • Itraconazole 200 mg qd po (if intolerant or failure with Fluconazole)
<p>Duration: Implant – change q 6-8 mo.</p> <p>Systemic: continue until inactive disease + CD4 > 100/mm³ x 3-6 mo.</p> <p>Immune recovery uveitis: Periocular steroids or short course oral prednisone.</p>

Adult OI Table 2. Treatment of Opportunistic Infections (Cont'd.)

Infection/Organism	Treatment
Cytomegalovirus – Colitis, Esophagitis, Pneumonia	Preferred: Valganciclovir (oral), ganciclovir (IV), foscarnet (IV) above doses for CMV retinitis x 14-21d
Cytomegalovirus – Neurologic Disease	Preferred: Ganciclovir + foscarnet above doses for CMV retinitis
Hepatitis B Virus	Preferred (No data for recommendation in HBV-HIV co-infection): HAART plus: 3TC 150 mg bid po x ≥ 1 year or 6 mo. post HBeAg seroconversion ± either : <ul style="list-style-type: none"> • Tenofovir, or • Adefovir, or • Interferon alfa 2a (or Peginterferon alfa 2b) 5 mil units SQ qd or 10 mil units 3x (wk x 16-24 wks (HBeAg pos) or ≥ 12 mo (HBeAg neg).
Hepatitis C Virus	Preferred: Peginterferon alfa 2b 1.5 mcg/kg (or Peginterferon alfa 2a) 180 mcg/kg SQ q wk + ribavirin 400 mg bid po x 48 weeks
Herpes Simplex Virus – Moderate or Severe Mucocutaneous	Preferred: Acyclovir 5 mg/kg q8h IV, then: <ul style="list-style-type: none"> • Fanciclovir 500 mg bid po, or • Acyclovir 400 mg 4-5x/d po when lesions begin to regress and continue until lesions healed.

Comment
<p>Maintenance: Consider after relapse</p>
<p>No antiretroviral therapy: Adefovir 10 mg qd po 3TC-experienced >1 year + HBeAg pos:</p> <ul style="list-style-type: none"> • Adefovir 10 mg qd po added to 3TC or to replace 3TC, <i>or</i> • Tenofovir 300 mg qd po + ART ± 3TC/FTC.
<p>Contraindication to Ribavirin: Peginterferon alone</p>
<p>Acyclovir-resistant HSV: Foscarnet 120-200 mg/kg qd IV in 2-3 daily doses</p>

Adult OI Table 2. Treatment of Opportunistic Infections (Cont'd.)

Infection/Organism	Treatment
Herpes Simplex – Keratitis	<p>Preferred: Trifluridine 1% ophthalmic soln q2h up to 9 gtts/d ≤ 21d</p>
Herpes Simplex – Encephalitis	<p>Preferred: Acyclovir 10 mg/kg q8h IV x 14-21d</p>
Microsporidia	<p>Preferred: HAART</p>
Mycobacterium avium	<p>Preferred: Clarithromycin 500 mg bid po + ethambutol 15 mg/kg qd po ± Rifabutin 300 mg qd po for severe disease.</p> <p>Alternative to Clarithromycin: Azithromycin 500-600 mg qd po Third/fourth drug: Ciprofloxacin 500-750 mg bid po or Levofloxacin 500 mg qd po or Amikacin 10-15 mg/kg qd IV</p>
Mycobacterium tuberculosis	<p>Preferred: Initial Phase – 8 weeks: <ul style="list-style-type: none"> • INH 300 mg qd po + pyridoxime 50 mg qd po, and • Rifampin 600 mg/qd (or rifabutin), and • Pyrazinamide < 55 kg: 1 gm/d, 56-75 kg: 1.5 gm/d > 76 kg 2 gm/d, and • Ethambutol < 55 kg: 800 mg; 56-75 kg: 1.2 gm; > 76 kg: 1.6 g qd Continuation phase – 18 weeks: <ul style="list-style-type: none"> • INH 300 mg qd po or 900 mg 2-3x/week, and • Rifampin 600 mg qd po or rifabutin </p>

Comment
<p>Enterocytozoon bieneusi: Fumagillin 60 mg qd po Microsporidia other than <i>E. bieneusi</i>: Albendazole 400 mg bid po until CD4 >200/mm³ Disseminated disease: Itraconazole 400 mg qd po + albendazole with Trachipleistophora or Brachiola</p>
<p>Duration: Lifelong unless:</p> <ul style="list-style-type: none"> • 12 mo treatment, and • asymptomatic, and • CD4 >100/mm³ x 3-6 mo.
<p>NOTE: DOT is preferred Continuation phase: rifampin ≥ 3x/week if CD4 <100</p> <p>INH resistance:</p> <ul style="list-style-type: none"> • Rif + PZA + EMB x 6 mo • Rif + EMB x 12 mo + PZA x ≥ 2 mo. <p>Rif resistance: INH + PZA + EMB + FQX ≥ 12 mo.</p> <p>Liver disease with AST > 3x ULN pre Rx:</p> <ul style="list-style-type: none"> • Standard Rx with careful monitoring, or • Rif + EMP + PZA x 6 mo, or • INH + Rif + EMB x 2 mo, then INH + Rif x 7 mo. <p>Severe liver disease: Rif + EMB x 12 mo ± FQ 1st 2 mo.</p>

Adult OI Table 2. Treatment of Opportunistic Infections (Cont'd.)

Infection/Organism	Treatment
<p>Pneumocystis jiroveci (formerly carinii)</p>	<p>Preferred:</p> <ul style="list-style-type: none"> • TMP-SMX 15-20 mg/kg q 6-8h po or IV, or • TMP-SMX 2 DS tid (TMP 15 mg/kg/d) x 21d (14 days with rapid response + toxicity) <p>Alternative-Severe disease: Pentamidine 3-4 mg/kg/d IV</p> <p>Alternative-moderate or mild disease:</p> <ul style="list-style-type: none"> • Dapsone 100 mg qd + TMP 5 mg/kg tid, or • Primaquine 15-30 mg qd + clindamycin 600-900 mg IV q 6-8h (or clindamycin 300-450 mg po q 6-8hr), or • Atovaquone 750 mg bid po
<p>Salmonella</p>	<p>Preferred: Ciprofloxacin 500-750 mg bid po (or gatifloxacin, moxifloxacin)</p> <p>Alternative:</p> <ul style="list-style-type: none"> • TMP-SMX po or IV, or • Ceftriaxone, or • Cefotaxime
<p>Toxoplasmosis</p>	<p>Preferred-Acute: Pyrimethamine 200 mg x 1 po, then 50 mg (<60 kg) or 75 mg (> 60 kg) qd po + sulfadiazine 1 g (< 60 kg) or 1.5 g (> 60 kg) qid po + leucovorin 10-20 mg qd po x ≥ 6 weeks.</p> <p>Alternative-Acute:</p> <ul style="list-style-type: none"> • Pyrimethamine + leucovorin (as above) +: <ul style="list-style-type: none"> o Clindamycin 600 g q6h po or IV, or o Atovaquone 1500 mg bid po, or o Azithromycin 900-1200 qd po • TMP-SMX 5 mg/kg bid IV or po, or • Atovaquone 1.5 g bid po ± sulfadiazine 1-1.5 g q6h po, or <p>Miscellaneous:</p> <ul style="list-style-type: none"> o Pyrimethamine + leucovorin + clarithromycin 500 mg bid po o 5 FU + Clindamycin; o Dapsone + pyrimethamine + leukovorin o Minocycline/doxycycline + either pyrimethamine or sulfadiazine or clindamycin <p>Preferred-Maintenance:</p> <ul style="list-style-type: none"> • Continue half dose indicated above for pyrimethamine + Sulfadiazine or clindamycin or TMP-SMX, or • Pyrimethamine 50 mg qd po + leucovorin 15 mg qd po + sulfadiazine 1 g q12h] 3x/week.

Comment
<p>Hypoxia (PaO₂ < 70 mm Hg or A-a O₂ gradient > 35 mm Hg):</p> <ul style="list-style-type: none"> • Prednisone: 40 mg bid days 1-5, 40 mg qd days 6-10, then 20 mg qd days 11-21, <i>or</i> • IV methylprednisolone as 75% prednisone dose.
<p>NOTE:</p> <p>Mild gastroenteritis only: Treat 7-14d</p> <p>CD4 <200/mm³ ± bacteremia: Treat ≥ 4-6 weeks</p> <p>Relapse: Treat several months or until immune reconstitution</p>

Adult OI Table 3. Immune Reconstitution Syndrome

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

Common Features

- MAC accounts for 1/3 of all reported cases.
- Usually occurs at 1-8 weeks post HAART initiation.
- Baseline CD4 count is usually <50 cells/mm³ and increases 2-4 fold in ≤12 months.
- May occur while treating OI or at time of OI clinical stability.
- Usual treatment is continued ART, antimicrobial therapy agents for the OI, and NSAIDS and/or steroids.

Agent	Clinical Features	Treatment
M. avium	Adenitis, pulmonary infiltrates, liver granuloma, mediastinitis, osteomyelitis, cerebritis, skin	ART, antibiotics, ± NSAIDS or steroids.
M. tuberculosis	Pneumonia, ARDS, adenitis, hepatitis, CNS TB, renal failure, epididymitis	ART, anti-TB meds, NSAIDS ± steroids.
M. leprae	Cutaneous	ART, dapsone.
Cryptococcus	Meningitis, palsy, hearing loss, abscess, mediastinitis, adenitis	ART, azole, steroids.
P jirovecii	Pneumonia	ART, anti-PCP meds, steroids.
HBV and HCV	Hepatitis flare	ART, ? d/c interferon.
JC virus	CNS lesions-inflammation (MRI)	ART, steroids, cidofovir.
HSV	Chronic erosive ulcers, encephalitis	ART, antivirals, steroids.
Varicella	Zoster flare	ART, antivirals.
CMV	Vitritis, cytooid 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 Testing:

- 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.

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

Treatment of Latent TB

- Rule out active TB based on symptoms and chest x-ray
- **Preferred Regimens:**
 - o INH 300 mg + pyridoxine 50 mg qd for 9 months (270 doses in ≤ 12 months); or
 - o INH 900 mg + pyridoxine 100 mg 2X/wk by directly observed therapy for 9 months (76 doses in ≤ 12 months)
- **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 sx suggesting hepatitis.
- LFTs (ALT and bilirubin) at baseline, 1 mo., 3 mo., and with symptoms of hepatitis. D/C IHN if asymptomatic and ALT increases to $\geq 5X$ ULN or if symptomatic and ALT increases to $\geq 3X$ 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.)

Adult OI Table 5. Treatment Drug-Susceptible Active Tuberculosis

Phase 1 (8 weeks)	Phase 2*: regimen, doses, minimal duration
<u>INH, RIF, PZA, EMB 8 weeks</u> • 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).
<u>INH, RIF, PZA, EMB 2 wk/6 week</u> 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)
<u>INH, RIF, PZA, EMB 8 weeks</u> 3 x/week for 8 weeks (24 doses)	INH/RIF 3x/week for 18 weeks (54 doses)
<u>INH, RIF, EMB 8 weeks</u> • 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 week (155 doses); or • INH/RIF 2x/wk for 31 weeks (62 doses).

INH = Isoniazide, RIF = Rifampin, 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 6: Special Considerations for TB Treatment with HIV Co-Infection

Identical for general population except:

- Always treat TB first in patients with dual infection. Problems with initiating therapy simultaneously is high pill burden (6-7 meds) including many with ADRs including hepatitis and the risk of immune reconstitution syndrome.
- Usually delay initiating HARRT based on CD4 count: CD4 <50 cells/mm³—delay ≥ 2 wks, CD4 50-200 cells/mm³—delay ≥8 wks, CD4 200-350 cells/mm³—delay until TB treatment completed.
- **CD4 <100 cells/mm³:** Continuation phase should be daily or 3x/week.
- **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 or RTV + SQV (Invirase or Fortovase). With other PIs and NNRTIs use rifabutin.
- Rifabutin combined with other PIs and NNRTI requires dose adjustment of both. See Drug Table 9. (www.cdc.gov/nchstp/tb/)
- 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 in 7-36%; clinical features - high fever; increased adenopathy, CNS lesions, pulmonary infiltrates and pleural effusions. Treatment is symptomatic; if severe give prednisone 1 mg/kg and reduce steroid dose at 1-2 weeks.

Adult OI Table 7. Doses Of Antituberculosis Drugs - First line drugs

Drug	Daily	l/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	1.5gm
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

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

Adult OI Table 8. Treatment of Hepatitis C

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 weeks post treatment) with genotype one of 14-29% [Chunk, 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 weeks with non-1 genotypes.

Pretreatment Evaluation

- Counsel patient on risks and benefits - if 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/mm³ and mean CD4 >500 cells/mm³).
- 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

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/mm³.

Regimen

- All genotypes treated with pegylated interferon and ribavirin x 48 weeks
- Peginterferon alfa 2a (Pegasys) 180 mg or alfa 2b (Peg-Intron) – 1.5 mg/kg SC qd x 48 weeks
- **Ribavirin:** 800 mg qd x 48 weeks*

Follow-up

- Reinforce birth control for now and 6 months post 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 log₁₀ IU/mL. Retest at end of treatment and 6 mos post treatment (wk 72) to determine SVR.
- Neuropsychiatric evaluation monthly \pm SSRI & consultation.
- **Thyroid:** TSH at 3 + 6 month intervals.
- **HIV:** CD4 count and viral load every 3-4 months.

* Failure to achieve no detectable HCV or a 2 log₁₀ IU/ml decrease at 12 weeks 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/nchstp/dstd/dstdp.html>

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
Urethritis	<ul style="list-style-type: none"> • Patient self-report sx • Review of hx at follow- up visits, including contact with other case. 	Confirm Urethritis and test for Gonorrhea and Chlamydia
Gonorrhea	<ul style="list-style-type: none"> • Patient self-report sx • Review of hx at follow- up visits, including contact with other case. • Many infections are asymptomatic in men and women: consider urinary NAAT for GC & CT in sexually active men and women 	Gram stain and/or culture (or other specific test) of urethral or cervical swabs. Urine NAAT tests are valid for urethral infections and may be more acceptable to patients.
Chlamydia	<ul style="list-style-type: none"> • Patient self-report sx • Review of hx at follow- up visits, including contact with other case. • Most infections are asymptomatic • Routine cervical tests for sexually active women <25 yrs. Consider routine NAAT urine test for GC & CT in sexually active women >25 yrs and men. • Consider repeat test annually or more often, especially if high risk behavior or prior positive test. 	Culture (or other specific test). Urine PCR/LCR tests are valid for urethral infections and may be more acceptable to patients.
Syphilis	<ul style="list-style-type: none"> • Patient self-report sx • Contact to case. • Screen at initial visit • Repeat screen annually 	<ul style="list-style-type: none"> • RPR(or VDRL) PLUS FTA-ABS if positive • Darkfield exam or DFA of lesion material or exudates (primary syphilis).

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

† Screening interval depends upon community prevalence, outcome of women's previous screening tests, and individual risk.

Treatment
For non-gonococcal urethritis treat for Chlamydia
<p>Urethral, endocervical, rectal: ceftriaxone 125 mg IM x 1 (also for pharyngeal), ciprofloxacin‡ 500 mg po x 1 (also for pharyngeal), ofloxacin* 400 mg po x 1, levofloxacin 250 po x 1; or cefixime 400 mg po x 1, PLUS azithromycin 1 gm po x 1 or doxycycline* 100 mg po bid x 7 days</p>
<p>Disseminated GC: Patients with disseminated GC infections are most appropriately treated in the hospital. Consult full-text of the guidelines for treatment recommendations.</p>
<p>azithromycin 1 gm po x 1 or doxycycline* 100 mg po bid x 7 days</p>
See table: STD/HIV Table 2. Management of Syphilis Co-Infection: Summary

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

Condition	Identification/Screening	Diagnosis
Herpes Simplex	<ul style="list-style-type: none">• Patient self-report sx• Review of hx at follow-up visits• Most common cause of genital ulcer disease in the US and the world• Many infections are asymptomatic unless history is targeted	Patients with lesions suspected to be herpes should be evaluated to rule out syphilis. Virologic Tests: Culture, DFA Serology for HSV-2

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

(Cont'd.)

Treatment
<p>Episodic therapy of recurring infection: Genital: acyclovir 200 mg po 5X per day for 5 days, or 400 mg po tid for 5 days, or 800 mg po bid for 5 days; famciclovir 125 mg po bid for 5 days; valacyclovir 1 gm po qd for 5 days, or 500 mg po bid for 3-5 days, Suppression: acyclovir 400 mg po bid; famciclovir 250 mg po bid; or valacyclovir 500 mg po qd, or 1 gm po qd HSV in HIV-coinfected patients with low CD4 counts show flares that are more severe, more common, more likely to be disseminated and more likely to involve acyclovir-resistant HSV. Many patients require IV acyclovir (15-30 mg.kg/day) or foscarnet for acyclovir- resistant HSV.</p>

‡ tetracycline, fluoroquinolones contraindicated in pregnancy

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

Form	Treatment	LP†
Primary syphilis	Initial: Benzathine penicillin G 2.4 mil units IM x 1 Pen. Allergic - doxycycline 100 mg po bid x 14 days Re-treatment Benzathine penicillin G 2.4 mil units IM x 3 (weekly)	Neuro sx Treatment failure
Secondary syphilis	Initial: Benzathine penicillin G 2.4 mil units IM x 1 Pen. allergic- doxycycline 100 mg po bid x 14 days Re-treatment Benzathine penicillin G 2.4 mil units IM x 3 (weekly)	Neuro sx Treatment failure
Early latent (<1 yr)	Initial: Benzathine penicillin G 2.4 mil units IM x 1 Pen. allergic- doxycycline 100 mg po bid x 14 days Re-treatment Benzathine penicillin G 2.4 mil units IM x 3 (weekly)	All HIV-infected patients
Late latent (>1 yr or unknown duration)	Benzathine penicillin, 2.4 mil units IM x 3 (weekly) Pen. allergic- doxycycline 100 mg po bid x 28 days ‡	All HIV-infected patients
Late syphilis (tertiary, not neurosyphilis)	Benzathine penicillin, 2.4 mil units IM x 3 (weekly) Pen. allergic- doxycycline 100 mg po bid x 28 days ‡	All patients
Neurosyphilis (or ocular syphilis)	Aq penicillin G, 18-24 mil units/day x 10-14 days administered as 3-4 million units IV q 4 hr or Procaine penicillin 2.4 million units IM qd + probenecid 500 mg po qd X10-14 days Some recommend benzathine penicillin, 2.4 million units IM weekly X 3 weeks after completion of IV course. Penicillin allergy: desensitization required.	Required

* 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.

Follow-up VDRL/RPR	Expectation VDRL/RPR	Indications to Re-treat
HIV: 3, 6, 9, 12 & 24 mos	Four-fold decrease at 6 mos	Titer increases four-fold and CSF negative. Titer fails to decrease four-fold at 6-12 mos. Symptoms persist or recur
HIV: 3, 6, 9 & 12 mos	Four-fold decrease at 6 mos	Titer increases \geq four-fold and CSF negative. Titer fails to decrease four-fold at 6-12 mos. Symptoms persist or recur
6, 12, 18, & 24 mos	Four-fold at 12 to 24 mos.	Titer increases four-fold Titer of >1:32 fails to decrease four-fold at 12-24 mos Develops signs or sx of syphilis
6, 12, 18, & 24 mos	Four-fold decrease in titer at 12-24 mos (lower initial titers may remain unchanged)	Titer fails to decrease four-fold at 12-24 mos. Increase titer by four-fold at any time after 3 mos.
6 & 12 mos	As above Granulomatous lesions should heal	As above Documentation of <i>T. pallidum</i> or other histologic feature of late syphilis
Every 6 mos. until negative	CSF WBC decrease at 6 mos and CSF normal at 2 yr	CSF WBC fails to decrease at 6 mos or if CSF VDRL is still positive. Persisting signs and symptoms.

‡ 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 insured, desensitization and tx with penicillin is recommended.

Occupational Post-Exposure Prophylaxis

The following are anticipated in the next edition of the CDC Guidelines for Occupational Post-Exposure Prophylaxis based on: Postexposure Prophylaxis Cardo, D 44th ICAAC, Washington, DC, 2004 Session 22(K) *Meet-the-Experts*.

Exposure	HIV Status of Source		
	HIV+, Low risk*	HIV+, High risk	Unknown HIV Status
Percutaneous			
Not severe	2 Drugs	3 Drugs	Consider 2 Drugs
Severe	3 Drugs	3 Drugs	Consider 2 Drugs
Mucocutaneous			
Small Volume	Consider 2 Drugs	2 Drugs	Consider 2 Drugs
Large Volume	2 Drugs	3 Drugs	Consider 2 Drugs

* Low Risk = Asymptomatic and/or HIV viral load <15,000 c/mL.

Regimen	Drug Choices
Two-Drug Regimens	3TC or FTC combined with AZT, TDF, or d4T
Three-Drug Regimens	2 NNRTIs (see above) combined with ritonavir-boosted PI: IDV, LPV/r, ATV, or SQV
Drugs to Avoid	NVP, ABC, ddC, DLV, APV

Initiation of Treatment: Start within 36 hours of exposure, preferably within 2 hours. Continue for 4 weeks.

Serology: Obtain at baseline, 6 weeks, 3 months, and 6 months. Do not use HIV PCR for routine detection of viremia prior to seroconversion.

When to Consult an Expert: Delayed report, pregnancy or breast-feeding in HCW, HIV resistance in source, and toxicity of drugs.