

The 2002
**Abbreviated
Guide**

to **Medical
Management**
of **HIV**
Infection

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*Federal guidelines exist

Note

This book is provided as a resource for physicians and other health care professionals in providing care and treatment to patients with HIV/AIDS. Every possible effort is made to ensure the accuracy and reliability of material presented in this book; however, 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 and confirm the information contained within this book. The author, reviewers, and production staff will not be held liable for errors, omissions or inaccuracies in information or for any perceived harm to users of this book. It is up to the individual physician or other health care professional to 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.

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Additional sources of information include the websites of the Johns Hopkins University Division of Infectious Diseases:

The Johns Hopkins AIDS Service: <http://hopkins-aids.edu>

The Hopkins ABX-Guide: <http://www.hopkins-abxguide.org>

The Johns Hopkins Center for Tuberculosis Research: <http://www.hopkins-tb.org>

Preface

The *Abbreviated Guide to Medical Management of HIV Infection* is intended for bedside clinical management decisions. The parent text, *Medical Management of HIV Infection*, provides the scientific foundation for recommendations. The *Abbreviated Guide* differs in several ways: 1.) It provides complete recommendations but without the background data and references of the parent text; 2.) This *Abbreviated Guide* came out 6 months later, so it is more up to date; 3.) New features in the drug section include “patient instructions” and “warnings.” The author thanks Greg Lucas, M.D., Joel Gallant, M.D., and Paul Pham, Pharm. D. for reviews, edits, and comments. *J.G. Bartlett, M.D.*

1 | Sources of Information and Resources for the HIV Care Provider

Postexposure Prophylaxis (PEP)

- National Clinicians' PEP hotline (available at all times): 888-448-4911 or <http://www.ucsf.edu/hivcntr>
- Hepatitis hotline: 888-443-7232 or <http://www.cdc.gov/hepatitis>
- Centers for Disease Control and Prevention (CDC): Reporting of occupationally acquired HIV: 800-893-0485

Federal Guidelines

- HIV/AIDS Treatment Information Service: <http://www.hivatis.org>

General Information

- Johns Hopkins AIDS Service: <http://www.hopkins-aids.edu>
- University of California San Francisco-HIV InSite: <http://hivinsite.ucsf.edu>
- National Library of Medicine: <http://sis.nlm.nih.gov/HIV/HIVMAIN.html>
- *Journal of the American Medical Association (JAMA)* HIV/AIDS Resource Center: <http://www.ama-assn.org/special/hiv>
- Medscape: <http://hiv.medscape.com/Home/Topics/AIDS/AIDS.html>
- The Body: <http://www.thebody.com>
- MEDLINE: <http://www.nlm.nih.gov/medlineplus/aids.html>

Food and Drug Administration (FDA)

- Report unusual or severe toxicity of antiretrovirals: 800-332-1088 or <http://fda.gov/medwatch>

Clinical Trials

- AIDS Clinical Trials Group (ACTG) Trials: <http://www.actis.org>
- AIDS Clinical Trials Information: 800-874-2572
- HIV/AIDS Treatment Information Service (ATIS): 800-448-0440; <http://www.hivatis.org>

Hotlines and Resources for Patients

- National Sexually Transmitted Diseases (STD) & AIDS Hotline: 800-342-AIDS, 24 hours/day, CDC; Spanish 800-344-SIDA
- National Institute on Drug Abuse: 800-662-4357
- CDC Prevention Information Network: 800-458-5231
- AIDS Clinical Trials Information Service: 800-874-2572
- HIV Treatment Information Service: 800-448-0440
- AIDS Treatment/Policy Project Inform: 800-822-7422 or <http://www.projectinform.org>
- National Association of People With AIDS (NAPWA): 202-898-0414 or <http://www.napwa.org>

2 | Classification and Natural History

Natural History of HIV Infection (without antiretroviral therapy [ART])

Viral transmission $\xrightarrow{2-3 \text{ weeks}}$ Acute retroviral syndrome* $\xrightarrow{2-3 \text{ weeks}}$ Recovery and seroconversion \longrightarrow Asymptomatic chronic HIV infection $\xrightarrow{\text{Avg. 8 years}}$ Symptomatic HIV infection/AIDS defining complication[†] $\xrightarrow{\text{Avg. 1.3 years}}$ Death

*Acute Retroviral Syndrome, see Table 2-1, below

[†]AIDS defining complications, see Table 2-2, below

■ TABLE 2-1: Acute Retroviral Syndrome

Symptomatic	50% to 90%
Symptoms	
Fever	96%
Adenopathy	74%
Pharyngitis (non exudative)	70%
Rash (morbilliform, maculopapular)	70%
Diarrhea	32%
Headache	30%
Nausea/vomiting	27%
Neurologic*	10%

*Guillain-Barré syndrome, encephalitis, aseptic meningitis

Diagnosis

Positive HIV RNA: 3% to 9% false positive at low titer <10,000 c/mL; titer should be high with acute retroviral syndrome, usually occurring within 2 to 4 weeks of transmission.

■ TABLE 2-2: AIDS Surveillance Case Definition for Adolescents and Adults (1993)

CD4 Cell Categories (cells/mm ³)	Clinical Categories		
	A: Asymptomatic, or PGL* or Acute HIV Infection	B: Symptomatic [†] (not A or C)	C: AIDS Indicator Condition (1987) [‡]
1. >500 (>29%)	A1	B1	C1
2. 200 to 499 (14% to 28%)	A2	B2	C2
3. <200 (<14%)	A3	B3	C3

*Persistent generalized lymphadenopathy

[†]All patients in categories A3, B3 and C1-3 are defined as having AIDS, based on the presence of an AIDS-indicator condition (see Table 2-3, p. 5) and/or a CD4 count <200 cells/mm³.

[‡]Symptomatic conditions not included in Category C that are a) attributed to HIV infection or indicative of a defect in cell-mediated immunity; or b) considered to have a clinical course or management that is complicated by HIV infection. Examples of B conditions include but are not limited to bacillary angiomatosis, thrush, vulvovaginal candidiasis which is persistent, frequent, or poorly responsive to therapy, cervical dysplasia (moderate or severe), cervical carcinoma *in situ*, constitutional symptoms such as fever (38.5° C) or diarrhea >1 month, oral hairy leukoplakia, herpes zoster involving two episodes or >1 dermatome, idiopathic thrombocytopenic purpura (ITP), listeriosis; pelvic inflammatory disease (PID) (especially if complicated by a tubo-ovarian abscess), and peripheral neuropathy.

■ TABLE 2-3: Indicator Conditions in Case Definitions of AIDS (Adults)*

Candidiasis of esophagus, trachea, bronchi, or lungs	16%
Cervical cancer, invasive	0.6%
Coccidioidomycosis, extrapulmonary	0.3%
Cryptococcosis, extrapulmonary	5%
Cryptosporidiosis with diarrhea >1 month	1.3%
CMV of any organ other than liver, spleen, or lymph nodes; eye	7%
Herpes simplex with mucocutaneous ulcer >1 month or bronchitis, pneumonitis, esophagitis	5%
Histoplasmosis, extrapulmonary	0.9%
HIV-associated dementia: Disabling cognitive and/or other dysfunction interfering with occupation or activities of daily living	5%
HIV-associated wasting: Involuntary weight loss >10% of baseline + chronic diarrhea (≥ 2 loose stools/day for ≥ 30 days) or chronic weakness and documented enigmatic fever ≥ 30 days	18%
Isosporiasis with diarrhea >1 month	0.1%
Kaposi's sarcoma (KS) in patient under 60 yrs. (or over 60 yrs.)	7%
<i>Mycobacterium avium</i> , disseminated	5%
<i>Mycobacterium tuberculosis</i> : Pulmonary, extrapulmonary	9%
<i>Pneumocystis carinii</i> pneumonia	38%
Pneumonia, recurrent-bacterial (≥ 2 episodes in 12 mos.)	5%
Progressive multifocal leukoencephalopathy	0.3%
<i>Salmonella</i> septicemia (nontyphoid), recurrent	0.3%
Toxoplasmosis of internal organ	4%

*% indicates approximate percentage of initial AIDS-defining diagnosis in reports to CDC during HAART era

■ TABLE 2-4: Correlation Between CD4 Count and HIV Complications

CD4 Count* (as cells/mm ³)	Infectious Complications	Non-infectious [†] Complications
>500	Acute retroviral syndrome Candidal vaginitis	PGL Guillain-Barré syndrome Myopathy Aseptic meningitis
200–500	Pneumococcal and other bacterial pneumonia Pulmonary tuberculosis (TB) Herpes zoster Oropharyngeal candidiasis (thrush) Cryptosporidiosis, self-limited KS Oral hairy leukoplakia	Cervical intraepithelial neoplasia (CIN) Cervical cancer B-cell lymphoma Anemia Mononeuronal multiplex ITP Hodgkin's lymphoma Lymphocytic interstitial pneumonitis (LIP)
<200	<i>Pneumocystis carinii</i> pneumonia (PCP) Disseminated histoplasmosis and coccidioidomycosis Miliary/extrapulmonary TB Progressive multifocal leukoencephalopathy (PML)	Wasting Peripheral neuropathy HIV-associated dementia Cardiomyopathy Vacuolar myelopathy Progressive polyradiculopathy
<100	Disseminated herpes simplex (HSV) Toxoplasmosis Cryptococcosis Cryptosporidiosis, chronic Microsporidiosis Candidal esophagitis	
<50	Disseminated cytomegalovirus (CMV) Disseminated <i>Mycobacterium avium</i> complex (MAC)	Central nervous system (CNS) lymphoma

*Most complications occur with increasing frequency at lower CD4 counts.

[†]Some conditions categorized as non-infectious are often microbially mediated, i.e., lymphoma (EBV), cervical carcinoma (HPV)

3 | Prevention

Mechanisms With Established Merit

- Perinatal Transmission: AZT, NVP, viral load reduction, C-section
- Healthcare Worker Postexposure Prophylaxis: AZT
- Safe sex (condom use)
- Needle exchange and syringe exchange for injection drug users

Mechanisms With Anticipated Benefit

- Reduction of viral load
- Treatment of STDs, especially genital ulcer disease, gonorrhea, and *C. trachomatis*
- Rehabilitation of injection drug users

Risk Reduction

Sexually Active Patients

- Condom use or abstinence
- Screen for and treat STDs: VDRL, urinary assay for *C. trachomatis*, and *N. gonorrhoeae* as surrogate marker of high risk and treatment for risk reduction. Recommended at baseline and annually for sexually active patients.
- Partner notification

Injection Drug Users

- Drug rehabilitation
- If rehabilitation is not possible: Needle exchange or non-sharing programs
- Partner notification

4 | Initial Evaluation and Monitoring

■ TABLE 4-1: Laboratory Test Battery for Patients With HIV

Test	Comment
Complete Blood Count (CBC)	Repeat at 3 to 6 months, more frequently for low values and with administration of marrow-toxic drugs.
Chemistry profile including liver and renal function tests.	Repeat annually or more frequently in patients with abnormal results and with administration of hepatotoxic or nephrotoxic drugs.
<i>Toxoplasma gondii</i> IgG	Screen all patients and repeat in seronegatives if CD4 cell count is <100/mm ³ and patient does not take TMP-SMX DS for PCP prophylaxis, or Sx suggest toxo encephalitis.
VDRL (or RPR)	Repeat annually.
Anti-hepatitis C virus	Confirm positive results with quantitative HCV RNA.
Anti-hepatitis B core	Purpose is to identify candidates for HBV vaccine. Anti-HBs Ag may also be used and is preferred if there is confusion about prior vaccination.
Purified protein derivative of tuberculin (PPD) (if no prior positive)	Repeat annually in previously PPD-negative patients who have risk for TB. (See HIV Co-Morbidities, Tuberculosis, p. 59)
PAP smear for female patients	Repeat at 6 months and then annually if results are normal.
Viral load at baseline (x2)	2 to 8 weeks, after initiating therapy or new regimen, then every 3 to 4 months, clinical event, or significant (≥3x) change in VL.
CD4 count	Every 3 to 6 months.
Chest x-ray	Indicated for symptoms and signs suggesting pulmonary disease or newly detected positive PPD.
<i>C. trachomatis</i> and <i>N. gonorrhoeae</i> urinary test	Repeat annually and as needed for patients with history of STDs, symptoms of STD, and multiple sex partners.
If Initiating Highly Active Antiretroviral Therapy (HAART)	
Fasting glucose	3 to 6 months after HAART
Fasting lipid profile (triglyceride, cholesterol, low-density lipoprotein [LDL], high-density lipoprotein [HDL])	3 to 6 months after HAART, then prn depending on changes in regimen, baseline values and risk for cardiovascular disease.
Indinavir: U/A and renal function	Periodically. Some advocate annual U/A for all patients to detect HIVAN.
Nevirapine: Liver function test (LFT).	LFTs every 2 weeks x2, then every month x12 weeks, then every 3 months.

■ TABLE 4-2: Laboratory Tests Characteristics

Test	Comment
HIV serology	<ul style="list-style-type: none"> ■ Sensitivity and specificity is >98%. ■ Indeterminate test results: Repeat in 2 to 3 months. ■ Most patients with low risk and indeterminate serology do not have HIV infection.
CBC and chemistry profile	<ul style="list-style-type: none"> ■ Standard for any patient.
VDRL or RPR	<ul style="list-style-type: none"> ■ Confirm positive results with fluorescent treponemal antibody absorption test (FTA-ABS). Biologic false positives are common, up to 6% of HIV infected patients. False negatives reported, but rare. ■ Indications for LP with positives: Late latent syphilis (>1 yr. or unknown duration); early syphilis (<1 yr.) + neurologic Sx/signs, treatment other than standard penicillin, therapeutic failures. ■ Cerebral spinal fluid (CSF) analysis may show mononuclear cells and/or elevated protein due to neurosyphilis or HIV with CNS involvement. CSF VDRL is diagnostic of neurosyphilis, but is negative in 30% of neurosyphilis cases.
Chest x-ray	<ul style="list-style-type: none"> ■ Considered mandatory with positive PPD. ■ Optional if asymptomatic, but often desired as baseline since rate of pulmonary complications is high.
HCV serology	<ul style="list-style-type: none"> ■ Usual screening test is anti-HCV, which is sensitive but not specific. ■ Confirm positives with HCV RNA PCR (preferred) or Recombinant Immunoblot Assay (RIBA). ■ Evaluation of HCV infection: Alanine aminotransferase (ALT), HCV VL ± genotype assay, biopsy (preferred).
Hepatitis A serology	<ul style="list-style-type: none"> ■ About 30% to 50% of adults are seropositive. ■ Negative serology is indication for HAV vaccine with HCV coinfection and possibly all HIV infected HAV seronegative patients.
Toxoplasmosis serology	<ul style="list-style-type: none"> ■ Usual screening test is anti-<i>Toxoplasma</i> IgG to define susceptibility to toxoplasmosis when CD4 is <100 cells/mm³.
PPD	<ul style="list-style-type: none"> ■ Test indicated in absence of history of TB or prior positive PPD. ■ Repeat if initial test is negative and CD4 increases to >200 cells/mm³ with HAART. ■ Criterion for positive test with HIV coinfection is ≥5 mm induration. ■ Positives need evaluation for active TB including chest x-ray. ■ Latent TB (positive PPD and negative evaluation for active TB) is indication for treatment of latent TB, usually isoniazid (INH) x 9 mos.
PAP smear	<ul style="list-style-type: none"> ■ National Cancer Institute guidelines (<i>JAMA</i> 1994; 271:1866). ■ Inflammation: Evaluate for infection; repeat PAP in 2 to 3 months. ■ Atypia (ASCUS): Follow-up PAP every 4 to 6 months x 2 yrs. until 3 are negative. Second report of ASCUS: Colposcopy. ■ Low grade squamous intraepithelial lesion (LSIL): Colposcopy or follow with PAP every 4 to 6 months. ■ High grade squamous intraepithelial lesion (HSIL): Colposcopy + biopsy. ■ HAART: Guidelines are unchanged.
CMV serology	<ul style="list-style-type: none"> ■ Seropositive in 50% of adults and in >90% in men who have sex with men (MSM) and injection drug users (IDUs). ■ Test may be useful in low risk patients.

TABLE 4-2: Laboratory Tests Characteristics—Continued

Test	Comment
G6-PD	<ul style="list-style-type: none"> ■ Danger with use of antioxidative drugs: (dapsone, primaquine, sulfonamides); may cause hemolysis in G6-PD deficient individuals. ■ Testing during hemolysis is usually negative: Must wait ~30 days after inducing agent is stopped. ■ Prevalence in black men—10%, black women—2%; Mediterranean variant causes more severe hemolysis.
CD4 count	<ul style="list-style-type: none"> ■ Barometer for susceptibility to OIs: Risk—CD4 <200; high risk—CD4 <50; normal—CD4 >500. ■ Minimal impact: Sex, age (adults), risk, stress, pregnancy. ■ Great variation: Some prefer CD4 percentage: CD4 500 = 29%, CD4 200 = 14%. ■ Repeat tests that are critical or don't make sense. ■ Inexplicably low CD4: Acute steroid administration or lab error. ■ Inexplicably high CD4: Splenectomy or human T-cell lymphotropic virus (HTLV-1) coinfection (not HTLV-2). ■ Reproducibility (95% confidence limits) = 30% (e.g., 200 cells/mm³ range of 118–337 cells/mm³).
HIV viral load (VL)	<ul style="list-style-type: none"> ■ Independent predictor of rate of progression. ■ Median in untreated patients 20,000–50,000 c/mL. ■ Usual goal of therapy is <20–50 c/mL. ■ Reproducibility (95% confidence limits) = 2–3x (0.3 log₁₀/mL): (e.g., 10,000 c/mL has 2 SD range of 3,100–32,000 c/mL). ■ Comparative merits of commercial assays, see below.
<i>C. trachomatis</i> and <i>N. gonorrhoeae</i> urinary test	<ul style="list-style-type: none"> ■ Surrogate marker for high risk behavior. Annual screening recommended. ■ Positive results require testing and counseling on HIV prevention and partner notification.
Lipid profile	<ul style="list-style-type: none"> ■ Indications are risk for heart disease or anticipated HAART. ■ CHD risks: Family history, smoking, obesity, hypertension, diabetes, prior elevated lipid levels, Hx stroke or MI. ■ Testing: Cholesterol, LDL and HDL cholesterol, triglycerides, glucose. ■ Fasting 8 to 12 hrs. is necessary for meaningful measurement of triglycerides, LDL cholesterol (calculated from triglycerides) and glucose. ■ Levels of concern: Fasting glucose >109 mg/dL, triglycerides >200 mg/dL (especially if >500), cholesterol >250 mg/dL; most important is LDL cholesterol >160 with minimal risk profile, or >130 with ≥2 risks, or >100 with high risk (diabetes, stroke, or coronary artery disease). ■ Interventions: See Tables 6-15 and 6-16, pp. 40–41.

■ TABLE 4-3: Comparison of VL Assays

	RT-PCR (Roche)	bDNA (Bayer)	Nuclisens (Organon)
Contact	800-526-1247	800-434-2447	800-682-2666 x152
Comparison	Version 2.0 is comparable to Version 3.0 bDNA	Version 3.0 is comparable to Version 2.0 RT-PCR	Comparability to other two is unknown
Versions	1.0, 1.5, 2.0; standard or ultrasensitive	2.0 and 3.0	—
Dynamic range	Standard 400–750,000 c/mL Ultrasensitive 50–75,000 c/mL	100–500,000 c/mL	40–10,000,000 c/mL depending on volume
Advantages	Version 1—FDA approved (only one)	Good dynamic range	May be used on non-blood specimens. Best dynamic range
Subtypes	Version 1: B only Version 1.5 and 2.0: A–G	A–G	A–G

■ TABLE 4-4: Indications for Resistance Testing

Recommended	<p>Chronically Infected Patient Receiving ART with:</p> <ul style="list-style-type: none"> ■ Failure to decrease VL >0.5 to $0.7 \log_{10}$ c/mL by 4 wks. ■ Failure to decrease VL $>1 \log_{10}$ c/mL by 8 wks. ■ VL >1000 c/mL after 16 to 24 wks. <p>Testing is recommended to determine the role of resistance in failure or suboptimal response and to maximize the number of effective drugs in and potency of new regimen.</p>
Consider	<ul style="list-style-type: none"> ■ Acute HIV syndrome to determine if resistant strains were transmitted.
Not recommended	<ul style="list-style-type: none"> ■ In treatment-naive patient with chronic HIV infection; may not detect minor resistant species. ■ In patient who has not received ART agents for >2 wks.; may not detect resistant strains in absence of selective pressure ("wild type" often returns at ≥ 2 wks.). ■ In patient with VL <1000 c/mL.

(U.S. Department of Health and Human Services [DHHS] Guidelines October 1, 2001, available at <http://www.hivatis.org> and at <http://www.hopkins-aids.edu>)

TABLE 4-5: Comparison of Genotypic and Phenotypic Assays

Genotypic Assays	
Advantages	Disadvantages
<ul style="list-style-type: none"> ■ Less expensive (\$300 to \$480/test)* ■ Short turnaround: 1 to 2 wks. ■ May detect presence of resistance mutations before they have resulted in phenotypic resistance. 	<ul style="list-style-type: none"> ■ Detect resistance only in dominant species (>20%) ■ Interpretation requires knowledge of mutational changes, e.g., expertise. ■ Technician experience influences results. ■ May show discrepancy with phenotype ■ Requires VL >1000 c/mL
Phenotypic Assays	
Advantages	Disadvantages
<ul style="list-style-type: none"> ■ Interpretation more analogous to resistance testing of bacteria ■ Assesses total effect, including mutations, mutational interactions. ■ Reproducibility is good. ■ Advantage over genotype when there are multiple mutations. 	<ul style="list-style-type: none"> ■ More expensive (usually \$800 to \$1,000). ■ Longer delay in reporting: 2 to 3 wks. ■ Thresholds to define susceptibility are arbitrary, nonstandardized, and do not always reflect achievable drug concentrations. ■ Detect resistance only in dominant species (>20%). ■ Require VL >500 to 1000 c/mL. ■ Current tests do not account for increased PI levels with RTV coadministration boost except with LPV/RTV.

*Cost: Medicare/Medicaid reimbursement per Health Care Financing Administration (HCFA) announcement January 8, 2001: Genotype test \$355.78 (code 87901); phenotype test \$675.29 (1st 10, code 8703), each additional drug \$36.02 (code 8704).

■ TABLE 4-6: Resistance Mutations

Drug	Codon Mutations	Comment
Nucleosides and Nucleotides		
AZT	41, 67, 69, 70, 151, 210, 215, 219	Mutations are thymidine analog resistance mutations (TAMS); reduce susceptibility to AZT, stavudine (d4T), abacavir (ABC).*
3TC	69, 151, 184	High level resistance. Increase activity of d4T, AZT.
d4T	41, 67, 69, 70, 75, 151, 210, 215, 219	The d4T specific mutation at 75 is seen mostly <i>in vitro</i> . <i>In vivo</i> resistance depends on the number of TAMS, which reduce susceptibility to d4T, AZT, and ABC
ddC	65, 69, 74, 151, 184	—
ddl	65, 69, 74, 151, 184	Presence of either 74 or 65 associated with intermediate level resistance to ddl. High level resistance associated with presence of both mutations. 184 causes low-level resistance.
ABC	41, 65, 67, 69, 70, 74, 115, 151, 184, 210, 215, 219	Resistance depends on number of TAMS: ≥ 3 TAMS = ABC resistance; ABC does not select for TAMS.
TDF	65, 69 insertion, ≥ 3 TAMS including 41, 210	Reduced activity with K65R and resistant with 69 insertion; active against most NRTI resistant strains.
Multinucleoside resistance-A (Q151M complex)	62, 75, 77, 116, 151	Resistance to all NRTIs but possibly not tenofovir.
Multinucleoside resistance-B (T69SSS insertion)	41, 62, 67, 69 insertion, 70, 210, 215, 219	Confers resistance to all NRTIs and tenofovir.
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)		
NVP	100, 103, 106, 108, 181, 188, 190, 230	Y181C is favored NVP resistance mutation; with AZT, K103N is favored.
DLV	103, 181, 230, 236	—
EFV	100, 103, 108, 188L, 190, 225, 230	Sensitive <i>in vitro</i> against 181 mutants; resistance with 188L but not 188C or 188H.

■ TABLE 4-6: Resistance Mutations—Continued

Drug	Codon Mutations		Comment
	Primary	Secondary [†]	
Protease Inhibitors (PIs)			
IDV	46, 82	10, 20, 24, 84, 90	Requires >3 mutations for >4x reduction in susceptibility.
NFV	30, 90	35, 36, 46, 71, 88	D30N most common; no PI cross resistance.
RTV	82	8, 10, 20, 33, 46, 54, 71, 84, 90	Cross resistance with IDV common.
SQV	48, 90	10, 24, 30, 46, 54, 64, 71, 73, 77, 81, 84, 88	90 develops 1st, then 48; 90 produces PI cross-resistance.
APV	50, 84	10, 32, 46, 47, 54	50 may not cause cross resistance.
LPV		10, 20, 24, 46, 53, 71, 82, 84, 90	Resistance correlated with number of mutations; ≥5 is significant.

(JAMA 2000; 283: 2417)

*TAMS are induced by exposure to AZT or d4T; there is increasing evidence of cross-resistance between AZT, d4T, and ABC.

[†]The distinction between primary and secondary resistance mutations has been eliminated for the RT gene (NRTIs and NNRTIs). For PIs, primary mutations usually develop first; secondary mutations contribute to resistance, but later and with less importance.

5 | Prevention of Opportunistic Infections

■ TABLE 5-1: Prevention of OIs (Masur H, et al: Guidelines for Prevention of HIV-related OIs. MMWR 1999; 48 [RR-10], updated Nov. 2001)

Condition	When to Start (CD4 count as cells/mm ³)	Preferred	Alternative
PCP	1 ⁰ : CD4 <200, thrush; consider if CD4 <250 or CD4% <14	<ul style="list-style-type: none"> ■ TMP-SMX 1 DS/day ■ TMP-SMX 1 SS/day 	<ul style="list-style-type: none"> ■ Dapsone 100 mg/day ■ Dapsone 50 mg/day + pyrimethamine 50 mg/wk. + leucovorin 25 mg/wk. ■ Dapsone 200 mg + pyrimethamine 75 mg + leucovorin 25 mg qwk. ■ Aerosolized pentamidine 300 mg/mo. ■ Atovaquone 1500 mg/day ■ TMP-SMX 1 DS 3x/wk.
TB	<ul style="list-style-type: none"> ■ PPD >5 mm ■ Prior positive PPD without Rx ■ Exposure 	INH 300 mg/day + pyridoxine 50 mg/day x 9 mos. or INH 900 mg + pyridoxine 100 mg 2x/wk.	<p>HAART: RBT* 300 mg/day + PZA 15–20 mg/kg/day x 2 mos.</p> <p>No HAART: RIF 600 mg/day x 4 mos. or PZA 15–20 mg/kg/day + RIF 600 mg/day x 2 mos.</p>
T. gondii	1 ⁰ : IgG + anti-toxoplasma IgG and CD4 <100	TMP-SMX 1 DS/day	<ul style="list-style-type: none"> ■ Dapsone + pyrimethamine + leucovorin (above doses) ■ Atovaquone 1500 mg/day ± pyrimethamine 25 mg/day + leucovorin 10 mg/day
MAC	1 ⁰ : CD4 <50	<ul style="list-style-type: none"> ■ Azithromycin 1200 mg/wk. or ■ Clarithromycin 500 mg PO bid 	<ul style="list-style-type: none"> ■ RBT* 300 mg/day or ■ Azithromycin 1200 mg/wk. + RBT* 300 mg/day
Varicella Zoster Virus (VZV)	Significant exposure + negative history ± negative serology	VZIG (varicella zoster immune globulin) 5 vials (6.25 mL) IM within 96 hrs.	—

5 Prevention of Opportunistic Infections

Condition	When to Start (CD4 count as cells/mm ³)	Preferred	Alternative
<i>S. pneumoniae</i>	CD4 >200	Pneumovax	
Hepatitis B Virus (HBV)	All with negative anti-hepatitis B c antigen (HBcAg) or anti-hepatitis B s antigen (HBsAg)	HBV vaccine in 3 doses	
Influenza	Annual; October–November preferably	Flu vaccine	<ul style="list-style-type: none"> ■ Oseltamivir 75 mg/day ■ Rimantadine 100 mg bid ■ Amantadine 100 mg bid
HAV	Anti HAV negative + risk (IDU, MSM, hemophilia, chronic liver disease or HCV, HBsAg)	HAV vaccine in 2 doses	
Cryptococcosis	1 ^o : Not indicated	2 ^o : Fluconazole 200 mg/day	Itraconazole 200 mg bid
Histoplasmosis	1 ^o : CD4 < 100 + endemic area with >10 cases/100 patient yrs.	2 ^o : Itraconazole 200 mg/day	
Coccidioidomycosis	1 ^o : Not recommended	2 ^o : Fluconazole 400 mg/day or itraconazole 200 mg bid	
CMV	1 ^o : Not recommended	2 ^o : Consult expert	

1^o refers to primary prophylaxis (no prior history of this infection); 2^o refers to secondary prophylaxis (history of prior infection)

* RBT dose adjustment with PIs and NNRTIs, see Table 9-2, p. 60.

■ TABLE 5-2: When to Stop and Restart OI Prophylaxis Based on Immune Reconstitution

Condition	When to Stop (CD4 count as cells/mm ³)	When to Restart
PCP	1 ⁰ : CD4 >200 >3 mos. 2 ⁰ : CD4 >200 >3 mos.	CD4 <200
Toxoplasmosis	1 ⁰ : CD4 >200 x 3 mos. 2 ⁰ : CD4 >200 x 6 mos. + completion of initial Rx + asymptomatic	1 ⁰ : CD4 <100–200 2 ⁰ : CD4 <200
<i>M. avium</i> complex	1 ⁰ : CD4 >100 x 3 mos. 2 ⁰ : CD4 >100 x 6 mos. + 12 mos. Rx + asymptomatic	CD4 <100
Cryptococcosis	2 ⁰ : CD4 >100–200 x 6 mos. + completion of initial Rx + asymptomatic	CD4 <100–200
Histoplasmosis	Not recommended	
Coccidioidomycosis	Not recommended	
CMV	2 ⁰ : CD4 >100–150 x 6 mos. + no active disease + regular ophthalmological exams	CD4 <100

1⁰ = primary prophylaxis (no previous disease)

2⁰ = secondary prophylaxis (prior infection with indicated agent)

Prevention of Opportunistic Infections ■ TABLE 5-3: Vaccines

Vaccine	Indicators—All Persons (schedule)	Cost/Series	HIV-infected Persons
Cholera	Travel to endemic area + requirement (x2 at 0 and 2 wks.)	\$2 x 2	No medical indications, but not contraindicated by HIV infection.
H. influenzae type B	Routine pediatric vaccine (x1)	\$22 x 1	Not indicated in adults (Most H. flu in patients with HIV is non-typable).
HAV	High risk: Travel, IDU, chronic liver disease, MSM	\$124/2 doses	Indicated for all anti-HAV negative HIV infected patients with HCV or chronic liver disease.
HBV	High risk patients including persons < 19 yrs., MSM, IDU, STDs, >1 partner in 6 mos. (x3 at 0, 1 and 6 mos.)	\$160/3 doses	Standard of care.
Influenza	High risk patients or anyone who requests it (annual, mid October to November)	\$3 x 1	Standard of care, vaccinate annually in mid October to late November (or later if necessary).
Japanese B	Travel to endemic area with stay > 1 month	\$200	Use if indicated.
Lyme	High risk: Endemic area + extensive tick exposure (x3 at 0, 1, and 12 mos)	\$184/3 doses	Use if indicated.
Measles	Routine childhood	\$17	Live virus vaccine, contraindicated.
Polio Inactivated (e/PV)	Travel to endemic area if not immunized.	\$14	Use if indicated.
Pneumococcal	<ul style="list-style-type: none"> ■ High risk patients (x1) ■ Pediatric vaccine, routine, 4 doses 	<ul style="list-style-type: none"> ■ \$13 x 1 ■ \$60/dose 	<ul style="list-style-type: none"> ■ Recommended with CD4 > 200 cells/mm³ ■ FDA approved only for pediatrics, but currently being tested in adults with HIV
Protein conjugated (7 valent)			

Vaccine	Indicators—All Persons (schedule)	Cost/Series	HIV-Infected Persons
Smallpox	Under discussion	—	Live virus, contraindicated
Tetanus-diphtheria (Td)	Routine every decade	\$3 x 1	Indicated with HIV, but serologic response is low with low CD4 count
Typhoid <ul style="list-style-type: none"> ■ Ty21a (Vivotif) ■ Typhoid inactivated ■ Typhoid V. polysaccharide (Typhim V_i) 	<ul style="list-style-type: none"> ■ Travel to endemic area ■ Travel to endemic area (2 doses at 0 and 1 mos.) ■ Travel to endemic area (x1) 	<ul style="list-style-type: none"> ■ \$33/4 doses ■ \$100 x 2 ■ \$32 x 1 	<ul style="list-style-type: none"> ■ Live virus, contraindicated ■ Use if indicated ■ Use if indicated: costs more, fewer side effects compared to typhoid inactivated
Varicella	Sero negative adults	\$62	Live virus, contraindicated
Yellow fever	Travel to endemic area (x1)	\$38 x 1	Live virus, contraindicated

6 | Antiretroviral Therapy

Prognosis

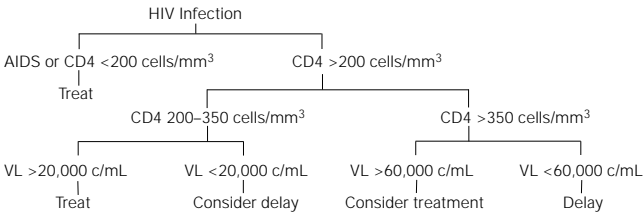
■ TABLE 6-1: Probability of Developing an AIDS-Defining OI Within 3 Years in the Absence of ART, Based on Baseline CD4 Count and VL.

Data from Multicenter AIDS Cohort Study (MACS)

VL (RT-PCR)* c/mL	% AIDS-Defining Complication			
	N	3 yrs.	6 yrs.	9 yrs.
CD4 <350 cells/mm³				
1,500–7,000*	30	0	18.8	30.6
7,000–20,000	51	8.0	42.2	65.6
20,000–55,000	73	40.1	72.9	86.2
>55,000	174	72.9	92.7	95.6
CD4 350–500 cells/mm³				
1,500–7,000	47	4.4	22.1	46.9
7,000–20,000	105	5.9	39.8	60.7
20,000–55,000	121	15.1	57.2	78.6
>55,000	121	47.9	77.7	94.4
CD4 >500 cells/mm³				
<1,500	110	1.0	5.0	10.7
1,500–7,000	180	2.3	14.9	33.2
7,000–20,000	237	7.2	25.9	50.3
20,000–55,000	202	14.6	47.7	70.6
>55,000	141	32.6	66.8	76.3

*Plasma HIV RNA levels in c/mL using RT-PCR. (Mellors J, et al. *Ann Intern Med* 1997;126:946)

Treatment Based on 15% Probability of AIDS-Defining Complication Within Three Years



When To Start Therapy

■ TABLE 6-2: Indications for the Initiation of ART (DHHS Guidelines, <http://www.hivatis.org>)

Clinical Category	CD4 Cell Count and HIV RNA	Recommendation*
Acute HIV or <6 mos. after seroconversion	All	Treat
Symptomatic (AIDS, thrush, unexplained fever)	All	Treat
Asymptomatic	CD4 <200 cells/mm ³	Treat
Asymptomatic	CD4 200–350 cells/mm ³	VL of <20,000 in this CD4 strata is associated with low rates of progression; some experts would defer therapy (see algorithm p. 23)
Asymptomatic	CD4 >350 cells/mm ³	Defer. Some experts would offer treatment to patients with VL >55,000 since this defines a >15% risk of an AIDS defining diagnosis in 3 years.

*Recommendations are based on CD4 count and VL thresholds that define a 15% probability of an AIDS-defining diagnosis within 3 yrs. (see Table 5-1, pp. 17–18). The strength of the recommendation depends on probability of adherence and prognosis for disease-free survival based on CD4 count and, to a lesser extent, on VL (see Table 5-1, pp. 17–18).

■ **TABLE 6-3: Initial Regimen—DHHS Guidelines (<http://www.hivatis.org>, Nov. 2001)**

(One from column A and one from column B in the preferred category)

	Column A	Column B
Preferred	EFV IDV NFV SQV/RTV LPV/RTV IDV/RTV	d4T/3TC AZT/ddI AZT/3TC d4T/ddI* ddI/3TC
Alternate	ABC APV DLV NVP RTV SQV (FTV) NFV/FTV	AZT/ddC
No recommendation (insufficient data)	HU RTV/APV RTV/NFV	TDF
Not recommended	SQV (INV) (except with RTV)	ddC/ddI ddC/d4T ddC/3TC AZT/d4T

*The combination of d4T & ddI should be avoided in pregnant women.

Drug Selection in Special Circumstances

BASELINE VL >100,000 c/mL

- **ESTABLISHED:** 2 NRTIs + EFV or 2 NRTIs + LPV/RTV
- **PROBABLE:** 3 NRTIs (AZT/3TC/ABC) + PI or NNRTI; 2 NRTIs + 2 PIs (RTV + IDV, SQV or APV); 2 NRTIs + NVP; 2 NRTIs + PI + NNRTI (+ induction → maintenance)

NUCLEOSIDE SPARING REGIMENS

- LPV/RTV + EFV
- EFV + IDV ± RTV
- SQV + RTV
- APV + RTV + EFV

LOW PILL BURDEN REGIMENS

- *Trizivir* 1 tab bid
- 2 NRTIs + EFV or NVP

■ TABLE 6-4: ART Regimens for Once Daily Dosing

Class	Established (FDA approved for once daily use)	Probable Adequacy Based on Pharmacology
NRTIs and NNRTIs	ddl 400 mg (empty stomach); TDF 300 mg	3TC 300 mg, ABC 600 mg
NNRTI	EFV 600 mg	NVP 400 mg
PIs		APV 1200 mg + RTV 100 mg FTV 1600 mg + RTV 100 mg LPV/RTV 800/200 mg IDV/RTV 1200/400 mg* SQV/RTV 1800/200 mg
Experimental		FTC, Atazanavir, T1249

*Dose adjusted by toxicity to IDV/RTV 800/400 mg (IDV toxicity) or IDV/RTV 1200/200 mg (RTV toxicity)

■ TABLE 6-5: ART Regimens for Methadone Recipients

Drugs	Methadone Levels ↓	No effect	Unknown	Other effects
NRTIs	ABC	ddl, d4T, AZT	—	↓ABC, ↓ddl 60% [†] ↓d4T 20%, ↑AZT 40%
NNRTI	EFV* NVP*			↑DLV
PI	APV, LPV, NFV, RTV, SQV		IDV	

*Anticipate need to ↑ methadone dose

[†]Anticipate need to increase ddl dose; effect on *Videx EC* not known

PREGNANCY ISSUES

- Avoid EFV, ddl + d4T, d4T + AZT
- Preferred: AZT-based regimen
- VL <1000: AZT monotherapy
- Contemplating pregnancy: Avoid EFV

THERAPEUTIC MONITORING

- IDV (risk of toxicity)
- NFV with bid dosing to ensure adequate antiviral levels

PI AND NRTI SPARING REGIMEN

- *Trivizir* 1 tab bid

When to Change Antiretroviral Therapy

Considerations

VIROLOGIC FAILURE

- Failure to suppress plasma HIV RNA levels to “below detection” with an arbitrary threshold of 20–50 c/mL. Some authorities accept higher virologic thresholds because the 20–50 c/mL level of suppression is deemed unrealistic due to individual patient idiosyncrasies, or because there is a need to preserve drug options, or because the threshold that defines risk of resistance is inadequately defined. Continued HAART is likely to cause and/or increase drug resistance at a frequency and level dependent on VL, time, and selective pressure.
- Failure to suppress plasma HIV RNA 1.5–2.0 log₁₀ at 8 to 16 weeks or to <500 c/mL at 24 weeks: Average time to <50 c/mL following HAART in previously treatment naïve patients is 60 to 90 days. This time interval depends on baseline VL, potency of the regimen and adherence.

DRUG TOXICITY OR INTOLERANCE

- If adequate viral suppression: Change responsible agent to alternative drug likely to have comparable potency.
- If inadequate viral suppression: Change regimen based on resistance tests.

ADHERENCE

- Most studies show that 95% of prescribed pills must be taken in order to achieve virologic success in most patients.

PREGNANCY

- Some authorities discontinue treatment in first trimester since this is the time of fetal organ formation.
- EFV should not be used.
- The combination of d4T + ddI should not be used.

Structured Treatment Interruption (STI)

All forms are considered experimental due to lack of controlled trial data that provides guidance and indications for when to stop, when to restart, and agents to use.

IMMUNE STIMULATION: Successful viral suppression (<50 c/mL) for sustained period (>6 mos., usually >2 yrs.) to permit “rebound viremia” with goal of stimulating HIV specific immune response and the long-term objective of immunologic control. Most trials show virologic rebound at 1 to 3 weeks without evolution of resistance. Data is strongest in patients treated during primary infection. Minimal evidence of benefit in patients with chronic infection.

VIROLOGIC FAILURE: Discontinuation of HAART usually results in rapid CD4 decline beginning at 2 to 4 weeks, and attributed to return of “wild type HIV”

which is more “fit” than resistant strains. The “wild type” HIV strain is usually sensitive to the drugs to which resistance had previously been demonstrated, and it responds to reintroduction of HAART. However, resistant strains are presumably retained as minority species and will eventually return with selective pressure.

STRUCTURED INTERMITTENT THERAPY (SIT): This is an experimental protocol in which patients who have achieved good virologic control with HAART are given the successful HAART regimen every other week in an attempt to decrease toxicity and cost. The experience to date shows preservation of CD4 level and viral suppression.

PULSE THERAPY: Patients who respond to HAART discontinue therapy due to concerns that these drugs are toxic, expensive, and possibly unnecessary in patients with high rebound CD4 counts. Indications for discontinuation and reinitiation of therapy are unknown.

What To Change To

■ TABLE 6-6: Change in Antiretroviral Therapy

Indication	Selection of New Antiretroviral Drugs
Virologic failure	Resistance testing; see Tables 4-4, 4-5, 4-6, pp. 12–14
Drug toxicity	Substitute responsible agent(s) using drugs that will provide comparable potency.
Adherence	New regimen selected for potency and individual need
Pregnancy	Avoid EFV, d4T + ddI
STI	
Immune stimulation	Restart same regimen*
Virologic failure	Restart regimen based on resistance testing
Structured intermittent regimen	Restart same regimen*
Pulse therapy	Restart same regimen or regimen selected on the basis of toxicity profile, resistance test results, availability of new drugs, or patient preference.

*Some advocate avoidance of NVP and EFV due to long half life with prolonged single drug exposure

Antiretroviral Agents, Combination Therapy, Other Drug-Drug Interactions

■ TABLE 6-7: ART Agents: Names, Manufacturers, FDA Approval

Agent	Brand Name	Manufacturer	FDA Approval
Nucleoside Reverse Transcriptase Inhibitors			
Abacavir (ABC)	<i>Ziagen</i>	GlaxoSmithKline	12/98
AZT/3TC	<i>Combivir</i>	GlaxoSmithKline	10/97
AZT/3TC/ABC	<i>Trizivir (TZV)</i>	GlaxoSmithKline	11/00
Didanosine (ddI)	<i>Videx, Videx EC</i>	Bristol-Myers Squibb	10/91
Lamivudine (3TC)	<i>Epivir</i>	GlaxoSmithKline	11/95
Stavudine (d4T)	<i>Zerit</i>	Bristol-Myers Squibb	06/94
Zalcitabine (ddC)	<i>HIVID</i>	Roche	06/92
Zidovudine (AZT, ZDV)	<i>Retrovir</i>	GlaxoSmithKline	03/87
Nucleotide Reverse Transcriptase Inhibitor			
Tenofovir (TDF)	<i>Viread</i>	Gilead	10/01
Protease Inhibitors			
Amprenavir (APV)	<i>Agenerase</i>	GlaxoSmithKline	04/99
Indinavir (IDV)	<i>Crixivan</i>	Merck	03/96
Lopinavir/Ritonavir (LPV/RTV)	<i>Kaletra</i>	Abbott	09/00
Nelfinavir (NFV)	<i>Viracept</i>	Agouron	03/97
Ritonavir (RTV)	<i>Norvir</i>	Abbott	03/96
Saquinavir (SQV, FTV)	<i>Fortovase</i>	Roche	11/97
Saquinavir mesylate (INV)	<i>Invirase</i>	Roche	12/95
Non-Nucleoside Reverse Transcriptase Inhibitors			
Delavirdine (DLV)	<i>Rescriptor</i>	Agouron	04/97
Efavirenz (EFV)	<i>Sustiva</i>	Bristol-Myers Squibb	09/98
Nevirapine (NVP)	<i>Viramune</i>	Boehringer Ingelheim	06/96
Other Drugs			
Hydroxyurea (HU)	<i>Droxia, Hydrea</i>	Bristol-Myers Squibb	—

Antiretroviral Therapy ■ TABLE 6-8: Antiretroviral Agents—Forms, Doses, Toxicities, and Monitoring

Drug Name	Form	Usual Dose	Toxicity (main toxicity italicized)	Monitor
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)				
Abacavir, ABC (Ziagen)	<ul style="list-style-type: none"> ■ 300 mg tab ■ 20 mg/mL PO solution 	<ul style="list-style-type: none"> ■ 300 mg bid ■ Food—no effect 	<ul style="list-style-type: none"> ■ Hypersensitivity reaction (HSR)—fever, rash, GI Sx, respiratory Sx, hyperlactatemia 	<ul style="list-style-type: none"> ■ Educate patient on signs/Sx of HSR and what to do; check Hx for prior reaction
Combivir, CBV	<ul style="list-style-type: none"> ■ AZT 300 mg + 3TC 150 mg (cap) 	<ul style="list-style-type: none"> ■ 1 cap bid ■ Food—no effect 	<ul style="list-style-type: none"> ■ AZT side effects, hyperlactatemia 	<ul style="list-style-type: none"> ■ CBC
Zalcitabine, ddC (HIVID)	<ul style="list-style-type: none"> ■ Tabs: 0.375, 0.75 mg 	<ul style="list-style-type: none"> ■ 0.75 mg tid ■ Food—no effect 	<ul style="list-style-type: none"> ■ Peripheral neuropathy, stomatitis, hyperlactatemia 	<ul style="list-style-type: none"> ■ Foot pain, paresthesias, deep tendon reflexes (DTRs)
Didanosine, ddi (Videx; Videx EC)	<ul style="list-style-type: none"> ■ Buffered tabs: 25, 50, 100, 150, 200 mg ■ Buffered powder: 100, 167, 250 mg ■ EC caps: 125, 200, 250, 400 mg 	<ul style="list-style-type: none"> ■ Wt >60 kg: Tabs—400 mg qd or 200 mg bid; powder—250 mg bid, EC 400 mg qd ■ Wt <60 kg: Tabs—250 mg qd or 125 mg bid, EC 250 mg/day; powder—167 mg bid ■ If tabs, must take at least 2 at a time for proper buffering ■ Food: ½ hr. before or 1 hr. after meal 	<ul style="list-style-type: none"> ■ GI intolerance: Pancreatitis, peripheral neuropathy, hyperlactatemia 	<ul style="list-style-type: none"> ■ Foot pain, paresthesias, DTRs, abdominal pain
Lamivudine, 3TC (EpiVir)	<ul style="list-style-type: none"> ■ 150 mg tab ■ 10 mg/mL PO solution 	<ul style="list-style-type: none"> ■ 150 mg bid ■ <50 kg: 2 mg kg bid ■ Food—no effect 	<ul style="list-style-type: none"> ■ Generally well tolerated; hyperlactatemia 	
Stavudine, d4T (Zerit)	<ul style="list-style-type: none"> ■ Caps: 15, 20, 30, 40 mg ■ 1 mg/mL PO sol'n 	<ul style="list-style-type: none"> ■ Wt >60 kg: 40 mg bid ■ Wt <60 kg: 30 mg bid ■ Food—no effect 	<ul style="list-style-type: none"> ■ Peripheral neuropathy, pancreatitis, hyperlactatemia 	<ul style="list-style-type: none"> ■ Foot pain, paresthesias, DTRs

Drug Name	Form	Usual Dose	Toxicity (main toxicity italicized)	Monitor
Trizivir, TZV	<ul style="list-style-type: none"> ■ 3TC 300 mg + ABC 150 mg + ABC 300 mg (tab) ■ Tabs: 100, 300 mg 	<ul style="list-style-type: none"> ■ 1 tab bid ■ Food—no effect 	<ul style="list-style-type: none"> ■ Abacavir: HSR, bone marrow suppression, GI intolerance, hyperlactatemia ■ GI intolerance, asthenia, headache, anemia, leukopenia 	<ul style="list-style-type: none"> ■ Educate patient on signs/Sxs of HSR and what to do; check Hx for prior reaction ■ CBC
Zidovudine, AZT, ZDV (Retrovir)	<ul style="list-style-type: none"> ■ Tabs: 100, 300 mg 	<ul style="list-style-type: none"> ■ 300 mg BID 		
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)				
Delavirdine, DLV (Rescriptor)	<ul style="list-style-type: none"> ■ Tabs: 100, 200 mg 	<ul style="list-style-type: none"> ■ 400 mg tid ■ Food—no effect 	<ul style="list-style-type: none"> ■ Rash 	<ul style="list-style-type: none"> ■ LFT[†]
Efavirenz, EFV (Sustiva)*	<ul style="list-style-type: none"> ■ Tabs: 50, 100, 200 mg tabs 	<ul style="list-style-type: none"> ■ 600 mg hs ■ Avoid high fat meal 	<ul style="list-style-type: none"> ■ CNS—disassociated state x 2 to 3 weeks, rash. Avoid in pregnancy. 	<ul style="list-style-type: none"> ■ LFT[†]
Nevirapine, NVP (Viramune)	<ul style="list-style-type: none"> ■ 200 mg tabs ■ 50 mg/5 mL PO susp. 	<ul style="list-style-type: none"> ■ 200 mg qd x 14 days, then 200 mg bid ■ Food—no effect 	<ul style="list-style-type: none"> ■ Rash, fulminant hepatitis 	<ul style="list-style-type: none"> ■ LFTs[†] q2 wks x 2, then qmo x 12, then q3mo
Nucleotide Reverse Transcriptase Inhibitor				
Tenofovir, TDF (Viread)	<ul style="list-style-type: none"> ■ 300 mg tabs 	<ul style="list-style-type: none"> ■ 300 mg qd ■ Food—improves absorption 		<ul style="list-style-type: none"> ■ LFTs
Protease Inhibitors (PIs)				
Ampranavir, APV, (Agenerase) ^{§§}	<ul style="list-style-type: none"> ■ Caps: 50, 150 mg ■ solution 15 mg/mL PO[†] 	<ul style="list-style-type: none"> ■ >50 kg: 1200 mg bid (caps); 1400 mg bid (PO solution) max. 2400 mg/day ■ <50 kg: 20 mg/kg bid (caps); <50 kg: 1.5 mL/kg bid (solution); max. 2800 mg/day ■ Avoid high fat meal 	<ul style="list-style-type: none"> ■ GI intolerance, rash, oral paresthesias, lipodystrophy 	<ul style="list-style-type: none"> ■ Lipid profile[†], LFTs ■ Do not take supplemental Vitamin E

6 Antiretroviral Therapy

Antiretroviral Therapy ■ TABLE 6-8: Antiretroviral Agents—Continued

Drug Name	Form	Usual Dose	Toxicity (main toxicity italicized)	Monitor
Indinavir, IDV (Crixivan)	<ul style="list-style-type: none"> ■ Caps: 200, 333, 400 mg 	<ul style="list-style-type: none"> ■ 800 mg q8h ■ Food: 1 hr. before or 2 hr. after meal or with low fat snack 	<ul style="list-style-type: none"> ■ GI intolerance, nephrolithiasis, benign increase in bilirubin, lipodystrophy 	<ul style="list-style-type: none"> ■ Lipid profile[†], LFTs, UA
Lopinavir/Ritonavir, LPV/RTV (Kaletra)	<ul style="list-style-type: none"> ■ LPV 133.3 mg + RTV 33.3 mg (cap) ■ LPV 80 mg + RTV 20 mg/mL PO solution 	<ul style="list-style-type: none"> ■ 400 mg LPV + 100 mg RTV bid (3 cap or 5 mL solution bid) ■ Take with meals 	<ul style="list-style-type: none"> ■ GI Intolerance (esp. diarrhea), asthenia, lipodystrophy 	<ul style="list-style-type: none"> ■ LFTs, Lipid profile[†]
Nelfinavir, NFV (Viracept)	<ul style="list-style-type: none"> ■ 250 mg tabs ■ 50 mg/g powder 	<ul style="list-style-type: none"> ■ 1250 mg bid or 750 mg tid ■ Take with meals 	<ul style="list-style-type: none"> ■ Diarrhea, lipodystrophy 	<ul style="list-style-type: none"> ■ LFTs, Lipid profile[†]
Ritonavir, RTV (Norvir)	<ul style="list-style-type: none"> ■ 100 mg caps ■ 600 mg/7.5 mL PO solution 	<ul style="list-style-type: none"> ■ 600 mg q12h ■ Food—improves GI tolerance 	<ul style="list-style-type: none"> ■ GI intolerance, paresthesia, hepatitis, lipodystrophy 	<ul style="list-style-type: none"> ■ LFTs, Lipid profile[†]
Saquinavir (SQV) <ul style="list-style-type: none"> ■ Fortovase (FTV) ■ Invirase (INV) 	<ul style="list-style-type: none"> ■ 200 mg soft gel caps ■ 200 mg hard gel caps 	<ul style="list-style-type: none"> ■ FTV—1200 mg tid ■ Food (FTV): Take with large meal ■ INV—400 mg bid + RTV[§] ■ Food (SQV+RTV): No effect 	<ul style="list-style-type: none"> ■ GI intolerance, lipodystrophy 	<ul style="list-style-type: none"> ■ LFTs, Lipid profile[†]
Combination/Other Drugs				
Hydroxyurea* (HU)	<ul style="list-style-type: none"> ■ 500 mg caps 	<ul style="list-style-type: none"> ■ 500 mg bid or 1000 mg qd ■ Food—no effect 	<ul style="list-style-type: none"> ■ GI intolerance, Marrow suppression 	<ul style="list-style-type: none"> ■ CBC

*EFV should be avoided in first trimester of pregnancy and used with caution in women with reproductive potential. The combination of ddI & d4T is contraindicated in pregnancy. The contraindication with APV applies only to the oral solution which contains large quantities of propylene glycol. More frequent monitoring required. Drug change or dose change could be considered on a case-by-case basis noting the risk of resistance with under dosing.

[†]PIs and possibly for NNRTIs: fasting triglycerides, cholesterol, LDL, HDL and glucose at baseline and at 3 to 6 months and then prn.

[§]INV taken with RTV, otherwise INV is not recommended.

^{§§}APV caps and solution are NOT interchangeable on mg per mg basis. Capsule is the preferred formulation due to high propylene glycol in the PO solution.

TABLE 6-9: PI-PI Combination Therapy, Dose Adjustments

PI	IDV	NFV	LPV/RTV	RTV	SQV*
APV	APV standard + IDV standard	Limited Data	APV 750 mg bid + LPV/RTV standard	APV 1200 mg bid [†] + RTV 100–200 mg bid APV 1200 mg + RTV 200 mg qd	Limited Data
IDV		IDV 1200 mg bid + NFV 1250 mg bid	IDV 600 mg bid + LPV/RTV standard	IDV 400 mg bid + RTV 400 mg bid or IDV 800 mg bid + RTV 100 mg bid	Limited Data
NFV			Limited Data	NFV 500–750 mg bid + RTV 400 mg bid	NFV standard + FTV 800 mg tid or 1200 mg bid
LPV/RTV					LPV/RTV standard + FTV 800 mg bid
RTV					RTV 400 mg bid + FTV 400 mg bid or RTV 100 mg bid + FTV 1600 mg qd [†] or FTV 1000 mg bid + RTV 100 mg bid

* SQV should be as FTV except in combination with RTV, when either INV or FTV are acceptable.

■ TABLE 6-10: PI-NNRTI Combination Therapy

Agent	DLV	EFV	NVP
APV	DLV ↓, APV ↑ Dose unclear	APV 600 mg bid + RTV 100–200 mg bid + EFV 600 mg hs <i>or</i> APV 1200 mg bid + RTV 200 mg bid + EFV 600 mg hs	Limited Data
IDV	DLV standard IDV 600 mg q8h	EFV standard + IDV 1000 mg q8h	NVP standard + IDV 1000 mg q8h
NFV	Limited Data	EFV standard + NFV standard IDV 800 mg bid/ RTV 200 mg bid/ EFV 600 mg qhs	NVP standard + NFV standard
LPV/RTV	Limited Data	EFV standard + LPV/RTV 4 caps bid	NVP standard + LPV/RTV 4 caps bid
RTV	Limited Data	EFV standard + RTV 500–600 mg bid	NVP standard + RTV standard
SQV	DLV standard FTV 800 mg tid	EFV standard + FTV 1000 mg bid + RTV 100 mg bid <i>or</i> EFV standard + FTV 400 mg bid + RTV 400 mg bid	NVP standard + FTV standard Limited Data

TABLE 6-11: Drug Interactions: Contraindicated Combinations

Class	Contraindicated Agent	ART Agents	Alternate
Ca ⁺⁺ channel blocker	■ Bepridil	■ RTV, APV	—
Antiarrhythmics	■ Flecainide, propafenone ■ Amiodarone, quinidine	■ RTV, LPV/RTV ■ RTV	—
Lipid lowering	■ Simvastatin, lovastatin	■ All PIs, DLV	■ Pravastatin, atorvastatin, possibly fluvastatin
Antimycobacterials	■ RIF ■ RBT	■ IDV, NFV, APV, LPV/RTV, SQV (unless given with RTV), DLV, NVP ■ DLV, SQV	■ Use RBT* with HAART or use RIF with RTV/SQV or EFV
Antihistamine	■ Astemizole, terfenadine	■ All PIs, DLV, EFV	■ Loratadine, fexofenadine or cetirizine
Gastrointestinal	■ Cisapride ■ H ₂ blockers, proton pump inhibitors	■ All PIs, DLV, EFV ■ DLV	—
Neuroleptic	■ Clozapine ■ Pimozide	■ RTV ■ LPV/RTV, RTV, APV	— —
Psychotropic	■ Midazolam, Triazolam	■ All PIs, DLV, EFV	■ Temazepam or lorazepam
Ergot alkaloids	■ Ergotamine, DHE + others	■ All PIs, DLV, EFV	—
Herbs	■ St. John's Wort ■ Garlic	■ All PIs & NNRTIs ■ SQV	■ Alternate antidepressants

*See Table 6-12 for RBT and antiretroviral dose adjustments

Antiretroviral Therapy ■ TABLE 6-12: Drug Interactions: Combinations Requiring Dose Modifications

Agent		ART
Antifungal	<ul style="list-style-type: none"> ■ Ketoconazole 	<ul style="list-style-type: none"> ■ IDV 600 mg tid; RTV + LPV/RTV–Ketoconazole ≤200 mg/day; NVP–Not recommended. APV–Ketoconazole/itraconazole <400 mg/day.
Oral contraceptives	—	<ul style="list-style-type: none"> ■ Alternative method of contraception recommended with: RTV, NFV, APV, EFV, LPV/RTV, NVP; no data–SQV, DLV.
Anticonvulsants	<ul style="list-style-type: none"> ■ Phenobarbital, phenytoin ■ Carbamazepine 	<ul style="list-style-type: none"> ■ Use with caution; combination may decrease PI and NNRTI plasma concentration. If given together, monitor levels of anticonvulsants. Consider alternative anticonvulsant. ■ IDV: Consider alternative agent.
Methadone	—	<ul style="list-style-type: none"> ■ NVP, EFV may cause withdrawal; monitor methadone levels or symptoms. ddi: Consider dose adjustment (↑ ddi). See Tables 6-5, p. 26 and 11-18, p. 124.
Antibiotics	<ul style="list-style-type: none"> ■ Clarithromycin 	<ul style="list-style-type: none"> ■ RTV, DLV: Decrease clarithromycin dose in renal failure. ■ EFV: Use alternative to clarithromycin.
Antimycobacterials	<ul style="list-style-type: none"> ■ Rifabutin 	<ul style="list-style-type: none"> ■ APV 1200 mg bid + RBT 150 mg/day or 300 mg 2–3x/wk. ■ EFV 600 mg/day + RBT 450–600 mg/day or 600 mg 2–3x/wk.* ■ IDV 1000 mg q8h + RBT 150 mg/day or 300 mg 2–3x/wk. ■ LPV/RTV 400/100 mg + RBT 150 mg qod ■ NFV 1000 mg tid + RBT 150 mg/day or 300 mg 2–3x/wk. ■ RTV 600 mg bid + RBT 150 mg qod or 150 mg 3x/wk. ■ RTV 400 mg + SQV 400 mg bid + RBT 150 mg 2–3x/wk. ■ NVP + RBT standard doses ■ SQV 400 mg bid + RTV 400 mg + RIF 600 mg/day or 2–3x/wk.
Miscellaneous	<ul style="list-style-type: none"> ■ Theophylline ■ Warfarin ■ Sildenafil ■ Desipramine 	<ul style="list-style-type: none"> ■ RTV: Monitor theophylline levels. ■ Monitor INR closely if given with any PI or NNRTI. ■ All PIs and DLV: ≤25 mg/48 hrs. ■ RTV: Consider desipramine dose reduction.

*These recommendations apply to regimens that do not include PIs, which substantially increase RBT levels

■ TABLE 6-13: Dosing of Antiretroviral Agents in Renal Failure

Agent	GFR in mL/min			Dialysis	
	>50 (mg)	10–50 (mg)	<10 (mg)	Hemo (mg)	Perit (mg)
NRTIs					
AZT	300 mg bid	300 mg bid	300 mg qd	300 mg qd	300 mg qd
ddI	Usual dose	50% dose	25% dose	25% dose	25% dose
q4T					
>60 kg	40 mg bid	20 mg q12h–q24h	20 mg qd	20 mg qd	20 mg qd
<60 kg	30 mg bid	15 mg q12h–q24h	15 mg qd	15 mg qd	15 mg qd
ddC	0.75 mg tid	0.75 mg tid	0.75 mg bid	ND	ND
3TC	150 mg bid	150 mg qd	150 mg, then 50 mg qd	150 mg, then 50 mg qd	50 mg qd
ABC	300 mg bid	300 mg bid	300 mg bid	300 mg bid	300 mg bid
TDF	300 mg qd	Avoid	Avoid	Avoid	Avoid
NNRTIs: EFV, NVP, DLV	Usual dose				
PIs: RTV, SQV, LPV, IDV, NFV, APV	Usual dose				

■ TABLE 6-14: Dosing of Antiretroviral Agents in Hepatic Failure

Agent	Regimen
AZT	200 mg bid
ddI	Consider dose reduction
d4T, ABC, ddC, 3TC, TDF	Usual dose, except ↓ ABC dose (No data for 3TC and d4T)
EFV, NVP, DLV	Consider empiric dose reduction
IDV	600 mg q8h
APV	Moderate failure—450 mg cap bid; Severe—300 mg cap bid
LPV, RTV, NFV, SQV	Consider empiric dose reduction

Adherence

Methods to Achieve Readiness to Start HAART and Maintain Adherence

PATIENT RELATED

- Negotiate a plan or regimen that the patient understands and to which s/he is committed.
- Take time needed, >2 visits, to ensure readiness before 1st prescription.
- Recruit family, friends, peer and community support.
- Use memory aids such as timers, pagers, written schedules, pill boxes/ medication organizers.
- Plan ahead: Keep extra meds in key locations, obtain refills.
- Use missed doses as opportunities to intervene 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.

PHYSICIAN RELATED

- Educate patient about goals of therapy, pills, food effects, and side effects.
- Assess adherence potential before starting HAART; monitor at each visit.
- Treat side effects.
- Ensure access during off-hours and weekends for questions or to address problems.
- Utilize full health care team; ensure med refills at pharmacy.
- Consider impact of events and new diagnoses on adherence.

REGIMEN RELATED

- Avoid adverse drug interactions.

- Simplify regimen, including dose frequency, pill burden, and food requirements.
- Inform patient about and anticipate side effects.

HEALTH TEAM RELATED

- 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 and patient community.

Class Adverse Drug Reactions (ADRs)

Lipodystrophy: Fat Redistribution

DIAGNOSIS

- Fat accumulation: Abdomen, dorsal neck (“buffalo hump”), breasts
- Fat atrophy: Extremities, buccal fat, buttocks

MEASUREMENT (Shevitz A, *Clin Infect Dis* 2001;32:1769)

- Dual-energy x-ray absorptiometry (DXA), computed tomography (CT) scan, or magnetic resonance imaging (MRI)
- Waist-hip ratio >0.85 (women) or >0.95 (men)
- Patient perception

INTERVENTION

- Results with changing therapy, including use of different classes, are inconclusive.

Hyperlipidemia

EVALUATION

- Baseline for patient at risk for cardiovascular disease and prior to HAART.

TRIGLYCERIDES

- Normal levels: <150 mg/dL
- Elevated levels: 200–499 mg/dL
- Very high levels requiring immediate intervention to prevent pancreatitis and reduce risk of cardiovascular disease: >500 mg/dL

DRUG SELECTION

- ACTG expert panel recommendations for statins with concurrent PI or NNRTI: Atorvastatin or pravastatin (*Clin Infect Dis* 2000;31:1216)

THERAPEUTIC SWITCH

- PIs and possibly NNRTI agents appear to be associated with increases in blood lipids, including cholesterol, LDL cholesterol, and triglycerides. Use of non-PI containing regimens may reverse these changes. Changing from a PI based regimen to an NRTI/NNRTI based regimen (NVP, EFV or AZT/3TC/ABC) may improve lipid profile.

■ **TABLE 6-15: LDL Cholesterol: National Cholesterol Education Program (Expert Panel, JAMA 2001;285:2486)**

Risk	LDL goal mg/dL	Threshold LDL (mg/dL) for Initiation of Drug Therapy [†]
Coronary heart disease (CHD) or other form of atherosclerotic disease or diabetes or multiple risks*	<100	>130 100–130: Drug therapy optional
Multiple risks: ≥2 of: <ul style="list-style-type: none"> Smoking High blood pressure (HBP) >140/90 or HBP meds HDL <40 Bad genes: 1st degree relative male with CHD <55, female <65 Age >45 male, >55 female 	<130	Threshold varies based on estimated risk* 10 yr. risk = 10% to 20%* >130 10 yr. risk <10%* >160
Risk factors: 0–1	<160	>190 (160–189 drug therapy optional)

*Determined by a complicated point system that factors age, cholesterol, HDL and systolic blood pressure (BP)

[†]Major interventions are therapeutic lifestyle changes (TLC) and drugs. TLC emphasizes diet with reduced saturated fat (<7% total calories) and cholesterol (<200 mg/day). Other TLCs are exercise, weight reduction, increased fiber (16–25 g/day) and LDL lowering plant stanols/sterols (2 g/day).

TABLE 6-16: Drug Therapy for Hyperlipidemia

Class	Effect	Side Effect	Contraindications
Statins*	<ul style="list-style-type: none"> ■ LDL ↓ 18% to 55% ■ HDL ↑ 5% to 15% ■ TG ↓ 7% to 30% 	<ul style="list-style-type: none"> ■ Myopathy, hepatitis 	<ul style="list-style-type: none"> ■ Liver disease ■ Concomitant P450 inhibitors ■ Lovastatin and simvastatin are contraindicated with CYP 3A4 inhibitors ■ ACTG expert panel recommends statins and/or fibrates (Clin Infect Dis 2000;31:1216)
Bile acid sequestrant†	<ul style="list-style-type: none"> ■ LDL ↓ 15% to 30% ■ HDL ↑ 3% to 5% ■ TG No change 	<ul style="list-style-type: none"> ■ GI intolerance 	<ul style="list-style-type: none"> ■ Triglyceride > 400
Fibric acid‡	<ul style="list-style-type: none"> ■ LDL ↓ 5% to 20% ■ HDL ↑ 10% to 20% ■ TG ↓ 20% to 50% 	<ul style="list-style-type: none"> ■ Dyspepsia, myopathy, gallstones 	<ul style="list-style-type: none"> ■ Renal failure, severe liver disease ■ ACTG expert panel recommends statins and/or fibrates
Nicotinic acid§	<ul style="list-style-type: none"> ■ LDL ↓ 5% to 25% ■ HDL ↑ 15% to 35% ■ TG ↓ 20% to 50% 	<ul style="list-style-type: none"> ■ Flushing, gout, ↑ glucose, GI intolerance, hepatitis 	<ul style="list-style-type: none"> ■ Chronic liver disease ■ Relative: diabetes, hyperuricemia, peptic ulcer disease

* Lovastatin (20–80 mg), pravastatin (20–40 mg), simvastatin (20–80 mg), fluvastatin (20–80 mg), atorvastatin (10–80 mg)

† Cholestyramine (4–16 gm), colestipol (5–20 gm)/day

‡ Gemfibrozil (600 mg bid), fenofibrate (≤160 mg/day), clofibrate (1000 mg bid)

§ Nicotinic acid: Immediate release (1.5–3.0 gm), extended release (1–2 gm), sustained release (1–2 gm)/day

Diabetes

RISK: PI use; all agents in class

FREQUENCY: 3–17% at median of 60 days.

CAUSE: Peripheral insulin resistance.

MONITORING: Fasting blood glucose at pre-HAART baseline; some recommend fasting glucose at 3 to 4 month intervals for the first year of PI therapy. Subsequent measurements based on baseline measurements and risks.

TREATMENT: Insulin sensitizers (metformin or glitazones) preferred over insulin or sulfonylureas based on mechanism of diabetes; most do not recommend changes in HAART unless there is severe diabetes.

Mitochondrial Toxicity: Lactic Acidosis ± Steatosis

(*Ann Intern Med* 2000;13:192)

RATE: 1.3 per 1000 patient years

RISK: Prolonged NRTI use, obesity, female sex, pregnancy, d4T > AZT, ddI > ABC, 3TC.

SYMPTOMS: Fatigue, nausea, vomiting, wasting, abdominal pain, dyspnea, diarrhea, anorexia, weakness, myalgias, paresthesias, hepatomegaly. May cause respiratory failure requiring ventilator therapy.

LAB: Lactic acid: Obtain without tourniquet, fist-clenching, or stasis; use pre-chilled fluoride-oxalate tubes. Transport on ice for processing within 4 hours.

- <2 mmol/mL: Normal
- 2–5 mmol/mL: d/c NRTI if symptomatic (after ruling out other causes of symptoms. At this low level, symptoms may be due to something else.
- >5 mmol/mL: d/c NRTI
- >10 mmol/mL: Potentially lethal

LAB, OTHER: Variable ↑ CPK, LDH, lipase, amylase, ALT, anion gap, ↓ HCO₃; CT scan or echo—fatty liver; liver biopsy—steatosis

TREATMENT: d/c NRTI or switch to NRTI with reduced frequency of lactic acidosis (ABC, AZT, tenofovir). NRTI-sparing regimens with established efficacy: LPV/RTV, EFV/IDV ± RTV, SQV/RTV, APV/RTV/EFV

RECOVERY: Mean time to normal lactic acid levels after stopping NRTIs: 50 days

■ TABLE 6-17: Drug Specific Toxicity (see Lancet 2000;356:1423)

Drug	Organ	Clinical Features	Rate	Lab	Intervention
AZT	<ul style="list-style-type: none"> ■ Muscles ■ Heart ■ Marrow 	<ul style="list-style-type: none"> ■ Fatigue, myalgias ■ Dilated cardiomyopathy ■ Anemia, neutropenia 	<ul style="list-style-type: none"> ■ 17% ■ Rare ■ 5% to 10% 	<ul style="list-style-type: none"> ■ CPK ↑ ■ Echo ■ WBC 	<ul style="list-style-type: none"> ■ d/c ■ d/c ■ d/c, EPO or G-CSF
d4T, ddI, ddC	Peripheral nerves	Pain, paresthesias	10% to 30%	DTRs, Sx	d/c
ddI	Pancreas	Abdominal pain	1% to 6%	Amylase ↑	d/c
d4T, ddI, others	Fat	Lipoatrophy	50%	Appearance	d/c?

Hepatotoxicity

DEFINITION: ALT or AST elevation to 3-5x ULN that is not otherwise explained.

FREQUENCY WITH HAART: 2% to 18%

MECHANISM: NRTI—mitochondrial toxicity; PI and NRTI—unclear. Liver biopsy usually not helpful.

AGENTS: All antiretroviral agents, especially RTV and NVP. Note: NVP associated hepatitis usually occurs in the first 12 weeks of therapy, may be asymptomatic, and in rare cases may progress to hepatic necrosis and death. ALT levels should be monitored (see p. 126). With PIs, the hepatotoxicity may occur at any time during treatment and the implicated drug should be stopped when the ALT is 5x ULN.

RISK: Chronic hepatitis with HCV, HBV, d4T use, alcoholism, and increased baseline transaminase levels. With HCV or HBV co-infection, the increased ALT may be due to immune reconstitution rather than drug toxicity.

DOSE MODIFICATION WITH HEPATIC FAILURE (ANY CAUSE): AZT, all PIs, all NNRTIs

Osteoporosis

RISK: Osteopenia in 25–50% of HAART recipients; osteoporosis in 5–10%

ROUTINE SCREENING: Not indicated

TREATMENT: Increase intake of calcium and vitamin D plus weight bearing exercises; if fractures—bisphosphonates, raloxifene, or calcitonin.

Avascular Necrosis

RATE: 0.3% to 1.3%

RISKS: ETOH abuse, hyperlipidemia, steroid use, hypercoagulability, hyperlipidemia, hemoglobinopathy; relationship with HAART is unclear.

DIAGNOSIS: MRI or CT scan

MOST FREQUENT SITES: femoral head, shoulder

Rash

MOST COMMON WITH NNRTIS: NVP, DLV, EFV; frequency—10% to 20%

- Most are cutaneous only and can be treated with antihistamines
- Severe or life threatening reactions include Stevens-Johnson syndrome and DRESS (drug rash, eosinophilia and systemic symptoms with fever, and multiple organ involvement)

INDICATION TO D/C NNRTI: Symptoms of DRESS or rash with fever, desquamation, mucous membrane involvement, blistering or arthritis (1% to 2%)

SAFETY OF ALTERNATIVE NNRTIS: Unknown; chemical structures of NNRTIs are very different and limited experience shows that a switch from NVP to EFV for rash is safe

PI MOST LIKELY TO CAUSE RASH: APV—22% (sulfonamide)

NRTI MOST LIKELY TO CAUSE RASH: ABC

TABLE 6-18: ART Agents: FDA Black Box Warnings

Drug	Warning
Nucleoside Reverse Transcriptase Inhibitors	
ABC	<ul style="list-style-type: none"> ■ Fatal hypersensitivity reactions reported. ■ Signs & Sx are fever, rash, fatigue, GI Sx, and respiratory Sx. If suspected, ABC should be stopped and should not be restarted. ■ Lactic acidosis and steatosis.
ddl	<ul style="list-style-type: none"> ■ Fatal and nonfatal pancreatitis; ddl should be held if pancreatitis is suspected & d/c if confirmed. ■ Lactic acidosis and steatosis. ■ Fatal lactic acidosis in pregnant women with ddl + d4T.
3TC	<ul style="list-style-type: none"> ■ Lactic acidosis and steatosis.
d4T	<ul style="list-style-type: none"> ■ Lactic acidosis and steatosis. ■ Fatal lactic acidosis in pregnant women with ddl + d4T. ■ Fatal and nonfatal pancreatitis with ddl + d4T+ HU.
ddC	<ul style="list-style-type: none"> ■ Severe peripheral neuropathy. ■ Pancreatitis; rare cases of hepatic failure & death with concurrent HBV. ■ Lactic acidosis and steatosis. ■ Rare cases of hepatic failure and death.
AZT	<ul style="list-style-type: none"> ■ Lactic acidosis and steatosis. ■ Hematologic toxicities including neutropenia & anemia. ■ Myopathy
TDF	<ul style="list-style-type: none"> ■ Lactic acidosis and steatosis
NNRTIs	
DLV	<ul style="list-style-type: none"> ■ None
EFV	<ul style="list-style-type: none"> ■ None
NVP	<ul style="list-style-type: none"> ■ Severe, life-threatening hepatotoxicity including fulminant and cholestatic hepatitis, hepatic necrosis & hepatic failure. ■ Severe, life-threatening & even fatal skin reactions. Monitor intensely during the first 12 wks. to detect hepatotoxicity and skin reactions.
PIs	
APV	<ul style="list-style-type: none"> ■ Large amount of the excipient propylene glycol in oral solution—contraindicated in pregnant women, patients with renal or hepatic failure, patients treated with disulfiram or metronidazole.
IDV	<ul style="list-style-type: none"> ■ None
LPV	<ul style="list-style-type: none"> ■ None
NFV	<ul style="list-style-type: none"> ■ None
RTV	<ul style="list-style-type: none"> ■ Co-administration with certain medications may cause serious or life-threatening events.
SQV	<ul style="list-style-type: none"> ■ None

7 Postexposure Prophylaxis

U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV and HIV and Recommendations for PEP (MMWR 2001; 50: RR-11)

Occupational Exposures

Risk

■ TABLE 7-1: Risk of Viral Transmission With Sharps Injury From Infected Source

Source	Risk
HBV (HBsAg positive + unvaccinated HCW) <ul style="list-style-type: none">■ Source HBeAg+■ Source HBeAg-	<ul style="list-style-type: none">■ 37% to 62%■ 23% to 37%
HCV	1.8%
HIV	0.3%

Management of Occupational Blood Exposure

IMMEDIATE CARE: Wash wounds with soap and water; flush mucous membranes with water.

RISK ASSESSMENT: Type of fluid and type of exposure.

EVALUATE SOURCE: Test source for HBsAg, anti-HCV, and HIV serology (rapid test if available).

EXPOSED PERSON

- HCV: No PEP.
- HBV: see Table 7-2, p. 48. Assess vaccine status and response.
- HIV: see Table 7-3, p. 50, initiate PEP as quickly as possible.

FOLLOW-UP TESTING IN EXPOSED PERSON

- HCV exposure (source anti-HCV positive):
 - Anti-HCV and ALT at baseline and at 4 to 6 mos.
 - HCV RNA at 4 to 6 wks. optional.
 - Confirm positive anti-HCV.
- HBV exposure (source HBsAg positive):
 - See Table 7-2, p. 48.
 - If vaccinating: Test anti-HBs at 1 to 2 mos. after last dose.

- HIV exposure (source positive HIV serology or acute HIV with positive HIV RNA):
 - See Table 7-3, p. 50.
 - HIV serology at baseline, 1.5, 3, and 6 mos.
 - Reevaluate and adjust regimen at 72 hrs. if taking PEP.
 - Monitor for drug toxicity.

■ **TABLE 7-2: HBV PEP Recommendations for Percutaneous Blood Exposures With HBV Infected Source (HBsAg positive) or Unknown HBV Status**

Vaccination Status of HCW	Features of Source	
	HBsAg Positive	Source Unknown
Unvaccinated	HBIG* + vaccine series (3 doses)	HBV vaccine (3 doses)
Vaccinated		
■ Responder [†]	■ No Rx	■ No Rx
■ Non-responder [†]	■ HBIG x 1 + vaccine series or HBIG x 2 [‡]	■ Rx as source positive if high risk
■ Antibody status unknown	Test for anti-HBs <ul style="list-style-type: none"> ■ Anti-HBs ≥ 10 mIU/mL: No Rx ■ Anti-HBs < 10 mIU/mL: HBIG x 1 + booster dose HBV vaccine 	Test for anti-HBs <ul style="list-style-type: none"> ■ Anti-HBs > 10 mIU/mL: No Rx ■ Anti-HBs < 10 mIU/mL: Booster, check titer in 1 to 2 mos.

*HBIG = Hepatitis B Immune Globulin; dose is 0.06 mL/kg IM. Should be given as soon as possible and within 7 days. HBIG and HBV vaccine are each 70% to 75% effective in preventing HBV transmission.

[†]Responder defined by antibody to HBsAg of ≥ 10 mIU/mL.

[‡]HBIG + the vaccine series is preferred for non-responders who did not complete the 3 dose series; HBIG x 2 doses is preferred if there were 2 vaccine series and no response.

HCV PEP

The reported risk from an HCV-infected source is 1.8% with a range of 0% to 7% in various reports. The following recommendations are made:

- Anti-HCV testing of the source.
- The exposed HCW should have baseline anti-HCV and ALT tests; follow-up testing at 4 to 6 months should include anti-HCV and ALT. Testing for HCV RNA (to detect acute infection prior to seroconversion) may be performed at 4 to 6 weeks.
- All positive results for anti-HCV should be confirmed with RIBA or HCV RNA.

- Postexposure Immune Globulin (IG) is not recommended because this has not proven effective in primate studies, no protective antibody response has been identified after HCV infection, and the ACIP has concluded that IG for HCV PEP is not indicated.
- Antiviral agents (interferon with or without Ribavirin) are not recommended because no trials have been done to show effectiveness, available data suggests that infection must be established before interferon can be effective, the drugs are not FDA-approved for this indication, and they have extensive side effects.

HIV PEP

- Through June 2000 there were 56 confirmed HIV transmissions from an infected source to a HCW. All involved blood, bloody body fluids or high titer viral cultures; 48 of 56 exposures were percutaneous (sharps) injuries; 5 were mucous membrane/non-intact skin exposures, and 2 had both type of exposure
- Potential sources of transmission (with no confirmed cases with occupational exposures): Semen, vaginal secretions, tissue or cerebrospinal, peritoneal, pericardial, synovial or amniotic fluid.
- PEP should be started as soon as possible; if the delay exceeds 36 hours expert consultation is suggested.
- Prophylaxis should be continued for 4 weeks if tolerated.
- The exposed person should be reevaluated within 72 hours as additional information about the source is obtained, including serologic status, VL, current treatment, any resistance test results, or information about factors that would modify recommendations.
- HIV EIA should be used to monitor for seroconversion, and this test should be performed at baseline and at 6 weeks, 3 months, and 6 months post exposure. VL tests for screening are not recommended in the HCW unless there is an illness compatible with the acute retroviral syndrome.
- If PEP is given, the HCW should be monitored for drug toxicity at baseline and at two weeks with a CBC, renal function tests, and hepatic function tests. For those receiving IDV, the tests should include urinalysis.
- HCWs are "asked to commit to behavioral measures, e.g., sexual abstinence or condom use for several weeks to two months." The greatest risk is during the first 6 to 12 weeks postexposure.
- Female HCWs with known or possible pregnancy should be treated as anyone else, except for the selection of drugs, which should involve a discussion of benefits and risks between HCW and care provider. EFV and the combination of d4T and ddI should be avoided.

- Specific recommendations for PEP are provided in the two tables below, one for percutaneous injuries and the second for exposures to mucous membranes or non-intact skin.

■ **TABLE 7-3: HIV PEP for Percutaneous Injuries**

Exposure	Status of Source		
	Low Risk*	High Risk*	Unknown
Not severe: Solid needle, superficial	2 drug PEP [†]	3 drug PEP [†]	Usually none; consider 2 drug PEP [‡]
Severe: Large bore, deep injury, visible blood on device, needle in patient artery/vein	3 drug PEP [†]	3 drug PEP [†]	Usually none; consider 2 drug PEP [‡]

*Low risk: Asymptomatic HIV or VL <1500 c/mL. High risk: Symptomatic HIV, AIDS, acute seroconversion, high VL.

[†]Concern for drug resistance: Initiate prophylaxis without delay and consult an expert.

[‡]Consider 2 drug PEP if source is high risk for HIV or exposure from unknown source when HIV infected source is likely.

■ **TABLE 7-4: HIV PEP for Mucous Membrane and Non-Intact Skin Exposures***

Exposure	Status of Source		
	Low risk [†]	High risk [†]	Unknown
Small volume (drops)	Consider 2 drug PEP	2 drug PEP	Usually no PEP; consider 2 drug PEP [‡]
Large volume (major blood splash)	2 drug PEP	3 drug PEP	Usually no PEP; consider 2 drug PEP [‡]

*Non-intact skin = dermatitis, abrasion, wound

[†]Low risk = Asymptomatic or VL <1500 c/mL. High risk = Symptomatic HIV, AIDS, acute seroconversion, high HIV viral load.

[‡]Consider if source has HIV risk factors or exposure from unknown source where HIV infected source is likely.

Drug Selection for PEP

Recommended Regimens for PEP

Decisions should be made based in part on information about the source, including ART, response to therapy, including VL, and any data on HIV resistance testing. Decisions should not delay initiation of PEP, and modifications can be made after information is obtained.

2 DRUG COMBINATIONS

- AZT + 3TC
- 3TC + d4T
- d4T + ddI

3 DRUG COMBINATIONS

- 2 nucleosides (above list) + IDV, NFV, EFV, ABC, RTV, FTV, APV, DLV or LPV/RTV. Preferred: NFV, EFV, ABC + LPV/RTV

Recommended Resources for Additional Information by Telephone or Internet

Occupational Exposure Management Resources

- National Clinicians' PEP Hotline (Health Resources and Services Administration [HRSA], AIDS Education Training Centers [AETC], CDC) (available at all times): 888-448-4911 or <http://www.ucsf.edu/hivcnt>
- Needlestick (University of California at Los Angeles [UCLA]): <http://www.needlestick.mednet.ucla.edu>
- Hepatitis Hotline: 888-443-7232 or <http://www.cdc.gov/hepatitis>
- CDC Reporting (Occupationally acquired HIV and PEP failures): 800-893-0485

8 | Pregnancy

■ TABLE 8-1: Prevention of OIs in Pregnancy

OI	Prevention Regimen
PCP	<ul style="list-style-type: none"> ■ TMP-SMX is recommended with dapson as the alternative. Due to theoretical concerns for teratogenicity providers may choose to withhold prophylaxis in the first trimester or use aerosolized pentamidine.
Toxoplasmosis	<ul style="list-style-type: none"> ■ Primary prophylaxis: TMP-SMX is recommended with theoretical concerns for teratogenicity in first trimester. Pyrimethamine regimens should be avoided. ■ Secondary prophylaxis: This is a risk : benefit issue with concerns for teratogenicity of pyrimethamine vs recurrent toxoplasmosis; most clinicians favor continued treatment. ■ Primary toxoplasmosis during pregnancy should be managed by specialist.
TB	<ul style="list-style-type: none"> ■ INH + pyridoxine regimens preferred for prophylaxis; some providers avoid INH in 1st trimester due to theoretical concerns for teratogenicity. ■ Chest x-ray to R/O active TB must be performed with lead apron shields. ■ RIF and RBT appear safe during pregnancy, but experience is limited. ■ PZA should be avoided, especially during the first trimester.
<i>M. avium</i> complex	<ul style="list-style-type: none"> ■ Primary prophylaxis: Azithromycin is preferred, but some providers withhold prophylaxis in 1st trimester. Experience with RBT is limited. Clarithromycin is teratogenic in animals, use with caution. ■ Secondary prophylaxis: Azithromycin + EMB is preferred.
<i>S. pneumoniae</i>	<ul style="list-style-type: none"> ■ Pneumovax may be given; due to the “ HIV viral burst” some delay vaccination until after HAART.
Travel	<ul style="list-style-type: none"> ■ Avoid fluoroquinolones; TMP-SMX may be used for prevention of travelers diarrhea.
Fungal infections	<ul style="list-style-type: none"> ■ General: Avoid azoles (fluconazole, ketoconazole and itraconazole) due to teratogenicity. ■ Cryptococcosis, histoplasmosis, coccidioidomycosis: For secondary prophylaxis, amphotericin B is preferred instead of azoles, especially during the 1st trimester.
CMV	<ul style="list-style-type: none"> ■ Standard recommendations apply.
HSV	<ul style="list-style-type: none"> ■ Oral acyclovir during late pregnancy to prevent perinatal HSV transmission is controversial, but usually not used; acyclovir prophylaxis to prevent severe recurrences may be indicated.
VZV exposure: Non-immune host	<ul style="list-style-type: none"> ■ VZIG within 96 hrs. of exposure is recommended.
Human papilloma virus (HPV)	<ul style="list-style-type: none"> ■ Avoid intravaginal 5 fluorouracil.

Antiretroviral Therapy

Recommendations for Pregnant Women and Their Infants

ACTG 076 PROTOCOL (SHOULD BE USED AS PART OF ART REGIMEN IN ALL PREGNANT WOMEN, IF POSSIBLE)

- **Antepartum:** AZT 300 mg bid PO or 200 mg tid PO, week 14 until delivery.
- **Intrapartum:** AZT 2 mg/kg IV over first hour then 1 mg/kg/hr. until delivery.
- **Postpartum:** (Infant): AZT syrup 2 mg/kg PO q6h (or 1.5 mg/kg q6h IV) x 6 wks.

REGIMEN FOR 2ND AND 3RD TRIMESTERS—STANDARD ART, BUT

- Include AZT for prevention of perinatal transmission, unless there are unacceptable side effects, toxicity, or factors requiring d4T-containing regimen.
- Treat based upon maternal clinical/immunologic status, but observe caution with: EFV, HU, AZT + d4T, d4T + ddl, APV solution, IDV (see notes below).

CHOICES FOR UNTREATED WOMEN PRESENTING IN LABOR AND THEIR INFANTS

- NVP 200 mg PO onset labor.
 - Infant: Single 2 mg/kg PO at 48 to 72 hrs.
- AZT 600 mg PO onset labor and 300 mg PO q3h until delivery + 3TC 150 mg PO onset labor and 150 mg PO q12h until delivery
 - Infant: AZT 4 mg/kg PO q12h *plus* 3TC 2 mg/kg PO q12h for 7 days.
- AZT 2 mg/kg IV bolus then 1 mg/kg/hr. IV infusion until delivery
 - Infant: AZT 2 mg/kg PO q6h for 6 wks. (ACTG 076 Protocol).
- NVP + AZT: NVP 200 mg PO onset labor + AZT 2 mg/kg IV bolus then 1 mg/kg/hr. IV infusion until delivery.
 - Infant: NVP single 2 mg/kg PO at 48 to 72 hrs. + AZT 2 mg/kg PO q6h for 6 weeks.

NOTES

- **AZT & d4T:** Pharmacologic antagonism, do not use together.
- **APV:** Oral solution (only) is contraindicated in pregnancy because it contains large quantities of propylene glycol, which may be toxic to the fetus.
- **d4T and ddl:** Concerns about lactic acidosis; use with caution, generally only when other NRTIs have failed or caused unacceptable side effects/toxicity (*N Eng J Med* 1999;340:1723).
- **EFV, HU:** Concerns about teratogenicity or birth defects: HU should be avoided in pregnancy; EFV should be avoided in 1st trimester.

- **IDV:** Theoretical concerns in late pregnancy for risk of neonatal hyperbilirubinemia, renal stones.

Drug Information: A listing of ART drugs with information pertinent to their use in pregnancy may be found in Table 2 of the *Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States* (January 24, 2001, <http://www.hivatis.org>).

Pregnancy Issues

Adverse Drug Reactions

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

Risk for Perinatal HIV Transmission

Plasma and genital tract VL (most significant), primary infection or late stage HIV, low CD4 count, STDs/other coinfections, pre-term delivery, increased duration of membrane rupture, placental disruption, invasive monitoring or assessment, vaginal delivery, and lack of AZT prophylaxis.

Postpartum Risk

Breastfeeding, not recommended in U.S.

Clinical Scenarios and Management, Including Cesarean Section

Untreated Pregnant Patient

PRESENTS EARLY IN PREGNANCY (<36 WKS.)

- Standard clinical, immunologic and virologic evaluation and resistance testing (same as other patients).
- If VL >1000 c/mL or CD4 <350 cells/mm³, HAART with AZT (ACTG 076 Protocol); see *Notes* under "ART and Delivery," above. May consider delaying ART until after 10 to 12 wks. gestation.
- VL <1000 c/mL and CD4 >350 cells/mm³, AZT monotherapy (ACTG 076 Protocol) after the first trimester for prevention of perinatal transmission (*J Infect Dis* 2001;183:539).
- Monitor VL and CD4 to plan for delivery.

PRESENTS LATE IN PREGNANCY (≥ 36 WKS.)

- Standard clinical, immunologic and virologic evaluation and resistance testing.
- If VL > 1000 c/mL or CD4 < 350 cells/mm³, HAART with AZT (ACTG 076 Protocol); see *Notes* under “ART and Delivery,” above.
- VL < 1000 c/mL and CD4 > 350 cells/mm³, AZT monotherapy (ACTG 076 Protocol) for prevention of perinatal transmission (*J Infect Dis* 2001;183:539).
- VL > 1000 c/mL: Counsel that C-section is likely to reduce risk of transmission to infant, but counsel about risks and benefits of all choices.

PRESENTS IN LABOR

- Initiate therapy (see recommendations for ART for Untreated Women Presenting in Labor, above).
- Postpartum immunologic and virologic evaluation of mother for ART.
- Infant should undergo diagnostic testing for HIV to determine need for ongoing ART.

PRESENTS POSTPARTUM

- Initiate the 6 week neonatal AZT protocol preferably within 6 to 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.

Treated Pregnant Patient

EARLY PREGNANCY (< 36 WKS.)

- Continue ART with standard monitoring, but:
- May consider discontinuation during 1st trimester: All drugs should be stopped and restarted simultaneously to reduce risk of resistance.
- Include AZT if tolerated; see cautions for antiretrovirals, in *Notes* under “ART and Delivery,” above.

LATE PREGNANCY (≥ 36 WKS.)

- Continue ART, including AZT, without interruption during labor and delivery.
- VL > 1000 c/mL: Counsel that C-section is likely to reduce the risk of transmission to infant, but counsel about risks and benefits of all choices.

C-SECTION PLANNED BUT PRESENTS IN LABOR OR WITH RUPTURED MEMBRANES

- Initiate ACTG 076 Protocol, intrapartum regimen, 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.

Delivery Procedures and Therapy

C-SECTION

- Schedule for week 38.
- If on ART: IV AZT starting 3 hrs. before C-section and continue all other ART agents.
- Infant: Use ACTG 076 Protocol, Postpartum regimen (infant), above.

VAGINAL DELIVERY

- If on ART: IV AZT with initiation of labor and continue all other ART agents.
- Avoid rupture of membranes, fetal scalp electrodes, forceps delivery, and vacuum extractor.
- Infant: If treated mother, use ACTG 076 Protocol, Postpartum (infant) regimen, above. If untreated mother, use regimen described above that matches maternal regimen.

Antiretroviral Pregnancy Registry

1410 Commonwealth Dr., Wilmington, NC 28402, TEL: 800-258-4263,
Fax 800-800-1052

9 | Co-Morbidities: TB, HCV, Pain, STDs

Tuberculosis

Latent TB

TESTING

Test all HIV infected persons without history of positive test; repeat annually if risk.

TREAT

- Positive PPD: 5 mm induration at 48 to 72 hrs.
- Confirmed history of positive PPD without Rx or
- High risk exposure: Repeat PPD at 12 wks. and d/c prophylaxis if negative at that time.

TREATMENT REGIMENS FOR LATENT TB

■ INH regimens

- INH 300 mg/day + pyridoxine 50 mg/day x 9 mos.
- INH 900 mg + pyridoxine 100 mg 2x/wk. (DOT) x 9 mos.

■ RBT/RIF + PZA

- HAART recipients: RBT (dose modified as indicated in Table 9–2) + PZA 15–20 mg/kg/day x 2 mos.
- No HAART (or EFV, SQV/RTV): RIF 600 mg/day + PZA 15–20 mg/kg/day x 2 mos.
- **Comments:** Short Course RBT/RIF + PZA has been associated with 6 hepatotoxic deaths, all in persons without HIV infection and without chronic liver disease (*MMWR* 2001;50:773). The CDC recommendation for HIV-infected patients with latent TB is INH regimen if completion of 9 month course is likely; otherwise, RBT/RIF + PZA x 2 mos. with bilirubin + ALT at baseline, 2, 4, and 6 weeks.

- **Contraindications to RBT/RIF + PZA:** Chronic liver disease or history of INH hepatotoxicity.

■ Alternative:

- RIF 600 mg/day x 4 mos.
- RBT 300 mg/day x 4 mos. (see Table 9–2).

- **INH resistant:** RBT/RIF ± PZA (see above)

■ TABLE 9–1: RBT Regimens

PI/NNRTI	RBT
IDV 1000 mg q8h	150 mg/day or 300 mg 2–3x/wk.
NFV 1000 mg tid or 1250 mg bid	150 mg/day or 300 mg 2–3x/wk.
APV 1200 mg bid	150 mg/day or 300 mg 2–3x/wk.
EFV 600 mg/day	450 mg/day or 600 mg 2–3x/wk.
NVP 200 mg bid	300 mg/day
RTV 600 mg bid	150 mg 2–3x/wk.
RTV 400 mg/SQV 400 mg bid	150 mg 2–3x/wk.
LPV 400 mg/RTV 100 mg bid	150 mg qod

Active TB (*MMWR* 1998;47:[RR–20]; *MMWR* 2000;49:185) —————

DOT PREFERRED

- **RIF-based regimens**, no PI or NNRTIs except EFV, RTV or RTV + SQV
 - INH/RIF/PZA/EMB (or SM) qd x 8 wks., then INH/RIF x 2–3x/wk. x 18 wks.
 - INH/RIF/PZA/EMB (or SM) qd x 2 wks., then 2 to 3x/wk. x 6 wks., then INH/RIF 2–3x/wk. x 18 wks.
 - INH/RIF/PZA/EMB 3x/wk. x 26 wks.
- **RBT-based regimens, concurrent PI or NNRTI** (see Table 9–2 for dose modification of RBT, PI, or NNRTI)
 - INH/RBT/PZA/EMB qd x 8 wks., then INH/RBT qd or 2x/wk. x 18 wks.
 - INH/RBT/PZA/EMB qd x 2 wks., then 2x/wk. x 6 wks., then INH/RBT 2x/wk. x 18 wks.
- **SM-based regimens, concurrent PI or NNRTI**
 - INH/SM/PZA/EMB qd x 8 wks., then INH/SM/PZA 2–3x/wk. x 30 wks.
 - INH/SM/PZA/EMB qd x 2 wks., then 2 to 3x/wk. x 6 wks., then INH/SM/PZA x 30 wks.

■ TABLE 9–2: Daily Dosing and Directly Observed Therapy (DOT):
2 to 3x/wk. x 26 wks. (total)

Drug	Daily	DOT 2x/wk.	DOT 3x/wk.
INH	5 mg/kg (300 mg)*	15 mg/kg (900 mg)*	15 mg/kg (900 mg)*
RIF	10 mg/kg (600 mg)*	10 mg/kg (600 mg)*	10 mg/kg (600 mg)*
PZA	15–30 mg/kg (2 gm)*	50–70 mg/kg (4 gm)*	50–70 mg/kg (3 gm)*
EMB	15–25 mg/kg (2 gm)*	50 mg/kg (4 gm)*	25–30 mg/kg (2.5 gm)*
SM	15 mg/kg (1 gm)*	25–30 mg/kg (1 gm)*	25–30 mg/kg (1 gm)*

*Maximum dose

HIV AND TB SPECIAL TREATMENT NOTES

- **Pregnancy:** INH regimens are preferred for pregnant women. Some experts would use RIF + PZA as an alternative regimen in HIV infected pregnant women. PZA should be avoided during the first trimester.
- **Multidrug Resistant TB (MDRTB) Exposure:** Expert consultation is recommended for persons who are likely to be infected with INH and RIF resistant TB (multidrug resistant TB, or MDRTB) and at high risk of reactivation.
- **ART/TB treatment interactions:** RBT should not be used with hard gel SQV or DLV.

MONITORING

- **Initial Evaluation:** Rule out active TB, include chest x-ray.
- **INH Prophylaxis:** Patient to receive DOT or contact provider every month to report Sx of hepatitis, etc.
 - Pyridoxine given concurrently.
 - LFTs at baseline, 3 mos., and as needed for Sx of hepatitis or if abnormal test results.
 - d/c INH if asymptomatic and ALT/AST $>5x$ ULN or symptomatic and ALT/AST $\geq 3x$ ULN.
- **RIF/RBT + PZA prophylaxis:** Monitor carefully for Sx and signs of hepatitis; deaths have been reported (*MMWR* 2001;50:733).
 - Patient should be seen at 2, 4, 6, and 8 weeks.
 - CBC and LFTs at 2, 4, and 6 weeks or with Sx.
 - d/c RIF/RBT + PZA if asymptomatic and ALT/AST $\geq 5x$ ULN or symptomatic and any elevation of ALT/AST.

MONITORING FOR DRUG TOXICITY

- **Clinical monitoring:** Patient should report any evidence of hepatitis (jaundice, dark urine, nausea, anorexia, vomiting, abdominal pain, fever >3 days). Patient should contact health care provider monthly.
- **Laboratory monitoring:** ALT, AST, bilirubin, CBC at baseline, at 3 mos., and as needed based on Sx and prior lab results.
- **Toxicity:** INH ALT/AST $>5x$ ULN or $>3x$ ULN + Sx: Discontinue INH, RIF and PZA and give EMB, SM + ofloxacin. When LFTs return to normal, reintroduce one at a time.

EVALUATION

- **Expected Response:**
 - Symptoms should improve in 4 wks.

- AFB smear & sputum culture: Obtain monthly until negative and expect negative results at 2 to 3 months.
- Positive smear/culture at 2 to 3 months: Suspect noncompliance or resistance.
- Patients with negative smear and culture at 2 months should have at least one additional smear at end of treatment.
- Some authorities recommend X-ray at 2 to 3 months.
- Extrapulmonary TB: As above for pulmonary TB, although some experts recommend monthly treatment for disseminated TB.
- Pregnancy: SM is contraindicated. PZA is not recommended in first trimester due to risk of teratogenicity; use INH, RIF + EMB.
- Lactation: No antituberculous drugs are contraindicated.
- Rx failure: Positive culture at 5 to 6 months: Suspect resistance or non-compliance.

INTERVENTION

- **Sensitive strain:** DOT
- **Resistant strain:** >2 active drugs x 12 to 24 mos.
- **Resistance:** (New cases, U.S., 1998): INH—8.4%, RIF—3.0%, PZA—3.0%, EMB—22%, SM—6.2%, INH + RIF (multiple-resistant)—2.2%

Hepatitis C

Management

DIAGNOSIS: EIA for anti-HCV (screening test) plus confirmatory quantitative HCV RNA PCR.

NATURAL HISTORY: Acute infection (clinically silent in 80%) → chronic HIV infection (80%) → cirrhosis in 20 years (20%) → lethal liver failure (25% or 4% of total infected population)

FACTORS THAT INCREASE RATES OF PROGRESSION: Alcoholism, coinfection with HBV or HIV, male sex, older age at HCV infection.

HIV COINFECTION: Increases risk of progression to cirrhosis: 25% in 15 yrs. compared to 7% in 15 yrs. without HIV coinfection. Impact of HCV on natural history of HIV is unclear. Coinfection often poses difficulties in distinguishing between changes in LFTs due to HCV and changes due to OIs or toxicity of anti-retroviral agents.

EVALUATION

- **Serology** to confirm diagnosis, as above.
 - **ALT:** Levels fluctuate, so single values are of limited use; levels do not correlate with pathology findings, and ALT should not be used for therapeutic decision.

- **Viral load:** Three commercial tests available (*Quantiplex HCV RNA Version 2.0*, *Cobas Ampliscreen*, *Amplicor HCV monitor Version 2.0*, and *Superquant HCV*), all are reliable but not comparable. VL has no prognostic value but is important in evaluating response to treatment.
- **Genotype:** Predicts response to treatment; genotype 1 has poor prognosis compared with 2 and 3.
- **Liver biopsy:** Gold standard for predicting prognosis, comparable to CD4 count in HIV. Main indication to treat is histologic evidence of bridging fibrosis or moderate inflammation and necrosis.

Treatment

INDICATIONS: Liver histology criteria + patient acceptance + lack of contraindications + stable HIV.

- Histologic criteria: Biopsy evidence of bridging fibrosis or inflammation and necrosis. Patients with compensated cirrhosis often benefit from therapy and should be considered for combination treatment. Patients with decompensated cirrhosis should not be treated except in controlled trials.
- Patients who are HCV treatment naïve, or who relapse after prior therapy with interferon alfa monotherapy.

CONTRAINDICATIONS: See Drug Profiles, interferon, p. 113 and ribavirin, p. 131

PATIENT ACCEPTANCE BASED ON THE FOLLOWING

- Side effects: All patients have side effects; 20% discontinue ribavirin for anemia, and 20% discontinue interferon.
- Probability of cure: 30% to 40% for HCV infected patients treated with interferon + ribavirin.
- Knowledge of natural history of HCV without treatment varies with liver biopsy results.
- Confounding of HAART due to hepatotoxicity of antiretroviral drugs.

REGIMENS: See Drug Profiles, interferon, p. 113 and ribavirin, p. 131.

- Ribavirin: Give 2x/day PO following any one of the 3 dosing schemes outlined below:
 - 10.6 mg/kg/day
 - Weight: >75 kg—600 mg; <75 kg—400 mg in A.M., 600 mg in P.M.
 - Weight: <40 kg—600 mg/day; 40–65 kg—800 mg/day; 65–85 kg—1000 mg/day; 85–105 kg—1200 mg/day; >105 kg—1400 mg/day
- Pegylated interferon
 - *Alfa 2a* (Roche): 180 µg SC qwk.
 - *Alfa 2b* (Schering): 1.5 µg/kg SC qwk.

HIV THERAPY

- Strength of recommendation to treat depends on CD4 count, VL, and HIV associated complications.
- All 14 antiretroviral drugs are potentially hepatotoxic; frequency of \uparrow ALT/AST to $>5x$ ULN is 10% independent of HCV; these drugs do not appear unusually hepatotoxic with chronic HCV, but the fluctuations in LFTs often confound treatment decisions.

Sequencing HIV and HCV Treatment**HIV TREATMENT NAÏVE + INDICATIONS FOR HCV TREATMENT**

- CD4 count >350 cells/mm³ (or 200–350 + VL $<20,000$ c/mL): Treat HCV x 24 to 48 weeks, then start HAART.
- CD4 count <200 cells/mm³ and stable: Treat both infections simultaneously but separate initiation by 1 to 2 months to avoid complications in interpreting drug toxicities.
- CD4 count <200 cells/mm³ and unstable HIV: Stabilize HIV prior to anti-HCV treatment.

HIV TREATMENT ONGOING

- Stable: Add HCV therapy.
- Unstable: Stabilize HIV first.
- HAART with drug hepatotoxicity: May consider ART interruption, initiate HCV treatment, reintroduce HAART later.

DRUG SELECTION

- HCV: Interferon \pm ribavirin.
- HIV: Consider avoiding RTV and NNRTIs (NVP + EFV) in coinfecting patients.

Pain***Principles**

- Aggressive treatment needed in late stages.
- Goal is prevention of pain.
- Addiction should not be a consideration.
- Avoid adverse effects of nausea/vomiting with antiemetic.
- Inform patient that sedation usually decreases after 3 to 5 days.

*World Health Organization (WHO) 3-step treatment model for chronic cancer pain; also found useful for late stage HIV

STEP 1: NONOPIOID ANALGESICS

- ASA 650 mg q4h–q6h
- Fenoprofen 200–400 mg qid
- Piroxicam 10 mg bid/20 mg/day
- Ibuprofen 200–400 mg qid
- Sulindac 150–200 mg bid
- Indomethacin 25–50 mg 2–4x/day
- Meclofenamate 100 mg tid/qid
- Diflunisal 500–1000 mg bid
- Mefenamic 250 mg qid
- Choline magnesium trisalicylate 500–750 mg tid
- Naproxen 250–500 mg bid, 500–750 mg bid or tid

STEP 2: WHEN STEP 1 DRUG FAILS, ADD WEAK OPIOID

- Codeine 30–65 mg q4h
- Oxycodone 5–10 mg PO q3h–q4h.
- Propoxyphene (*Darvon*) 65 mg PO q3h–q4h
- Acetaminophen with narcotic (*Empracet* with codeine; *Percocet*; *Roxicet*)
- Phenaphen with codeine; *Tylenol* with codeine; *Tylox*, *Vicodin*

STEP 3: WHEN NECESSARY, USE STRONG OPIOID, USUALLY WITH A NONOPIOID

- Morphine: immediate release 10–30 mg q4h, sustained release (MS Contin) 30 mg q8h–q12h, suppositories (*Roxanol*): 10–20 mg q6h
- Oxycodone: 10–30 mg q4h
- Oxycodone with acetaminophen or ASA: *Percocet*, *Roxicet*, *Roxiprin*, *Percodan*: 1 tab q6h
- Hydromorphone (*Dilaudid*): Tabs 2–4 mg q4h–q6h, suppositories 3 mg q6h–q8h
- Methadone: 2.5–10 mg PO q6h–q8h
- Levorphanol: 2 mg PO q4h–q6h
- Fentanyl patch (*Duragesic*): 25 mcg/hr. q72h

ADJUNCTIVE MEDICATIONS

- Hydroxyzine (*Vistaril*): 10–25 mg PO q4h–q6h
- Diazepam (*Valium*): 5–10 mg PO tid
- Baclofen: 5 mg PO tid

SEVERE PAIN

- Methadone 20 mg tid or qid
- Morphine SO₄: 10–30 mg PO q4h; 30–60 mg (long acting) PO q8h-q12 h; 4–15 mg IM or SC q4h; 10–20 mg q4h prn
- Hydromorphone (*Dilaudid*): 1–6 mg q4h-q6h PO; 2–4 mg IM q4h-q6h; SC or IV: 3 mg q6h-q8h prn
- Fentanyl patch: 25–100 mcg/hr
- Narcotic equivalence: Morphine SO₄ 10 mg IM

■ TABLE 9-3: Equivalence of Opiate Doses

Drug	Oral	IM
Morphine	30–60 mg	10 mg
Codeine	200 mg	—
Heroin	60 mg	5 mg
Meperidine	300 mg	75 mg
Methadone	20 mg	—
Oxycodone	15–30 mg	—
Fentanyl	—	0.1–0.2 mg

■ TABLE 9-4: Equivalence of Fentanyl Patches

Oral MS (mg)	Fentanyl (pg/hr.)	Oral MS (mg)	Fentanyl (pg/hr.)
45–134	25	495–584	150
135–224	50	675–764	200
225–314	75	855–994	250
315–404	100	1035–1124	300

STDs**Special Considerations in HIV-infected Patients**

- Development of a new STD in an HIV infected patient signals the need for additional patient counseling to prevent further spread of both HIV and the STD at hand. Development of an ulcerative STD carries an increased risk of HIV transmission.
- Some STDs (esp. syphilis) in HIV-infected patients may require more careful and extensive management and follow-up than in patients who are not infected with HIV.

Additional Information

The information presented here does not address all STDs that may be encountered by the provider nor does it address all presentation or diagnostic contingencies. Please consult the following for additional information and guidance:

- CDC Guidelines for the Treatment of Sexually Transmitted Diseases: Available on the CDC web site at <http://www.cdc.gov/nchstp/dstd/dstdp.html>
- 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 (PTCs): Check the web site: <http://depts.washington.edu/nnptc/> for a list of the PTCs.

Co-Morbidities: STDs ■ TABLE 9-5: STD Identification and Treatment*

Condition	Identification/Screening	Diagnosis	Treatment
Urethritis	<ul style="list-style-type: none"> ■ Patient self-report Sx ■ Review Hx at follow-up visits, including contact with other case. 	<ul style="list-style-type: none"> ■ Confirm urethritis and test for gonorrhea and chlamydia. 	<ul style="list-style-type: none"> ■ For non-gonococcal urethritis treat for chlamydia.
Gonorrhea	<ul style="list-style-type: none"> ■ Patient self-report Sx ■ Review Hx at follow-up visits, including contact with other case. 	<ul style="list-style-type: none"> ■ Gram stain and/or culture (or other specific test). 	<p>Urethral, endocervical, rectal:</p> <ul style="list-style-type: none"> ■ Ceftriaxone 125 mg IM x 1 (also for pharyngeal); ciprofloxacin[†] 500 mg PO x 1 (also for pharyngeal); cefixime 400 mg PO x 1; ofloxacin[†] 400 mg PO x 1; or ■ Levofloxacin 250 mg PO x 1 plus Azithromycin 1 gm PO x 1 or doxycycline[†] 100 mg PO bid x 7 days <p>Disseminated GC:</p> <ul style="list-style-type: none"> ■ Ceftriaxone 1 gm/day IV or IM ■ Alternatives: Cefotaxime 1 gm IV q8h; ceftizoxime 1 gm IV q8h or β lactam allergic: ciprofloxacin 400 mg IV q12h or ofloxacin 400 mg IV q12h, spectinomycin 2 gm IM q12h <p>Duration: Parenteral Rx until 24 to 48 hrs. after Sx resolve, then cefixime 400 mg PO bid or ciprofloxacin[†] 500 mg PO bid to complete >1 wk. treatment</p>
Chlamydia	<ul style="list-style-type: none"> ■ Patient self-report Sx ■ Review Hx at follow-up visits, including contact with other cases. ■ Routinely screen^{††} women if sexually active and <25 yrs., any age with >1 partner, and/or Hx of STD 	<ul style="list-style-type: none"> ■ Culture (or other specific test) 	<ul style="list-style-type: none"> ■ Azithromycin 1 gm PO x 1 or idoxycycline[†] 100 mg PO bid x 7 days

Condition	Identification/Screening	Diagnosis	Treatment
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) + FTA-ABS ■ Darkfield exam or DFA of lesion material or exudates. 	<ul style="list-style-type: none"> ■ See table: "Management of Syphilis," below
HSV	<ul style="list-style-type: none"> ■ Patient self-report Sx ■ Review Hx at follow-up visits 	<ul style="list-style-type: none"> ■ Virologic tests: Culture, DFA ■ Type Specific Serologic Test: Accurate type-specific assays for HSV antibodies must be based on the HSV-specific glycoprotein G-2 for Dx of HSV-2 and glycoprotein G-1 for Dx of HSV-1. 	<p>Episodic Therapy of Recurring Infection:</p> <ul style="list-style-type: none"> ■ Genital: Acyclovir 200 mg PO 5x/day or 400 mg PO tid; famciclovir 250 mg PO tid; or valacyclovir 1 gm PO bid. Give for 5 to 10 days. ■ Suppression: Acyclovir 400-800 mg PO bid or tid, famciclovir 250 mg PO tid; valacyclovir 500 mg PO bid.

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

†Tetracycline, fluoroquinolones contraindicated in pregnancy.

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

Co-Morbidities: STDs ■ TABLE 9-6: Management of Syphilis*

Form	Treatment	LP†	Follow-up VDRL/RPR	Expectation—VDRL/RPR	Indications to Re-treat
Primary syphilis (Chancre)	<ul style="list-style-type: none"> ■ Initial: Benzathine penicillin (pen) 2.4 mil units IM x 1 ■ Pen Allergic: Doxycycline 100 mg PO bid x 14 days ■ Re-treatment: Benzathine pen 2.4 mil units IM x 3 (weekly) 	<ul style="list-style-type: none"> ■ Neuro Sx ■ Treatment failure 	<ul style="list-style-type: none"> ■ HIV: 3, 6, 9, 12, & 24 mos. 	<ul style="list-style-type: none"> ■ Four-fold decrease at 6 mos. 	<ul style="list-style-type: none"> ■ Titer increases 4-fold and CSF negative ■ Titer fails to decrease 4-fold at 6 to 12 mos. and CSF negative. ■ Symptoms persist or recur
Secondary syphilis (Rash)	<ul style="list-style-type: none"> ■ Initial: Benzathine pen 2.4 mil units IM x 1 ■ Pen Allergic: Doxycycline 100 mg PO bid x 14 days ■ Re-treatment: Benzathine pen 2.4 mil units IM x 3 (weekly) 	<ul style="list-style-type: none"> ■ Neuro Sx ■ Treatment failure 	<ul style="list-style-type: none"> ■ HIV: 3, 6, 9, 12, & 24 mos. 	<ul style="list-style-type: none"> ■ Four-fold decrease at 6 mos. 	<ul style="list-style-type: none"> ■ Titer increases 4-fold and CSF negative. ■ Titer fails to decrease 4-fold at 6 to 12 mos. and CSF negative. ■ Sx persist or recur
Early latent (<1 yr.)	<ul style="list-style-type: none"> ■ Initial: Benzathine pen 2.4 mil units IM x 1 ■ Pen Allergic: Doxycycline 100 mg PO bid x 14 days ■ Re-treatment or HIV infection: Benzathine pen 2.4 mil units IM x 3 (weekly) 	<ul style="list-style-type: none"> ■ Neuro Sx ■ Treatment failure 	<ul style="list-style-type: none"> ■ 6, 12, 18, & 24 mos. 	<ul style="list-style-type: none"> ■ Four-fold at 12 to 24 mos. 	<ul style="list-style-type: none"> ■ Titer increases 4-fold ■ Titer of > 1:32 fails to decrease four-fold at 12 to 24 mos. ■ Develops signs or symptoms of syphilis
Late latent (>1 yr. or unknown duration)	<ul style="list-style-type: none"> ■ Benzathine pen 2.4 mil units IM x 3 (weekly) ■ Pen allergic: Doxycycline 100 mg PO bid x 28 days 	<ul style="list-style-type: none"> ■ Indicated before treatment or retreatment 	<ul style="list-style-type: none"> ■ 6, 12, 18, & 24 mos. 	<ul style="list-style-type: none"> ■ Four-fold decrease in titer at 12 to 24 mos. (lower initial titers may remain unchanged) 	<ul style="list-style-type: none"> ■ Titer fails to decrease 4-fold at 12 to 24 mos. ■ Increase titer by 4-fold at any time after 3 mos.

Form	Treatment	LP†	Follow-up VDRL/RPR	Expectation— VDRL/RPR	Indications to Re-treat
Late syphilis (tertiary, not neurosyphilis)	<ul style="list-style-type: none"> ■ Benzathine pen 2.4 mil units IM x 3 (weekly) 	<ul style="list-style-type: none"> ■ Indicated 	<ul style="list-style-type: none"> ■ 6, 12, 18, & 24 mos. 	<ul style="list-style-type: none"> ■ As above ■ Granulomatous lesions should heal 	<ul style="list-style-type: none"> ■ As above ■ Documentation of T. pallidum or other histologic feature of late syphilis.
Neurosyphilis (or ocular syphilis)	<ul style="list-style-type: none"> ■ Aq pen G 18–24 mil units/day x 10 to 14 days administered as 3–4 mil units IV q4h ■ Pen Allergic: Desensitize or Ceftriaxone 2 g/day IM or IV x 10 to 14 days ■ Some experts recommend benzathine pen 2.4 mil units IM after completion of IV course. 	<ul style="list-style-type: none"> ■ Required 	<ul style="list-style-type: none"> ■ Every 6 mos. 	<ul style="list-style-type: none"> ■ CSF WBC decrease at 6 mos. and CSF normal at 2 yrs. 	<ul style="list-style-type: none"> ■ CSF WBC fails to decrease at 6 mos. or CSF still abnormal at 2 yrs. ■ Persisting signs and Sx. ■ Consider if 4-fold increase in CSF VDRL at >6 mos.

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

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

9 Co-Morbidities: STDs

10 | Management of Complications of HIV Infection

■ TABLE 10-1: Management of Opportunistic Infections

Pathogen or Disease	Treatment	Alternative
Aspergillosis (invasive)	<ul style="list-style-type: none"> ■ Amphotericin B 0.7–1.4 mg/kg/day IV <i>or</i> ■ Lipid formulations: <i>Abelcet</i> 5 mg/kg/day, <i>Amphotec</i> 4–6 mg/kg/day <i>or</i> ■ <i>AmBisome</i> 5 mg/kg/day IV 	<ul style="list-style-type: none"> ■ Itraconazole 200 mg PO tid x 3 days then 400 mg/day* ■ Caspofungin 70 mg IV day, then 50 mg IV/day
<i>Bartonella</i>	<ul style="list-style-type: none"> ■ Erythromycin 500 mg PO qid ■ Doxycycline 100 mg PO bid x >3 wks. 	<ul style="list-style-type: none"> ■ Azithromycin 0.5–1 gm PO/day x 1 to 3 mos. ■ Erythromycin or doxycycline + RIF 300 mg PO bid
<i>C. difficile</i>	<ul style="list-style-type: none"> ■ Metronidazole 250 mg PO qid x 10 days 	<ul style="list-style-type: none"> ■ Vancomycin 125 mg PO qid x 10 days
<i>Candida</i>	<p>Thrush</p> <ul style="list-style-type: none"> ■ Clotrimazole troches 10 mg 5x/day x 14 days ■ Nystatin 500,000/mL units susp. 5 mL gargled or 200,000 units pastilles to suck 4–5x/day x 14 days ■ Misc: HAART, d/c steroids, d/c antibiotics <p>Vaginitis</p> <ul style="list-style-type: none"> ■ Intravaginal: Miconazole 200 mg suppository/day x 3 days; clotrimazole 100 mg tab vaginal bid x 3 days or qd x 7 days; clotrimazole 1% cream or miconazole 2% cream qd x 7 days ■ Fluconazole 150 mg PO x 1 <p>Esophagitis</p> <ul style="list-style-type: none"> ■ Fluconazole 200 mg/day up to 400 mg/day x 2 to 3 wks. then maintenance with fluconazole 100–200 mg/day (maintenance optional due to resistance concern) 	<ul style="list-style-type: none"> ■ Fluconazole 50–100 mg PO/day x 14 days ■ Amphotericin B 4x/day swish and swallow (100 mg/mL) ■ Itraconazole 100 mg/day liquid solution to gargle* ■ Ketoconazole 200 mg PO/day x 7 days or bid x 3 days ■ Ketoconazole 200–400 mg PO bid x 2 to 3 wks. + maintenance 200 mg/day ■ Itraconazole 200 mg PO* x 2 to 3 wks. + maintenance ■ Amphotericin B 0.3–0.5 mg/kg/day IV

■ TABLE 10-1: Management of Opportunistic Infections—Continued

Pathogen or Disease	Treatment	Alternative
Cytomegalovirus	<p>Gastrointestinal</p> <ul style="list-style-type: none"> ■ Ganciclovir 5 mg/kg IV bid x 2 to 3 wks., then either ganciclovir IV 5 mg/kg/day or valganciclovir 900 mg PO with meals bid x 3 wks then 900 mg PO/day meals ■ Foscarnet IV 90 mg/kg q12h x 3 wks., then IV 90 mg/kg/day <p>Retinitis (<i>Arch Intern Med</i> 1998; 158:957)</p> <ul style="list-style-type: none"> ■ Intraocular ganciclovir device + oral valganciclovir 900 mg PO bid with meal x 3 wks. then 900 mg/day ■ Ganciclovir 5 mg/kg IV q12h x 14 to 21 days, then 5 mg/kg IV, 5 to 7 days/wk. ■ Foscarnet 90 mg/kg IV q12h x 14 to 21 days, then IV 90–120 mg/kg/day <p>Neurologic</p> <ul style="list-style-type: none"> ■ Ganciclovir and/or foscarnet (above doses) (Combination is possibly superior, but poor quality of life) 	<ul style="list-style-type: none"> ■ Cidofovir: see CMV retinitis (below) ■ Cidofovir 5 mg/kg/wk. IV x 2, then 5 mg/kg every 2 wks.; each dose with probenecid 2 gm PO 3 hrs. before each dose and 1 gm at 2 & 8 hrs. after. ■ Fomivirsen 330 mg intravitreal injection days 1 & 15, then monthly + valganciclovir.
Coccidioidomycosis	<ul style="list-style-type: none"> ■ Amphotericin B 1.0 mg/kg/day IV x 14 days then maintenance fluconazole or itraconazole 400 mg PO/day ■ Fluconazole 400 mg PO/day 	<ul style="list-style-type: none"> ■ Itraconazole 200 mg PO bid*
Cryptococcosis	<p>Meningitis</p> <ul style="list-style-type: none"> ■ Amphotericin B 0.7–1.0 mg/kg/day + 5-FC 25 mg/kg PO qid x 14 days, then fluconazole 400 mg/day x 8 wks., then 200 mg/day ■ CSF pressure: OP >250 mm H₂O—drain until ½ initial pressure or <200; repeat daily until <200 mm H₂O 	<ul style="list-style-type: none"> ■ Fluconazole 400–800 mg/day PO + 5-FC 25 mg/kg PO qid x 6 to 10 wks., then fluconazole 200 mg/day ■ <i>AmBisome</i> 4 mg/kg/day IV + 5-FC 25 mg PO qid x 10 days, then, fluconazole 400 mg/day x 8 wks., then 200 mg/day ■ Refractory cases: Intrathecal Amphotericin B ■ Alternative for maintenance: Itraconazole 200 mg/day* or Amphotericin B 0.6–1 mg/kg IV 1–2x/wk.

■ TABLE 10-1: Management of Opportunistic Infections—Continued

Pathogen or Disease	Treatment	Alternative
Cryptosporidiosis [IDSA: <i>Clin Inf Dis</i> 2001;32:331]	<p>Non-meningeal (Neg LP)</p> <ul style="list-style-type: none"> ■ Fluconazole 200–400 mg/day PO ■ Paromomycin 500 mg PO tid with food x 14 to 28 days <i>or</i> ■ Paromomycin 1 gm PO bid with food + azithromycin 600 mg PO/day x 4 wks., then paromomycin alone x >8 wks. ■ Misc: HAART, antiperistaltic (<i>Lomotil</i>, <i>Loperamide</i>, paretoric), food supplements 	<ul style="list-style-type: none"> ■ Itraconazole 200 mg PO bid* ■ Atovaquone 750 mg bid with food
Herpes simplex	<p>Initial: Mild and Moderately ill</p> <ul style="list-style-type: none"> ■ Acyclovir 400 mg PO tid or famciclovir 250 mg PO tid or valacyclovir 1 gm PO bid, all 7 to 10 days <p>Prophylaxis</p> <ul style="list-style-type: none"> ■ Acyclovir 400 mg PO bid ■ Famciclovir 250–500 mg PO bid ■ Valacyclovir 500 mg PO bid <p>Recurrent</p> <ul style="list-style-type: none"> ■ Acyclovir 400 mg PO tid or 800 mg PO bid x 5 days ■ Famciclovir 500 mg PO bid x 5 days ■ Valacyclovir 500 mg PO bid x 5 days <p>Severe or Refractory</p> <ul style="list-style-type: none"> ■ Acyclovir 15–30 mg/kg/day IV x >7 days ■ Valacyclovir 1 gm PO bid ■ Acyclovir resistance: Foscarnet 60 mg/kg IV q12h x 3 <p>Visceral</p> <ul style="list-style-type: none"> ■ Acyclovir 30 mg/kg/day IV x 14 to 21 days 	<ul style="list-style-type: none"> ■ Foscarnet 60 mg/kg q12h x 3 wks. ■ Cidofovir 5 mg/kg IV q2 wks. + probenecid ■ Topical trifluridine (1% ophthalmic solution) q8h ■ Topical cidofovir 3% gel q8h ■ Foscarnet 60 mg/kg IV q8h x >10 days ■ Valacyclovir 1.0 gm PO tid
Histoplasmosis	<ul style="list-style-type: none"> ■ Amphotericin B 0.7–1.0 mg/kg/day x 3 to 14 days, then itraconazole 200 mg PO bid* 	<ul style="list-style-type: none"> ■ Amphotericin B induction, then maintenance with fluconazole 800 mg/day PO or Amphotericin B 1 mg/kg/wk. IV ■ <i>AmBisome</i> 3 mg/kg/day IV

■ TABLE 10-1: Management of Opportunistic Infections—Continued

Pathogen or Disease	Treatment	Alternative
<i>Isospora</i>	<ul style="list-style-type: none"> ■ TMP-SMX 2 DS PO bid or 1 DS tid x 2 to 4 wks. + maintenance TMP-SMX 1–2 DS/day PO 	<ul style="list-style-type: none"> ■ Pyrimethamine 50–75 mg/day PO + folinic acid 5–10 mg/day x 1 mo. + maintenance pyrimethamine 25 mg + folinic acid 5 mg/day
Microsporidia	<ul style="list-style-type: none"> ■ Albendazole 400–800 mg Amphotericin PO bid x >3 wks. (<i>S. intestinalis</i> only) ■ Misc: HAART, nutritional supplements, antiperistaltic agents (<i>Lomotil</i>, <i>Imodium</i>, paregoric, etc.) 	<ul style="list-style-type: none"> ■ Metronidazole 500 mg PO tid ■ Atovaquone 750 mg PO bid with meals ■ Thalidomide 100 mg PO/day
<i>Mycobacterium avium</i>	<ul style="list-style-type: none"> ■ Clarithromycin 500 mg PO bid + EMB 15 mg/kg/day ■ Azithromycin 600 mg/day + EMB 15 mg/kg/day +/- RBT 300 mg/day; adjust RBT dose for concurrent PI (see Table 9–2, p. 60). 	<ul style="list-style-type: none"> ■ Clarithromycin or azithromycin + EMB + amikacin 15 mg/kg/day or ciprofloxacin 500–750 mg bid
<i>Mycobacterium kansasii</i>	<ul style="list-style-type: none"> ■ INH 300 mg PO/day + RIF 600 mg/day (or RBT) + EMB 15–25 mg/kg/day >18 mos. 	<ul style="list-style-type: none"> ■ Regimen with ciprofloxacin 750 mg bid and/or clarithromycin 500 mg bid
<i>Mycobacterium tuberculosis</i>	<ul style="list-style-type: none"> ■ See HIV Co-Morbidities, Tuberculosis, p. 59. 	
<i>Nocardia</i>	<ul style="list-style-type: none"> ■ TMP-SMX 10–15 mg/kg/day (TMP) PO or IV x 3 to 6 wks., then 5–10 mg/kg/day to complete >6 mos. ■ Sulfadiazine 6–12 gm/day PO 	<ul style="list-style-type: none"> ■ Amikacin 10–15 mg/kg/day ■ Imipenem or meropenem 1 gm q6–8h ■ Ceftriaxone, cefuroxime or cefotaxime, or one of these + imipenem or amikacin ■ Minocycline 100–200 mg bid ■ Amoxicillin-clavulanate 875 mg tid
<i>P. carinii</i> pneumonia	<ul style="list-style-type: none"> ■ TMP-SMX 15 mg/kg/day (trimethoprim) PO or IV x 21 days + PO₂ <70 mm Hg or A-a gradient >35 mm Hg; prednisone 40 mg bid x 5 days, then 40 mg/day x 5 days, then 20 mg/day to completion of Rx. 	<ul style="list-style-type: none"> ■ TMP 15 mg/kg/day PO + dapsone 100 mg/day x 21 days ■ Pentamidine 4 mg/kg/day IV x 21 days ■ Clindamycin 600 mg IV q8h or 300–450 mg PO q6h + primaquine 15–30 mg base/day x 21 days ■ Atovaquone 750 mg PO bid with meal x 21 days

■ TABLE 10-1: Management of Opportunistic Infections—Continued

Pathogen or Disease	Treatment	Alternative
PML	<ul style="list-style-type: none"> ■ HAART 	<ul style="list-style-type: none"> ■ Interferon alpha 3 MU/day IV
<i>Rhodococcus equi</i>	<ul style="list-style-type: none"> ■ Vancomycin 1 gm IV bid + RIF 300 mg bid ■ Imipenem 0.5 gm IV q6h + RIF 300 mg bid ■ Ciprofloxacin 750 mg PO/IV q 12 h 	
<i>Salmonella</i> (IDSA: <i>Clin Infect Dis</i> 2001;32:331)	<p>Need <i>in vitro</i> susceptibility tests</p> <ul style="list-style-type: none"> ■ Ciprofloxacin 500 mg PO/400 mg IV bid x >14 days ■ TMP-SMX 1 DS bid x 5 to 7 days x >14 days ■ Ceftriaxone 2 gm/day IV x 2001;32:331)>14 days 	
<i>Staph aureus</i>	<p>Methicillin sensitive: Oxacillin/Nafcillin, Cefazolin, Cephalexin, dicloxacillin</p>	<ul style="list-style-type: none"> ■ Clindamycin, fluoroquinolone, TMP-SMX
Folliculitis	<p>Methicillin resistant: Vancomycin</p> <ul style="list-style-type: none"> ■ Cephalexin or dicloxacillin 500 mg PO qid x 7 to 21 days 	<ul style="list-style-type: none"> ■ Linezolid (not endocarditis) ■ Add RIF 600 mg/day if severe or refractory
Endocarditis	<ul style="list-style-type: none"> ■ MSSA: Naf/ox 2 gm IV q4h x 4 to 6 wks. + gent 1 mg/kg IV q8h x 3 to 5 days ■ Tricuspid valve: Naf/ox 2 gm IV q4h x 2 to 4 wks. + gent 1 mg/kg ■ Pen allergy or MRSA: Vancomycin 1 gm IV q12h x 4 wks. 	<ul style="list-style-type: none"> ■ Cefazolin IV 2 gm q8h x 4 to 6 wks. + gent IV 1 mg/kg q8h x 3 to 5 days ■ Ciprofloxacin 750 mg PO bid + RIF 300 mg PO bid x 4 wks.
<i>Strep pneumoniae</i>	<ul style="list-style-type: none"> ■ Cefotaxime 2 gm IV q6h ■ Ceftriaxone 2 gm/day IV ■ Amoxicillin 750 mg PO tid ■ Fluoroquinolone: Levofloxacin 500 mg PO/IV qd; gatifloxacin 400 mg PO/IV qd; moxifloxacin 400 mg PO/day 	<ul style="list-style-type: none"> ■ Macrolide (azithromycin, clarithromycin, erythromycin) ■ Vancomycin
Toxoplasmosis	<ul style="list-style-type: none"> ■ Pyrimethamine 100 mg, then 50–100 mg/day PO + folinic acid 10 mg/day + sulfadiazine 4–8 gm/day x >6 wks., then maintenance pyrimethamine 25–50 mg/day PO + folinic acid 10–25 mg/day + sulfadiazine 5–1 gm PO aid 	<ul style="list-style-type: none"> ■ Pyrimethamine + folinic acid (see preferred regimen) + clindamycin 900–1200 mg IV q6h or PO 300–450 mg q6h ■ Pyrimethamine + folinic acid (see preferred regimen) + azithromycin 1200 mg/day PO or clarithromycin 1 am PO bid or atovaquone 750 mg PO qid with food

■ TABLE 10-1: Management of Opportunistic Infections—Continued

Pathogen or Disease	Treatment	Alternative
Toxoplasmosis (cont'd)		<ul style="list-style-type: none"> ■ Maintenance doses: Clindamycin 300–450 mg PO qid, atovaquone 750 mg 2–3x/day, azithromycin 600 mg/day clarithromycin 500 mg bid
Varicella Zoster (VZV)	<p>Dermatomal</p> <ul style="list-style-type: none"> ■ Valacyclovir 1 gm PO tid >7 days ■ Famciclovir 500 mg PO tid >7 days <p>Disseminated, Visceral or Ophthalmic Nerve</p> <ul style="list-style-type: none"> ■ Acyclovir 30–36 mg/kg/day IV >7 days 	<ul style="list-style-type: none"> ■ Acyclovir 800 mg PO 5x/day x >7 days ■ Acyclovir 30 mg/kg/day IV ■ Foscarnet 60 mg/kg/day IV (acyclovir resistant) ■ Foscarnet 60 mg/kg/day IV (acyclovir resistant)

*Itraconazole: Oral solution should be taken on empty stomach; capsule form should be taken with meal. Gastric acid is necessary for absorption of caps—avoid concurrent H₂ blockers, antacids, omeprazole, sucralfate, buffered ddi; may need concurrent acidic drink such as cola or orange juice, etc.

■ TABLE 10-2: Non-Infectious and Miscellaneous Infectious Complications

Condition	Treatment
Cardiac	
Cardiomyopathy	<ul style="list-style-type: none"> ■ Ace inhibitors, enalapril 2.5 mg bid titrated to 20 mg/day or captopril 8.25 mg tid titrated to 20–50 mg tid ± diuretics ± digoxin ■ HAART
Pericardial disease	<ul style="list-style-type: none"> ■ Pericardiocentesis or biopsy—major causes: Bacterial, MAC, TB, cryptococcosis, CMV, treat microbial cause
Pulmonary	
Lymphoid interstitial pneumonia	<ul style="list-style-type: none"> ■ HAART, prednisone
Pneumothorax	<ul style="list-style-type: none"> ■ PCP is usual cause ■ Manage with tube thoracostomy ± pleurodesis ■ ± Rx for PCP
Renal	
HIV-associated nephropathy (HIVAN)	<ul style="list-style-type: none"> ■ HAART ■ Hemodialysis ■ ACE inhibitors: Captopril 6.25 titrated up to 25 mg PO tid ■ Prednisone: 60 mg/day x 2 to 11 wks., taper to 10 mg/day

■ TABLE 10-2: Complications—Continued

Condition	Treatment
Neurologic	
Peripheral neuropathy	<p>Usual Treatment</p> <ul style="list-style-type: none"> ■ d/c d4T, ddl, and/or ddc ■ Nortriptyline 10 mg, increase by 10 mg/day q 5 days to max. 75 mg/day ■ Gabapentin 300–1000 mg PO tid ■ Ibuprofen 600–800 mg tid ■ Topical capsaicin ointments (<i>Zostrix</i>) or lidocaine 20% to 30% ointment ■ Lamotrigine (<i>Lamictal</i>) 25 mg PO/day increased to 300 mg/day over 6 wks. <p>Alternative Treatments: Phenytoin 200–400/day or carbamazepine 200–400 mg PO bid</p> <p>Severe Pain: Methadone, up to 20 mg qid or Fentanyl patch 25–100/hr. (2.5–10 mg/cm² x q 3 days)</p>
Myopathy	<ul style="list-style-type: none"> ■ d/c AZT ■ For inflammatory myopathy: Prednisone 40–60 mg/day
HIV-associated dementia	<ul style="list-style-type: none"> ■ HAART ■ Selegiline 5 mg bid or 10 mg
Hematologic	
Idiopathic Thrombocytopenia	<p>Asymptomatic</p> <ul style="list-style-type: none"> ■ HAART ■ Discontinue any contributing drugs <p>Hemorrhage: Packed red blood cells/platelets + prednisone 60–100 mg/day or IVIG 1 g/kg days 1, 2, 14 then q 2 to 3 wks.</p> <p>Persistent and Symptomatic</p> <ul style="list-style-type: none"> ■ HAART ■ Discontinue contributing agents ■ Prednisone 30–60 mg/day with rapid taper to 5–10 mg/day ■ IVIG 400 mg/kg, days 1, 2, & 14, then q 2 to 3 wks.
Anemia	<p>HIV: HAART</p> <p>Address Cause: Marrow infiltrating tumor (lymphoma, KS); infection (MAC, TB, CMV, parvovirus B19, fungi, esp. <i>Histoplasma</i>), drugs (AZT, amphotericin, ganciclovir, pyrimethamine, dapsone, ribavirin, interferon), anemia of chronic disease; deficiency state (Fe, folic acid, B12), HIV inhibition of precursors.</p> <p>AZT: d/c AZT or add EPO if EPO levels <500 μ/mL (EPO - Rx if hematocrit is <33%). Start with 40,000 units SC/wk. and titrate down.</p>
Neutropenia	<p>Address Cause: AZT, ganciclovir, foscarnet, ribavirin, 5-FC, and ganciclovir.</p>

■ TABLE 10-2: Complications—Continued

Condition	Treatment
Neutropenia	AZT: d/c AZT and/or add G-CSF. G-CSF 5 µg/kg/day SC: usually 1 µg/kg/day with increase of 1 µg/kg/day at 5 to 7 day intervals to maintain ANC > 1000/mm ³ .
Tumors	
Kaposi's sarcoma	HAART Local therapy <ul style="list-style-type: none"> ■ Topical liquid nitrogen ■ Intra-lesional vinblastine, (0.010–0.002 mg/lesion q 2 wks. x 3) ■ Radiation or laser Systemic: Widespread skin involvement with >25 lesions; failure of local Rx, and/or symptomatic visceral organ involvement. <ul style="list-style-type: none"> ■ Liposomal daunorubicin (<i>DaunoXome</i>) ■ <i>Taxol</i> (100–500 mg/M²) ■ <i>Adriamycin</i>, bleomycin + either vincristine or vinblastine ■ Vincristine/vinblastine ■ Bleomycin/vinca alkaloids
Non-Hodgkin's Lymphoma	<ul style="list-style-type: none"> ■ EPOCH (<i>JAMA</i> 2001;285:1882): Etoposide, vincristine, and doxorubicin + cyclophosphamide + prednisone ■ Various combinations of methotrexate, bleomycin, doxorubicin, cyclophosphamide, adriamycin, vincristine, corticosteroids ± cranial radiation ■ CHOP & BACOD + GM-CSF
CNS Lymphoma	<ul style="list-style-type: none"> ■ Cranial radiation + high dose corticosteroids ± chemotherapy
Castleman disease	<ul style="list-style-type: none"> ■ Interferon alfa 5 x 10⁶ units 3 x weekly (1 case report: <i>Clin Infect Dis</i> 2000;31:602)
Dermatologic	
Bacillary angiomatosis	<ul style="list-style-type: none"> ■ See <i>Bartonella</i>, Table 10-1, p. 73
Dermatophytic fungi	<ul style="list-style-type: none"> ■ Topical miconazole or clotrimazole ■ Refractory: Ketoconazole 200 mg PO/day x 1 to 3 mos. or itraconazole 100 mg/day x 1 to 3 mos. ■ Nails: Terbinafine 250 mg PO/day x 6 wks. (fingernails) or 12 wks. (toenails) or itraconazole 200 mg PO bid 1 wk./mo. x 2 (fingernails) or x 3 to 4 mos. (toenails) FDA warning regarding hepatotoxicity with terbinafine and itraconazole for triviral infection, check pre-treatment LFTs; itraconazole may have negative inotropic effect as well.
Eosinophilic folliculitis	<ul style="list-style-type: none"> ■ Astemizole 10 mg/day + topical steroids ■ Ultraviolet light ■ Antihistamine (first generation-sedating antihistamines)

■ TABLE 10-2: Complications—Continued

Condition	Treatment
<i>Molluscum contagiosum</i>	<ul style="list-style-type: none"> ■ HAART, cryotherapy, electrosurgery, curettage, topical cantharidin, or cidofovir
Scabies	<ul style="list-style-type: none"> ■ Permethrin cream 5% x 12 hrs.; Repeat 3 to 7 days later (must apply to all skin surfaces); ■ Topical lindane: Apply to all surfaces but face ■ Ivermectin 200 mcg/kg x 1
Seborrhea	<ul style="list-style-type: none"> ■ Steroid cream (hydrocortisone 1%) ± precipitated sulfur (desonide cream) or topical ketoconazole bid ■ Scalp-shampoo with selenium sulfide, zinc pyrithione, salicylic acid, coal tar applied daily or ketoconazole shampoo
<i>Staph. folliculitis</i>	<ul style="list-style-type: none"> ■ Cephalexin or dicloxacillin 500 mg PO qid x 7 to 21 days
Gastrointestinal	
Anorexia	<ul style="list-style-type: none"> ■ d/c meds that could be responsible ■ Megesterol 400–800 mg/day or dronabinol (<i>Marinol</i>) 2.5–5.0 mg bid
Nausea/vomiting	<ul style="list-style-type: none"> ■ <i>Compazine</i> 5–10 mg PO q6h–q8 h ■ <i>Tigan</i> 250 mg PO q6h–q8 h ■ <i>Dramamine</i> 50 mg PO q6h–q8h ■ <i>Ativan</i> 0.025–0.05 mg/kg IV or IM ■ Haloperidol 1–5 mg PO bid or IM bid ■ Ondansetron (<i>Zofran</i>) – 0.2 mg/kg IM, IV, or PO bid or tid ■ Dronabinol (<i>Marinol</i>) 2.5–10 mg bid
Pancreatitis	<ul style="list-style-type: none"> ■ d/c implicated drugs (esp. ddi ± d4T or HU; others – pentamidine, sulfonamides, steroids, PIs with ↑ triglycerides) ■ Deal with non-drug causes: ETOH, high triglycerides (level dependent risk), ERCP, cholelithiasis, morbid obesity ■ Rx infections: MAC, TB, toxoplasmosis, cryptosporidia ■ There is no good medical or surgical treatment of pancreatitis <i>per se</i>
Oral and Esophageal Lesions	
Aphthous ulcers	<p>Standard</p> <ul style="list-style-type: none"> ■ Topical fluocinonide (<i>Lidex</i>) 0.05% ointment mixed 1:1 with Orabase to facilitate application ■ Mouth washes with dexamethasone (0.5 mg/mL), <i>Dyclone</i> (10%), <i>Benadryl</i> or viscous lidocaine (2%) (Mile's solution) ■ Prednisone 40 mg/day PO x 1 to 2 wks., then taper (severe cases) or <i>Decadron</i> 0.5 mg/5 mL elixir rinse 1–3x/day

■ TABLE 10-2: Complications—Continued

Condition	Treatment
	<p>Refractory</p> <ul style="list-style-type: none"> ■ Thalidomide 200 mg PO/day x 4 to 6 wks., then 100 mg 2x/wk. ■ Colchicine 1.5 mg/day
Oral hairy leukoplakia	<ul style="list-style-type: none"> ■ Usually not treated ■ Acyclovir 800 mg PO 5x/day x 2 to 3 wks., then 1.2–2 gm/day (famciclovir, valacyclovir, valganciclovir, foscarnet and ganciclovir should be effective) ■ Tretinoin (<i>Retin A</i>) 0.025–0.05% solution applied 2–3x/day
Salivary gland enlargement	<ul style="list-style-type: none"> ■ Xerostomia: Sugarless gum + artificial saliva ± pilocarpine for refractory cases ■ Painful, disfiguring lesions: Needle aspiration.
Gingivitis/periodontitis	<ul style="list-style-type: none"> ■ Dental curettage and debridement + topical antiseptic, i.e., <i>Povidine</i>, iodine solution, or chlorhexidine (<i>Peridex</i>) mouth rinses ■ Metronidazole 250 mg PO tid or 500 mg PO bid x 7 to 14 days or clindamycin 300 mg tid.
Esophagitis	<p>Candida: Fluconazole, see Table 10-1, p. 73 CMV: Ganciclovir, see Table 10-1, p. 74 HSV: IV Acyclovir, see Table 10-1, p. 75 Aphthous: Prednisone 40 mg/day x 2 wks. then taper slowly or thalidomide 200 mg/day</p>
Diarrhea (<i>Clin Infect Disease</i> 2001;32:331)	
Microbial Agent Specific	<p>Cryptosporidiosis: Paromomycin + atovaquone, see Table 10-1, p. 75 Isospora: TMP-SMX, see Table 10-1, p. 76 Microsporidia: Albendazole (<i>septata intestinalis</i> only), see Table 10-1, p. 76 Salmonella: Need <i>in vitro</i> susceptibility tests; ciprofloxacin 500 mg PO bid x >14 days; TMP-SMX 1 DS bid x >14 days; cefotaxime 4–8 g/day IV Shigella: TMP-SMX 1 DS bid x 3 days; ciprofloxacin 500 mg PO bid x 3 days Aeromonas: TMP-SMX 1 DS bid x 3 days; ciprofloxacin 500 mg PO bid x 3 days E. coli (Traveler's diarrhea): ciprofloxacin 500 mg PO bid x 3 days or TMP-SMX 1 DS tid x 3 days E. coli 0157 (enterohemorrhagic) <i>E. coli</i> with bloody diarrhea and no fever. Must avoid antibiotics. C. jejuni: Erythromycin 500 mg PO bid x 5 days C. difficile: d/c implicated antibiotic; metronidazole 250 mg PO qid or 500 mg tid x 10 days or vancomycin 125 mg PO qid x 10 days E. histolytica: Metronidazole 750 mg IV or PO x 5 to 10 days + paromomycin 500 mg PO tid x 7 days</p>

■ TABLE 10-2: Complications—Continued

Condition	Treatment
Protease Inhibitor	<p>Giardia: Metronidazole 250–750 mg PO tid x 7 to 10 days</p> <p>Most likely: NFV, LPV, buffered ddl; some routinely prescribe <i>Imodium</i> 4–8/day ± fiber supplement (<i>Metamucil</i>, <i>Citrucel</i>, or <i>Fibercon</i>) or calcium (<i>TUMS</i>, etc.)</p> <p>OTC preps: <i>Imodium</i> (4 mg, than 2 with each loose stool up 16 mg/day), psyllium 1 tsp/day bid or 2 bars/day bid, Oat bran 1500 mg bid, calcium 500 mg bid</p>
Symptomatic treatment	<ul style="list-style-type: none"> ■ Diet modification: Avoid caffeine, fat and milk and/or milk products ■ Diphenoxylate/atropine (<i>Lomotil</i>), loperamide, paregoric (Antiperistaltic agents are contraindicated with <i>C. difficile</i> or <i>E. coli</i> 0157)
Hepatobiliary	
HIV cholangiopathy	<ul style="list-style-type: none"> ■ Papillary stenosis: ERCP + sphincterotomy ■ Cholangiopathy without papillary stenosis: Ursodeoxycholic acid 300 mg PO tid ■ Isolated bile duct stricture: Endoscopic stenting
Hepatitis	<p>HCV</p> <ul style="list-style-type: none"> ■ Indications to treat: Biopsy evidence of bridging fibrosis or moderate inflammation and necrosis + no contraindication to drugs (depression, etc) + patient acceptance + stable HIV ■ Peginterferon: 180 mcg/wk. (Roche) or 1.5 mcg/kg/wk. (Schering), each with ribavirin 10.6 mg/kg/day x 48 wks. <p>HBV</p> <ul style="list-style-type: none"> ■ 3TC 150 mg bid (with concurrent HIV treatment) or 100 mg PO/day or Interferon 30–35 mil U/wk. x 4 mos.; famciclovir and adefovir also active
Wasting	<p>Enteral Feedings</p> <ul style="list-style-type: none"> ■ Polymeric formulas: <i>Ensure</i>, <i>Sustacal</i>, <i>Enrich</i>, etc. <p>Appetite Stimulants</p> <ul style="list-style-type: none"> ■ Megestrol: 400–800 mg/day; usually 800 mg/day ■ Dronabinol: 2.5 mg PO bid to 10 mg bid <p>Anabolic Steroids</p> <ul style="list-style-type: none"> ■ Nandrolone 100–200 mg IM q 2 wks. (men) or 25–100 mg IM q 2 wks. (women); ■ Oxandrolone 20 mg/day (men and women) ■ Oxymetholone 100–150 mg/day up to 300 mg/day <p>Testosterone (men only)</p> <ul style="list-style-type: none"> ■ <i>Androderm</i> patch 5 mg/day ■ <i>Testoderm</i> ITS patch 5 mg/day ■ <i>AndroGel</i> topical 5 mg/day ■ Testosterone enanthate or testosterone cypionate 200–400 mg IM q 2 wks. or 100–200 mg/wk. IM by self injection

■ TABLE 10-2: Complications—Continued

Condition	Treatment
	<p>Resistance Exercise</p> <ul style="list-style-type: none"> ■ 20–120 min./day 3x/wk. <p>Cytokine Suppression</p> <ul style="list-style-type: none"> ■ Thalidomide 100 mg/day PO, up to 400 mg/day <p>Growth Hormone (<i>Serostim</i>)</p> <ul style="list-style-type: none"> ■ 6 mg/day SC x 12 wks. (@ \$30,000)
Psychiatric	
Anxiety	<ul style="list-style-type: none"> ■ Buspirone 5 mg PO tid ■ Nortriptyline: Titrate level of 70–125 ng/dL ■ Desipramine: Titrate levels up to 75–150 ng/dL (75–150 mg)
Depression	<ul style="list-style-type: none"> ■ Fluoxetine 10 mg, increasing to 20 mg/day ■ Nortriptyline 10–25 mg hs increasing to 50–150 mg hs; promotes sleep ■ Desipramine 10–25 mg hs increasing to 50–200 mg hs ■ Sertraline 25–50 mg/day increasing to 50–150 mg/day ■ Paroxetine 20–50 mg/day ■ Bupropion 20 mg/day, increasing up to 150 mg bid ■ Mirtazapine 15 mg/day; titrate q wk to 15–45 mg/day ■ Nefazodone 100 mg bid increase to 300–600 mg/day ■ Venlafaxine 37.5–75 mg/day, increasing to 75–150 mg/day (max. 225 mg)
Delirium	<ul style="list-style-type: none"> ■ Haloperidol 0.5–1 mg hs
Psychosis	<ul style="list-style-type: none"> ■ Olanzapine 5–10 mg/day; titrate to 10–15 mg/day ■ Haloperidol 1–5 mg/day in 2 to 3 doses; titrate to effect
Insomnia	<ul style="list-style-type: none"> ■ Diphenhydramine 25–50 mg hs ■ Trazodone 25–100 mg hs ■ Chloral hydrate 500–1000 mg hs ■ Zolpidem 5–10 mg hs ■ Nortriptyline or amitriptyline 25–50 mg hs
Apathy/Fatigue	<ul style="list-style-type: none"> ■ Ritalin 7.5 mg bid with weekly increase to intolerance (hyperactivity) or 60 mg/day (maximum) ■ Pemoline 18.75 mg (1 cap) bid with weekly increase to intolerance (shakiness) or maximum 112.5 mg/day

11 | Drug Profiles

Abacavir (ABC): *Ziagen* (GlaxoSmithKline); related: *Trizivir* (TZV)

CLASS: NRTI

INDICATIONS: Most potent NRTI.

FORMS AND PRICE: Tabs: 300 mg at \$6.41. As TZV: AZT 300 mg/3TC 150 mg/ABC 300 mg at \$16.75

PATIENT ASSISTANCE: 800-722-9294

REGIMEN: 300 mg bid. Renal failure: Standard.

PATIENT INSTRUCTIONS: No food restrictions. Warn about hypersensitivity reactions expressed as fever (usually 39° to 40°C), rash (maculopapular, often subtle), fatigue, nausea, vomiting, diarrhea, abdominal pain, muscle/joint pain, paresthesias, cough and/or dyspnea. The highest risk is in the first 6 weeks but can occur at any time. A common concern is that every cold or side effect from a drug taken concurrently is interpreted as a side effect of ABC. Fever is nearly always present with ABC hypersensitivity. Patients should be advised to contact provider with questions prior to d/c. Warn of lipodystrophy and fat redistribution.

WARNINGS: HSR, may be severe, resulting in hypotension and possible death. Warning card is available from pharmacists. Next dose will illicit same or worse Sx, may wish to administer next dose under observation. Remember that once this drug is stopped for suspected hypersensitivity it is often lost forever.

SIDE EFFECTS: HSR with above Sx; complications include anaphylaxis, renal failure, hepatic failure, hypotension and death. Rechallenge has resulted in 3 deaths. GI intolerance. Class ADR: Lactic acidosis and hepatic steatosis. To report HSR or for more information, call: 800-270-0425.

DRUG INTERACTIONS: ETOH increases ABC AUC 41% (clinical significance unknown); ABC may ↑ methadone CI; ↑ methadone dose may be required.

PREGNANCY: Category C

Acyclovir: *Zovirax* (GlaxoSmithKline); related: *Famciclovir* (*Famvir*) and *Valacyclovir* (*Valtrex*)

CLASS: Antiviral

INDICATIONS: Treatment and prophylaxis of HSV and VZV.

FORMS AND PRICE

Acyclovir: Caps: 200 mg at \$1.05, 400 mg at \$2.13, and 800 mg at \$1.26; IV vials: 500 mg at \$10, 1 gm at \$20

Famciclovir: Tabs: 125 mg at \$2.80, 250 mg at \$3.33, 500 mg at \$6.70

Valacyclovir: Tabs: 500 mg at \$3.09, 1 gm

REGIMENS:

■ **TABLE 11-1: Acyclovir Regimens (oral unless IV acyclovir indicated)**

Genital HSV	Acyclovir	Famciclovir	Valacyclovir
Initial (7 to 14 days)	400 mg tid	250 mg tid	1 gm bid
Recurrent (5 days)	400 mg tid	125 mg bid	500 mg bid
Suppression	400 mg bid	125–250 mg bid	0.5–1 gm/day
Severe disease	15–30 mg/kg/day IV	—	1 gm tid
Perirectal (5 days)	800 mg tid	—	—
Mucocutaneous	400 mg 5x/day	—	1 gm tid
Progressive (7 to 14 days)	5 mg/kg/day IV	—	—
Encephalitis (10 to 14 days)	30 mg/kg/day IV	—	—
Varicella Zoster			
Dermatomal (7 days)	800 mg 5x/day 30 mg/kg/day IV	500 mg tid	1 gm tid
Disseminated	30 mg/kg/day IV	—	—

■ **TABLE 11-2: Acyclovir Dose Adjustment for Renal Failure**

CrCl (mL/min.)		Acyclovir (PO and IV)			
Usual Dose	800 mg 5x/day	500 mg tid	30 mg/kg/day		
40–60	800 mg tid	500 mg bid	20 mg/kg IV		
20–40	800 mg tid	500 mg/day	10 mg/kg IV		
<20	800 mg tid	250 mg/day	5–10 mg/kg IV		
CrCl (mL/min.)		Famciclovir (PO)		Valacyclovir (PO)	
Usual Dose	500 mg tid	125 mg bid	1 gm tid	0.5 gm bid	
40–60	500 mg bid	125 mg bid	1 gm bid	0.5 gm bid	
20–40	500 mg/day	125 mg/day	1 gm/day	0.5 gm/day	
<20	250 mg/day	125 mg/day	0.5 gm/day	0.5 gm/day	

PATIENT INSTRUCTIONS: Genital HSV is an STD, with increased shedding and risk of transmission with ulcerative lesions. VZV is as contagious as chickenpox via aerosol. Persons with AIDS and others with reduced cell mediated immunity

and no Hx and/or serology indicating chickenpox are considered vulnerable. These drugs will reduce shedding of HSV and VZV and will sometimes hasten healing. They will not cure VZV or HSV.

WARNINGS: HSV: Take within 24 hrs. of onset Sx. VZV: Take within 4 days or while new lesions are still forming. Hydrate well for IV acyclovir. Agents are category C for pregnancy, use based on risk-benefit ratio. CDC advocates acyclovir only for life-threatening disease in pregnancy. Famciclovir and valacyclovir are presumably similar.

ACYCLOVIR REGISTRY: Registry experience with 601 pregnant women showed no increase in fetal abnormalities (*MMWR* 1993:42:806).

RELATIVE MERITS OF ACYCLOVIR, FAMCICLOVIR AND VALACYCLOVIR: Acyclovir: Only IV formulation (ointment form available, but indications for topical are nil). Valacyclovir: Prodrug of acyclovir and probably preferred to acyclovir for conditions treated with high dose oral agent. Famciclovir: Appears comparable to other two. Acyclovir-resistant strains of HSV and VZV: Resistant also to famciclovir, valganciclovir, and ganciclovir. Most resistant strains are treated with foscarnet (HSV and VZV); other options for HSV are cidofovir and topical trifluridine.

■ TABLE 11–3: Relative Activity of Acyclovir, Cidofovir, Famciclovir, Foscarnet, Ganciclovir, and Valacyclovir

	Acyclovir					
	HSV	Resistant HSV	VZV	EBV	CMV	HHV 6–8
Acyclovir	++	–	+	+	–	–
Cidofovir	+	+	+	++	+	++
Famciclovir	++	–	+	+	–	–
Foscarnet	+	+	+	++	+	+
Ganciclovir	++	–	+	++	++	+
Valacyclovir	++	–	+	+	–	–

SIDE EFFECTS: Rare: CNS toxicity. IV acyclovir: Irritation at infusion site and risk of fluid overload with high doses; renal toxicity in high doses—crystal nephropathy.

DRUG INTERACTIONS: None

PREGNANCY: Category B. Valacyclovir: Category B

Albendazole: *Albenza* (GlaxoSmithKline)

CLASS: Anthelmintic

INDICATIONS: Microsporidiosis due to *Septata intestinalis*.

FORMS AND PRICE: Tabs: 200 mg at \$1.32

REGIMENS: 400–800 mg PO bid >3 weeks (usually 3 weeks).

PATIENT INSTRUCTIONS: Must take with fatty meal which increases absorption by 5x.

WARNINGS: Hepatotoxic and marrow suppression: Get LFTs and CBC every 2 weeks. Effective against *E. septate*, which causes 20% of microsporidia cases. Not active against *E. bieneusi*, which accounts for 80% of cases.

DRUG INTERACTIONS: May increase theophylline levels.

PREGNANCY: Category C; teratogenic in animals.

Amphotericin B: *Amphotericin B* (Abbott), *Fungizone* (Apothecon), *Amphotec* (Sequus)

CLASS: Antifungal

FORMS AND PRICE: Vials: 50 mg at \$11.64

REGIMENS

- Aspergillosis: 0.5–1.5 mg/kg/day
- Candidiasis: 0.2–0.8 mg/kg/day
- Coccidioidomycosis: 0.5–1.0 mg/kg/day
- Cryptococcosis: 0.7–1.0 mg/kg/day, usually 0.7 mg/kg
- Histoplasmosis: 0.5–1.0 mg/kg/day

ADMINISTRATION: Slow infusion: 1st dose 1 mg in 50 mL D5W given over 30 min. with vital signs monitoring q 30 min. x 4 hrs.; then daily maintenance dose.

PATIENT INSTRUCTIONS: Warn of infusion-related side effects.

WARNINGS: Infusion-related side effects. Chills: Treat with hydrocortisone 10–50 mg added to infusion if necessary or give meperidine, ibuprofen prior to infusion. Nausea/vomiting usually 1 to 3 hrs. post infusion, treat with *Compazine*, etc. Hypotension: Monitor BP. Nephrotoxicity in up to 80% + nephrocalcinosis, K wasting, renal tubular acidosis. Reduce risk with pretreatment hydration, avoid concurrent nephrotoxic drugs, and Na⁺ or Mg⁺⁺ loading. Suspend therapy if creatinine increases to >3 mg/dL or use lipid amphotericin preps. Electrolyte changes: Depletion of K⁺, Mg⁺⁺ and Ca⁺⁺. Anemia.

MONITOR: CBC, electrolytes, creatinine.

SIDE EFFECTS: Infusion related: Chills, fever, headache, hypotension, nausea, which improve with subsequent dosing. Nephrotoxicity (see above). Electrolyte depletion. Anemia.

INDICATIONS FOR LIPID FORMULATION: (IDSA Guidelines, *Clin Infect Dis* 2000; 30: 60)

- Serious, life-threatening infections caused by molds: *Aspergillus*, *Mucor* or *Fusaria*.

- Pre-existing renal failure or Amphotericin B related renal failure with serum creatinine >2.0–2.5 mg/dL.
- Intolerable infusion-related toxicity.
- Disease progression after >500 mg Amphotericin B.

■ **TABLE 11–4: Comparison of Lipid Formulations of Amphotericin B**

Agent	Amphotericin B	Abelcet	Amphotec	AmBisome
Dose (mg/kg/day)	0.5–1.0	5	3–4	3–5
Cost/dose	12	\$776	\$480 to \$740	\$942
Side effects				
Infusion	++++	+++	++++	+
Nephrotoxicity	++++	++	++	++

DRUG INTERACTIONS: Caution or avoid drugs associated with renal failure, marrow suppression, digitalis (K depletion); additive K depletion, mineralocorticoids, and diuretics.

PREGNANCY: Category B

Amprenavir (APV): Agenerase (GlaxoSmithKline)

CLASS: PI

INDICATIONS: PI with activity against many PI resistant strains.

FORMS AND PRICE: Caps: 50 mg, 150 mg at \$1.39 (\$155/week, standard dose). Oral solution 15 mg/mL at \$33.30/240 mL bottle.

PATIENT ASSISTANCE: 800–722–9294

REGIMENS: 1200 mg bid. Renal failure: Standard. Hepatic failure/liver disease: 450 mg bid. Severe cirrhosis: 300 mg bid.

PATIENT INSTRUCTIONS: 1200 mg bid (eight 150 mg caps bid) can be taken with or without food, but avoid high fat meal. Avoid supplemental vitamin E. Women should not rely on birth control pills for contraception. Warn of rash. Warn of lipodystrophy and fat redistribution. Ask if history of sulfonamide allergy.

WARNINGS: Reduce dose to 450 mg bid with liver disease and to 300 mg bid with severe cirrhosis. Oral solution contains 55% propylene glycol and is contraindicated in renal failure, hepatic failure, pregnancy, children <4 years old, and with disulfiram, metronidazole or alcohol. Always use caps when feasible. Avoid large amounts of vitamin E. See drug interactions, below.

SIDE EFFECTS: GI intolerance: Nausea: 43–74%; Vomiting: 24–34%; Diarrhea: 39–60%; Rash: 20–27%, including cases of Stevens-Johnson Syndrome. APV is a sulfonamide, but patients with adverse reactions to TMP-SMX or sulfas

usually tolerate APV. Headache—6%, mood disorders. Oral or peripheral paresthesias—28%. Class ADR: Lipodystrophy.

DRUG INTERACTIONS: Contraindicated in combination with astemizole, bepridil, cisapride, dihydroergotamine, ergotamine, midazolam, terfenadine, triazolam, RIF, simvastatin, lovastatin, St. John's Wort. Dose reduction: RBT 150 mg/day or 300 mg 2–3x/week. PI/NNRTI combinations, see Tables 6–9 and 6–10, pp. 33–34.

PREGNANCY: Category C

Atorvastatin: *Lipitor* (Parke-Davis)

CLASS: Statin

INDICATIONS: Elevated total or LDL cholesterol or triglycerides LDL cholesterol.

FORMS AND PRICE: Tabs: 10 mg, 20 mg, 40 mg at \$3.49, 80 mg

REGIMENS: Initiate at 10 mg/day with increase at 2 to 4 week intervals to maintenance dose of 10–80 mg/day in one daily dose depending on response.

PATIENT INSTRUCTIONS: Treatment should be combined with lifestyle changes including diet modification, exercise, weight loss if appropriate, d/c smoking, diabetes control, HBP control, etc. Take at evening with or without food. Warn about myopathy with muscle tenderness and pain + fever, malaise. Warn about symptoms of hepatitis. Must avoid pregnancy.

WARNINGS: Concurrent use with IDV, SQV, RTV and APV is considered safe. Atorvastatin levels increase 6x with LPV/RTV, use combination with caution or use pravastatin instead. If patient reports muscle pain or tenderness d/c atorvastatin and evaluate including CPK.

SIDE EFFECTS: Myopathy with muscle pain, tenderness, and elevated CPK; rhabdomyolysis reported. Transaminase levels increase in 1% to 2% - d/c atorvastatin if >3x ULN x2.

DRUG INTERACTIONS: Niacin and gemfibrozil: Increased risk of myopathy and rhabdomyolysis.

PREGNANCY: Category X

Atovaquone: *Mepron* (GlaxoSmithKline)

CLASS: Antiprotozoal

INDICATIONS: Treatment and prevention of *P. carinii* pneumonia.

FORMS AND PRICE: 750 mg/5 mL, \$668/210 mL bottle (21 day supply)

REGIMENS: 750 mg (5 mL) PO bid (PCP prophylaxis and treatment) or 1500 (10 mL) mg/day (prophylaxis). Renal or hepatic failure: No data.

PATIENT ASSISTANCE: 800-722-9294

PATIENT INSTRUCTIONS: 750 mg (mL) bid with meals, preferably a fatty meal which increases absorption 2x.

WARNINGS: Drug interactions with LPV/RTV, RIF, and RBT. Expensive compared to alternative PCP prophylactic drugs (\$10,600/year vs \$100/year for dapsone).

SIDE EFFECTS: Rash—20%. GI intolerance—20%

DRUG INTERACTIONS: RIF and possibly RBT decrease atovaquone levels 50%; presumably need atovaquone dose increase or avoid combination. LPV/RTV induces atovaquone metabolism.

PREGNANCY: Category C

Azithromycin: *Zithromax* (Pfizer)

CLASS: Macrolide

INDICATIONS: Common respiratory tract infections; treatment and prophylaxis of MAC.

FORMS AND PRICE: Caps: 250 mg at \$6.97; Tabs: 600 mg at \$16.73; IV vials: 500 mg at \$25.23

PATIENT ASSISTANCE: 800-646-4455

REGIMENS

- MAC prophylaxis: 1.2 gm (two 600 mg tabs)
- MAC Rx: 600 mg/day + EMB ± RBT
- Pneumonia: 500 mg/day IV or PO
- Sinusitis: 500 mg x 1, then 250 mg PO/day x 4 (Z PAC)
- *Chlamydia trachomatis*: 1-1.2 gm x 1
- Gonorrhea (uncomplicated): 2 gm x 1 (poorly tolerated)
- Toxoplasmosis: 600-1200 mg/day + pyrimethamine
- Renal failure or hepatic failure: Standard dose with caution

PATIENT INSTRUCTIONS: Take 250 mg caps 1 hr. before or 1 hr. after meal. Food has no effect on absorption of 600 mg tabs and powder, but may improve GI tolerance. (Food decreases azithromycin AUC of caps by 40%, and does not effect AUC of tabs). Avoid concurrent use of antacids with Mg⁺⁺ or Al⁺⁺.

WARNINGS: GI intolerance, especially with high doses (1-2 gm doses).

SIDE EFFECTS: GI intolerance—4%. With 1200 mg dose—diarrhea, abdominal pain, nausea. Reversible ototoxicity.

DRUG INTERACTIONS: Antacids with Mg⁺⁺ or Al⁺⁺ decrease absorption of caps and should be taken >1 hr. before or >2 hrs. after. Increases levels of theophylline and warfarin.

PREGNANCY: Category B

Benzodiazepines

INDICATIONS: Anxiety and insomnia.

PATIENT INSTRUCTIONS: Warn of abuse potential and dependency, which correlates with dose and duration. Early signs include amnesia, anxiety, confusion, depression, abnormal thinking. Avoid alcohol and other CNS depressants. Warn of daytime sedation, dizziness, incoordination, ataxia, blurred vision, incontinence, and hangover. Warn that activities requiring coordination, alertness and judgment may be impaired. Pregnancy: Risk of congenital malformations in first trimester and neonatal dependency: Avoid.

WARNINGS: Major concern is abuse potential with dependency, tolerance, and withdrawal symptoms which depend on dose and duration. Agent selection should be based on indication (anxiety or insomnia) and need for rapid response (short T_{max}). Regimen selection: Use smallest dose for shortest time; increase dose prn. with caution. Specific concern for patients who use/abuse ETOH and other sedative-hypnotic agents. If used for more than several weeks, reduce dose by 20% to 30%/week adjusted by symptoms and facilitated by antidepressants or hypnotics. Withdrawal: Recurrence of pretreatment Sx over days–weeks; rebound Sx within hours or days or “benzodiazepine withdrawal syndrome,” autonomic Sx, disturbed equilibrium. Avoid triazolam and midazolam with PIs and DLV. Rx dependence: Taper over 4 to 16 weeks.

SIDE EFFECTS: See above. Visual problems. Memory loss, confusion, disinhibition and bizarre behavior. Autonomic nervous system dysfunction blurred vision, incontinence, hypotension. Potentiates CNS depressants including ETOH.

DRUG INTERACTIONS: Increase benzodiazepine levels: Itraconazole, ketoconazole, cimetidine, fluoxetine, nefazodone, propoxyphene, ranitidine, verapamil (not lorazepam, oxazepam, or temazepam). Increase carbamazepine.

PREGNANCY: Category D (clonazepam, diazepam, lorazepam, halazepam); Category X (quazepam, temazepam, triazolam). Avoid.

Bupropion: *Wellbutrin, Wellbutrin SR, Zyban* (GlaxoSmithKline); generics (various manufacturers)

CLASS: Atypical antidepressant

INDICATIONS: Depression; smoking cessation.

FORMS AND PRICE: Tabs: 75 mg, 100 mg at \$0.96; SR tab 150 mg at \$1.60

REGIMENS

- Depression: 150 mg/day x4, then SR formulation 150 mg bid
- Smoking cessation: 150 mg/day x 3 days, then 150 mg bid x 7 to 12 weeks. Continue smoking 1st week to establish steady state; d/c smoking 2nd week.

■ TABLE 11-5: Benzodiazepines—Forms, Characteristics, and Doses

Agent	Trade Name	Anxiety	Insomnia	T _{max} hrs.	T _{1/2} hrs.	Forms mg	Regimen
Alprazolam	Xanax	+	-	1-2	11	0.25, 0.5, 1, 2	0.75-1.5 mg/day 3 doses
Chlordiazepoxide	Librium	+	-	0.5-4	10	5, 10, 25	15-100 mg/day hs or 3 to 4 doses
Clorazepate	Tranxene	+		1-2	73	3.7, 7.5, 11, 23	15-60 mg/day hs or 2 to 3 doses
Diazepam	Valium	+	+	1.5-2	73	2, 4, 5, 10	15-60 mg/day hs or 2 to 3 doses
Flurazepam	Dalmane	-	+	0.5-2	74	15, 30	15-30 mg/day 2 to 4 doses
Quazepam	Doral	-	+	2	74	7.5, 15	30 mg hs
Lorazepam	Ativan	+	+	2	14	0.5, 1, 2	0.25-0.5 mg tid
Oxazepam	Serax	+	+	1-4	7	10, 15, 30	10-30 mg/day 2 to 3 doses
Temazepam	Restoril	-	+	1-1.5	13	15, 30	7.5-30 mg hs
Triazolam	Halcion	-	+	1-2	3	0.125, 0.25	0.125-0.5 mg hs

PATIENT INSTRUCTIONS: Warn of requirement for treatment up to 4 weeks for antidepressant effect. Warn of GI toxicity and weight loss.

WARNINGS: May induce seizures: Do not use >150 mg/dose; do not exceed 450 mg/day, and use with caution with seizure-prone patients and with patients whose ETOH or other antidepressants. Contraindicated in patients with a history of seizures.

SIDE EFFECTS: Agitation, insomnia, depersonalization. GI toxicity: Nausea, vomiting, weight loss—up to 25%.

DRUG INTERACTIONS: Metabolized by P450 2B6; inducers will decrease bupropion levels (carbamazepine); inhibitors will increase risk of seizures. Concurrent use with MAO inhibitors is contraindicated: d/c MAOI \geq 14 days before starting bupropion. Medications that decrease seizure threshold increase risk of seizures with bupropion.

PREGNANCY: Category B

Buspirone: *BuSpar* (Bristol-Myers Squibb)

CLASS: Nonbenzodiazepine-nonbarbiturate antianxiety agent

INDICATIONS: Anxiety, not controlled.

FORMS AND PRICE: Tabs: 5 mg, 10 mg at \$1.50, 15 mg, 30 mg at \$4.05

REGIMENS: 5 mg PO tid, increase 5 mg/day q 2 to 4 days. Usual effective dose is 5 mg tid or 15 mg bid. Maximum dose is 60 mg/day. Onset of response at 1 week and full effect at 4 weeks. Renal failure: Reduce dose 25% to 50% with creatinine clearance <10 mL/min. Hepatic failure: Monitor closely.

PATIENT INSTRUCTIONS: Advantages compared to other antianxiety agents: No dependency liability, does not potentiate antidepressants, and less confusion than with benzodiazepines. Decreased libido, muscle relaxation, fatigue and confusion. May impair activities that require coordination and alertness. May require up to 1 month for maximum effectiveness.

WARNINGS: See above. Use with care with hepatic failure and with MAOIs.

SIDE EFFECTS: Fewer side effects than benzodiazepines, but considerable individual patient variation, including insomnia, headache, dizziness, increased or decreased libido, depression. GI intolerance.

DRUG INTERACTIONS: Erythromycin increases buspirone AUC 6x; itraconazole increases buspirone AUC 19x. P450 3A4 plays significant role in metabolism.

PREGNANCY: Category B

Capsaicin: *Zostrix* (Medicus)

CLASS: Analgesic, topical

INDICATIONS: Neuropathic pain.

FORMS AND PRICE: Cream 0.025% at \$9.98/20 oz.; Lotion 0.075% at \$9.76 (over the counter only)

REGIMENS: Topical application 3–4x/day; use sparingly and rub well into skin so there is none left on the surface of the skin. Apply only to intact skin.

PATIENT INSTRUCTIONS: May cause stinging or burning at site of application, which may last days or weeks, and may decrease with continued application. Wrappings, clothing, or bathing may make it worse. Pain relief usually requires 2 to 4 weeks. If drug is discontinued, pain of neuropathy returns. Wash hands after use and avoid eye contact with capsaicin.

WARNINGS: Stinging and burning in first 2 to 4 weeks may be reduced with pre-treatment use of topical lidocaine.

DRUG INTERACTIONS: None

Cidofovir: *Vistide* (Gilead)

CLASS: Antiviral

INDICATIONS: CMV disease, also active vs VZV, EBV, HHV 6 and 8 and ganciclovir resistant CMV; less vs HSV.

FORMS AND PRICE: Vials: 375 mg/mL at \$846

REGIMENS

- Induction: 5 mg/kg IV over 1 hr. weekly x 2
- Maintenance: 5 mg/kg IV over 1 hr. q 2 weeks. Serum creatinine increase 0.3–0.4 mg/dL: Reduce dose to 3 mg/kg. Serum creatinine increase >0.5 mg/dL or >3 + protein: Discontinue.
- Probenecid: 2 gm given 3 hrs. prior to cidofovir and 1 gm given at 2 and 8 hrs. post infusion (total 4 gm) + >1L 0.9% N saline over 1 to 2 hr. immediately before cidofovir infusion.
- In case of pre-existing renal disease, see table below:

■ TABLE 11–6: Cidofovir Dosing for Pre-existing Renal Disease (experience is limited)

CrCl (mL/min.)	Induction: 2x per wk.	Maintenance
41–55	2 mg/kg	2 mg/kg
30–40	1.5 mg/kg	1.5 mg/kg
20–29	1 mg/kg	1 mg/kg
<19	0.5 mg/kg	0.5 mg/kg

PATIENT INSTRUCTIONS: Warn about side effects: Neutropenia, renal failure, ocular hypotony (decreased vision). ADRs from Probenecid.

WARNINGS: Dose dependent nephrotoxicity: Avoid concurrent nephrotoxic drugs. If receiving nephrotoxic drugs, need 7 day "washout." Probenecid causes side effects (fever, chills, headache, rash, nausea) in 50%; most resolve in 12 hrs. May reduce with antipyretics, antiemetics, antihistamines or food. Renal failure with creatinine >1.5 mg/dL is contraindication.

MONITOR: CBC, creatinine, U/A, electrolytes q 1 to 2 weeks, visual acuity and intraocular pressure.

SIDE EFFECTS: Dose limiting nephrotoxicity with proteinuria, decreased creatinine clearance in 50%. Fanconi's syndrome with $\text{NaHCO}_3 < 16 \text{ mEq/mL}$ + renal tubular damage—9%. Neutropenia with $\text{ANC} < 500 \text{ c/mm}^3$ —20%. Ocular hypotony.

DRUG INTERACTIONS: Avoid nephrotoxic drugs.

PREGNANCY: Category C

Clarithromycin: *Biaxin, Biaxin XL* (Abbott)

CLASS: Macrolide

INDICATIONS: Common respiratory tract infections; treatment and prophylaxis of MAC.

FORMS AND PRICE: Tabs: 250 mg, 500 mg at \$3.95; XL tabs: 500 mg at \$4.42 (for qd dosing); Suspension 250 mg/mL at \$68.93/100 mL

PATIENT ASSISTANCE: 800-659-9050

REGIMENS

- Sinusitis, pneumonia, etc.: 250–500 mg PO bid or 1 gm/day (two 500 mg XL tabs)
- MAC prophylaxis: 500 mg PO bid
- MAC treatment: 500 mg PO bid (+ EMB)
- Toxoplasmosis: 500 mg PO bid + pyrimethamine (experimental)
- *H. pylori*: 500 mg tid + omeprazole 40 mg/day x 14 days, then omeprazole 20 mg/day x 14 additional days (may substitute ranitidine 400 mg bid x 14 days, then 400 mg/day x 14 additional days)

PATIENT INSTRUCTIONS: Food: No effect. Drug interactions, see below. May decrease AZT levels.

WARNINGS: Drug interactions: See below; 10% to 20% of *S. pneumoniae* strains are resistant to macrolides.

SIDE EFFECTS: GI intolerance—4%. Transaminase elevation—1%

DRUG INTERACTIONS: Avoid RBT, RIF, carbamazepine, cisapride, terfenadine, pimozone. EFV and NVP induce clarithromycin metabolism and reduce AUC by

30% to 40%, but increase levels of 14 OH clarithromycin by 25% to 35%; effect on efficacy is uncertain. RTV and LPV/RTV increase clarithromycin levels—reduce clarithromycin dose by 50% if CrCl 30–60 mL/min., and by 75% if CrCl <30–60 mL/min. Warfarin may increase INR.

PREGNANCY: Category C

Clindamycin: *Cleocin* (Pharmacia); generic (various manufacturers)

CLASS: Antibacterial, antiprotozoal

INDICATIONS: Most GPC except Enterococcus and MRSA. Most anaerobes are sensitive. Alternative Rx for toxoplasmosis and PCP.

FORMS AND PRICE: Caps: 75 mg, 150 mg at \$1.18, 300 mg at \$4.20; IV form: 150 mg/mL at \$13.84/600 mg

REGIMENS

- PCP: 600–900 mg IV q6h–q8h or 300–450 mg PO qid (+ primaquine 15 mg base)
- Toxoplasmosis: 900–1200 mg IV q6h or 300–450 mg PO qid (+ pyrimethamine + folinic acid)
- Bacterial Infections: 600 mg IV q8h or 150–300 mg PO qid
- Dose modification with renal or hepatic failure: None

PATIENT INSTRUCTIONS: Warn about high rate of diarrhea.

WARNINGS: Diarrhea—10% to 30% with IV or oral form. *C. difficile* induced in 6% of all clindamycin recipients—avoid antiperistaltic, d/c clindamycin and Rx with metronidazole (500 mg bid or 250 mg tid x 10 days). High rate of rash in HIV-infected patients.

SIDE EFFECTS: Diarrhea most common cause of *C. difficile* colitis (fever leukocytosis, fecal WBC + ileus or toxic megacolon). Rash—rare. Hepatotoxicity—rare.

DRUG INTERACTIONS: Avoid concurrent use of antiperistaltic drugs.

PREGNANCY: Category B

Clotrimazole: *Gyne-Lotrimin* (Schering), *Lotrimin* (Schering), *Mycelex* (Bayer)

CLASS: Antifungal

INDICATIONS: Mucocutaneous candidiasis.

FORMS AND PRICE: Troche: 10 mg at \$.82; Vaginal tabs: 100 mg at \$1.71 (\$7.45/3 days), 500 mg at \$13.88 (single dose); 1% Cream.

ACTIVITY: *Candida albicans*

REGIMENS

- Thrush: 10 mg troche 5x/day until symptoms resolve, usually 10 to 14 days
- Vaginitis: 100 mg tab (topical) bid x 3 or 500 mg tab x 1
- Dermatophytic infections (candidiasis, *tinea corporis*, *T. cruris*, *T. pedis*): Apply cream bid.

PATIENT INSTRUCTIONS: Thrush: Must dissolve in mouth.

WARNINGS: Monitor LFTs with oral administration, esp. if prior liver disease.

SIDE EFFECTS (TROCHES): AST elevated—15%; nausea + vomiting—5%

DRUG INTERACTIONS: None

PREGNANCY: Category C

Dapsone: generic (Jacobus)

CLASS: Synthetic sulfone

INDICATIONS: Treatment and prophylaxis of *P. carinii* pneumonia.

FORMS AND PRICE: Tabs: 25 mg at \$.19, 100 mg at \$.20

REGIMENS:

- PCP prophylaxis: 100 mg/day PO
- PCP treatment: 100 mg/day PO + TMP 15 mg/kg/day PO x 3 weeks
- PCP + toxoplasmosis prophylaxis: 50 mg/day + pyrimethamine 50 mg/week + folinic acid 25 mg/week
- Renal or hepatic failure: Standard regimen

PATIENT INSTRUCTIONS: Avoid concurrent gastric acid neutralization—buffered ddi, antacids, H₂ blockers, omeprazole.

WARNINGS: High rates of adverse reactions, including rash, pruritus, hepatitis, anemia. Dose dependent hemolytic anemia with or without G6-P Ddeficiency (see side effects). GI intolerance common.

MONITOR: Hematocrit, esp. with G6-PD deficiency; if anemic, get methemoglobin level.

SIDE EFFECTS: Rash, pruritus, hepatitis, and/or fever—20% to 40%. Hemolytic anemia with hemolysis + methemoglobinemia. Acute: Dyspnea, fatigue cyanosis with high PaO₂ by blood gas (variable O₂ sat by pulse oximetry) + chocolate-colored blood. Chronic: Methemoglobinemia levels elevated related to dose and duration; TMP increases levels. Methemoglobin levels <25% are usually well tolerated, except with lung disease. Risk increases with G6-PD deficiency; African race is not a contraindication to dapsone, but is a risk and should monitor hematocrit + get methemoglobin if anemia is noted; Mediterranean variety of G6-PD is contraindication. Dx: Hemolytic anemia with methemoglobin. Rx: Acute-O₂, packed RBCs, d/c implicated drugs; if methe-

moglobin >30%—activated charcoal (20 mg qid) to decrease dapsone; in absence of G6-PD—methylene blue 3–5 mg/kg PO q4h–q6h.

DRUG INTERACTIONS: Gastric acid neutralization: Decreased dapsone absorption. Decreased dapsone levels: RIF and RBT. Increased dapsone levels: TMP, Probenecid. Warfarin: Increased hypothermia.

PREGNANCY: Category C

Delavirdine, DLV: *Rescriptor* (Agouron)

CLASS: NNRTI

INDICATIONS: Infrequently used due to tid regimen, limited experience, and cross resistance with other NNRTIs; potential benefit is increased levels of PIs: IDV (40% increase AUC), RTV (70%), FTV (5x), NFV (2x).

FORMS AND PRICE: Tabs: 100 mg, 200 mg at \$1.62

PATIENT ASSISTANCE: 888–777–6637

REGIMENS: 400 mg PO tid. Renal failure: Standard regimen. Hepatic failure: Consider empiric dose reduction.

PATIENT INSTRUCTIONS: Take without regard for meals. Warn of pill burden (6/day) and rash. Avoid concurrent H₂ blockers and buffered ddl. Warn of lipodystrophy and fat redistribution.

WARNINGS: Extensive list of drugs contraindicated for concurrent use, see below. Rash—18%, usually within 1st six weeks. DLV inhibits activity of CYP3A.

SIDE EFFECTS: Rash—18%, sufficiently severe to d/c Rx—4%. Discontinue DLV if blistering, fever, mucous membrane involvement, swelling, arthritis. Increased transaminase. Class ADRs: Rash; lipodystrophy (not well characterized).

DRUG INTERACTIONS: Contraindicated: RIF, RBT, ergot, astemizole, cisapride, midazolam, triazolam, simvastatin, lovastatin, H₂ blockers, proton pump inhibitors. Decrease DLV levels: Carbamazepine, phenobarbital, phenytoin, antacids, buffered ddl, H₂ blockers, NFV. DLV increases AUC of dapsone, clarithromycin, quinidine, warfarin, sildenafil. PI combinations: see Table 6–10, p. 34.

PREGNANCY: Category C

Didanosine, ddl: *Videx, Videx EC* (Bristol-Myers Squibb)

CLASS: NRTI

INDICATIONS: Major advantages are qd dosing, extensive experience, and a different resistance profile from thymidine analogs.

FORMS AND PRICE

- *Videx EC* (enteric coated) tabs: 125 mg at \$89.56/30, 200 mg at \$143.29/3, 250 mg at \$179.11/30, 400 mg at \$236.57/30
- Buffered ddl tabs: 25 mg at \$0.49, 50 mg at \$0.99, 100 mg at \$1.98, 150 mg and 200 mg

- Buffered powder packets: 100 mg at \$59.45/30, 167 mg at \$99.29/30, 250 mg at \$148.62/30

REGIMENS

■ TABLE 11-7: *ddl* Dosing

Weight	<i>Videx EC</i>	Buffered Tabs	Powder
>60 kg	400 mg/day	200 mg bid or 400 mg/day	250 mg bid
<60 kg	250 mg/day	125 mg bid or 250 mg/day	167 mg bid

■ TABLE 11-8: Dosing for Renal failure: *Videx EC* and Buffered Tabs

Weight	Creatinine Clearance (mL/min.)			
	>50	26–49	10–25	<10
>60 kg	400 mg/day	200 mg/day	100 mg/day; EC 125/day	100 mg/day; EC 125/day
<60 kg	250 mg/day	125 mg/day	50 mg/day; EC 125/day	50 mg/day; EC avoid

PATIENT INSTRUCTIONS: All formulations must be taken on empty stomach (EC formulation is preferred; it is better tolerated and has fewer drug interactions). Warn about side effects—pancreatitis (abdominal pain) and peripheral neuropathy (pain and paresthesias). Powder form to be mixed in 4 oz water; buffered tab should be chewed or crushed in 1 oz water. Warn of lipodystrophy and fat redistribution.

WARNINGS: Pancreatitis—1% (most do not monitor amylase in absence of abdominal pain) but special caution with ETOH, hypertriglyceridemia, (>1000 mg/dL), history of pancreatitis; d/c if amylase >2x ULN. Peripheral neuropathy—5% to 12%. Drug interactions, including reduced *ddl* levels with methadone (see Methadone). Avoid *ddl* + d4T in pregnancy. Tabs and powder have 50–60 mEq (1000–1400 mg) Na/day. Caution with requirement for Na restriction—CHF, HBP, cirrhosis.

MONITOR: Peripheral neuropathy: Pain, paresthesias, and reduced/absent ankle jerks.

SIDE EFFECTS: Pancreatitis and peripheral neuropathy, esp. if given with d4T. Class ADRs: Lactic acidosis + hepatic steatosis, lipatrophy. GI intolerance (frequent): Nausea, vomiting, abdominal pain.

DRUG INTERACTIONS: Buffered forms (powder and tabs other than *Videx EC*) decrease absorption of dapsone, IDV, RTV, DLV, ketoconazole, tetracycline, fluoroquinolones. Avoid drugs that cause pancreatitis—ETOH (use with caution), EMB, pentamidine. Avoid drugs that cause peripheral neuropathy: EMB, INH, vincristine, gold, disulfiram, cisplatin, ddC. Oral ganciclovir increases *ddl* AUC

by 100%; clinical significance is unknown. Methadone reduces dDI AUC 41%; clinical significance is unknown and effect on *Videx EC* is unknown. Tenofovir increases dDI levels 41%; significance and need for dose adjustment are unclear.

PREGNANCY: Category B

Dronabinol: *Marinol* (Roxane)

CLASS: Appetite stimulant, psychoactive component of marijuana.

INDICATIONS: Wasting attributed to anorexia.

FORMS AND PRICE: Caps: 2.5 mg, 5 mg at \$6.63, 10 mg at \$14.80.

REGIMENS: 2.5 mg bid to 5 mg bid before lunch and dinner. Renal failure: No change.

PATIENT INSTRUCTIONS: Psychoactive component of marijuana; dose related CNS effects including "high," paranoia, somnolence, depersonalization, confusion, etc. CNS depression with concurrent use of alcohol, benzodiazepines, barbiturates, etc. Avoid driving and machine operation until safety and tolerance are established. Changes in mood, confusion and somnolence usually resolve in 1 to 3 days. Take before meal. Withdrawal Sx (irritability, insomnia, restlessness) within 12 hours when dose of 20 mg/day is given for 16 consecutive days.

WARNINGS: Duration of psychoactive effect is 4 to 6 hours; duration of appetite increase is >24 hours. Caution or avoid with substance abuse, psychiatric illness, patients receiving sedatives or hypnotics, elderly (limited experience) or cardiac disease (hypotension). Weight gain in clinical trials is modest or nil and mostly fat. Schedule I agent with potential for abuse. Despite concerns, long term use in AIDS patients has not shown abuse, personality change, abnormal social functioning, or withdrawal reactions, even in those with a history of substance abuse.

SIDE EFFECTS: CNS (see above). Cardiovascular: Hypotension, vasodilation, tachycardia.

DRUG INTERACTIONS: Sympathomimetic agents, anticholinergic agents, CNS depressants.

PREGNANCY: Category C

Efavirenz, EFV: *Sustiva* (Bristol-Myers Squibb)

CLASS: NNRTI

INDICATIONS: Potent anti-HIV agent; one of few triple agent regimens with comparable antiviral activity with baseline VL above or below 100,000 c/mL in treatment naïve patients.

FORMS AND PRICE: Caps: 50 mg, 100 mg, 200 mg at \$4.39

REGIMENS: 600 mg (three 100 mg tabs) hs. Renal failure or hepatic failure: Standard

PATIENT INSTRUCTIONS: Take without regard to meals except that high fat meals should be avoided because they increase absorption. If switching from PI to EFV, some experts suggest an overlap of 1 week to achieve therapeutic EFV levels. Avoid in pregnancy and in women contemplating pregnancy. Warn of potential side effects of bad dreams and “disconnected” feeling, with the anticipation that if these occur, they will occur with the first dose and will usually resolve in 2 to 4 weeks. Women cannot depend on oral contraceptives when taking EFV. Warn of lipodystrophy, fat redistribution, and rash.

WARNINGS: Avoid in 1st trimester of pregnancy and in women contemplating pregnancy; birth control pills may be unreliable due to interaction with EFV. CNS side effects in >50% in first 2 to 3 weeks and may be profound with confusion, vivid dreams, depersonalization, etc. Impact of ETOH, prior mental illness, or psychoactive drugs not well characterized. May need to avoid driving and other potentially dangerous activities during first 2 to 4 weeks. May cause false positive cannabinoid test (confirmatory tests are negative). Drug interactions, see below.

SIDE EFFECTS: Rash—15% to 27%, sufficiently serious to d/c drug in 1% to 2%; d/c if rash is associated with fever, blistering, desquamation, mucous membrane involvement, arthritis or Stevens-Johnson syndrome (rare). CNS effects, see above. Hepatitis with ALT >5 x ULN in 2% to 3%. Class ADRs: Rash, lipodystrophy (not well characterized), cholesterol and HDL increase.

DRUG INTERACTIONS: Contraindicated: Astemizole, terfenadine, midazolam, triazolam, cisapride, clarithromycin and ergot. EFV reduces levels of RBT, increase RFB dose to 450–600 mg/day or 600 mg 2x/week. Minimal RIF interaction, use standard doses of each. EFV reduces methadone levels, monitor for withdrawal Sx. Possibly significant interactions: Ethinyl estradiol (use alternative method of birth control) and warfarin (monitor pro-time). PIs: see Table 6–10, p. 34.

PREGNANCY: Category C, but birth defects in cynomolgus monkeys; avoid in women contemplating pregnancy and in first trimester of pregnancy. Some avoid throughout pregnancy.

Erythropoietin, EPO: *Procrit* (Ortho Biotech), *Epogen* (Amgen)

CLASS: Antianemic

INDICATIONS: Anemia with renal failure, drugs (AZT, ribavirin, etc.) HIV, cancer chemotherapy.

FORMS AND PRICE: Vials: 2,000 units, 3,000 units, 4,000 units, 10,000 units at \$120; 20,000 units and 40,000 units at \$11.13/1000 units.

REGIMENS: Initial dose 40,000 units SC q week. Response with increased hematocrit in 2 to 6 weeks; response correlates with degree of anemia, baseline EPO

level, EPO dose and iron stores. Supplemental Fe if ferritin levels <100 mg/mL. At 4 weeks if Hgb increases <1 gm/dL, increase dose to 60,000 USC/week. If increase in Hgb is still <1 gr/dL after another 4 weeks, d/c. Expect full response to require >4 weeks. If response is adequate, titrate maintenance dose. If HCT >40% or Hgb >13 g/dL, decrease EPO 10,000 U/week or d/c. If no response, consider Fe deficiency, occult blood loss, folic acid, B₁₂ deficiency, or hemolysis.

PATIENT INSTRUCTIONS: Requires SC injections at weekly intervals; most patients prefer self injections.

WARNINGS: Must evaluate cause of anemia: bleeding—stool guiac; hemolysis (TTP, drugs)—smear, LDH, retic count; Fe deficiency—Fe/IBC; drug related—AZT, amphotericin B, ganciclovir, HU, pyrimethamine, interferon, sulfas, dapsone, ribavirin, primaquine—d/c and expect response <1 week; parvovirus B₁₉ infection—PCR of blood for virus; infection involving marrow (MAC, TB, histo, CMV); tumor—involving marrow (KS, lymphoma) marrow biopsy; major causes—AZT, HIV. Avoid continued use of EPO without attempt to titrate down or d/c when drug is ineffective or desired results have been achieved.

SIDE EFFECTS: Minor: Headache, arthralgias, flu-like Sx, edema, fatigue. EPO is contraindicated with uncontrolled hypertension

PREGNANCY: Category C

Ethambutol: *Myambutol* (Dura Pharmaceuticals, Wyeth-Lederle)

CLASS: Antimycobacterial

INDICATION: Infections due to MAC and *M. tuberculosis*.

FORMS AND PRICE: Tabs: 400 mg at \$1.99

REGIMENS

- TB: 15–25 mg/kg up to 2 g/day or 50 mg/kg up to 4.0 gm twice/week (some use 2.5 gm as the peak dose for DOT)
- MAC: 15 mg/kg, usually 800 or 1200 mg/day
- Dose modification in renal failure: CrCl 10–50 mL/min.: 15–25 mg/kg/24 to 36 hrs.; CrCl <10 mL/min.: 15–25 mg/kg/48h

PATIENT INSTRUCTIONS: Dose related ocular toxicity with decreased acuity, scotomata, decreased color discrimination, usually after >2 months and usually reversible. May be taken with food.

WARNINGS: With 25 mg/kg dose many advise baseline screening for visual activity and red-green color perception with repeat at monthly intervals; may be unilateral, so test both eyes. Gouty arthritis with ↑ uric acid levels. Dose reduction with renal failure.

DRUG INTERACTIONS: Al⁺⁺⁺ containing antacids decrease absorption.

PREGNANCY: Category C, use with caution.

Famciclovir: See Acyclovir, p. 85

Fenofibrate: *Tricor* (Abbott)

CLASS: Fibrate

INDICATIONS: Hypertriglyceridemia; risk of pancreatitis with levels >2000 mg/dL, possibly >1000 mg/dL.

FORMS AND PRICE: Caps: 67 mg at \$0.83

REGIMENS: 67 mg/day; increase as necessary at 4 to 8 week intervals to maximum 201 mg/day. Renal failure: Consider dose adjustment.

PATIENT INSTRUCTIONS: Take once daily with meal. Combine with lifestyle changes, diet, exercise, weight loss, etc. Contact provider if symptoms of myositis with muscle pain, tenderness or weakness.

WARNINGS: Myositis with muscle weakness, tenderness or pain + fever and malaise—get CPK and d/c if Sx typical. Dose-related hepatotoxicity—d/c if ALT >3 x ULN (most return to normal with or without continued Rx). Increased risk of rhabdomyolysis with renal failure and statins. Avoid or use with caution with gallbladder disease, hepatic disease or renal failure.

MONITOR: Blood lipids; d/c if no response to maximum dose (201 mg for ≥2 mos.). LFTs if dose is 134–201 mg/day. Creatinine kinase in any patient with muscle pain, weakness, or tenderness.

SIDE EFFECTS: Myositis; rhabdomyolysis—rare. Hepatitis with ALT >3 x ULN in 3% of recipients of 134–201 mg/day. Flu-like syndrome.

DRUG INTERACTIONS: Warfarin—potentiated. Statins—increased risk of myositis and rhabdomyolysis. Cholestyramine or colestipol bind fenofibrate, take fenofibrate >1 hr. before or 4 to 6 hrs. after.

PREGNANCY: Category C; not recommended unless benefit justifies risk.

Fentanyl: *Duragesic* (Janssen), *Fentanyl Oralet* (Abbott)

CLASS: Opiate, Schedule II

INDICATION: Chronic pain requiring opiate.

FORMS AND PRICE: Transdermal patches: 25 at \$12.20 (to deliver 25 mcg/hr. with 2.5 mg/cm²), 50 at \$20.40 (50 ug/hr.), 75 at \$32.60 (75 ug/hr.), 100 at \$40.60 (100 ug/hr.)

REGIMENS: Initial dose is 25 µg/hr. patch q72h in opiate naive patients and in those previously receiving ≤135 mg oral morphine. With 25, delivery is 25

µg/hour at constant rate; peak level of 0.3–1.2 µg/mL at 12 to 24 hours which is sustained 72 hours. Peak levels with 50 µg/hour patch: 0.6–1.8 ng/mL; 100 µg/hour: 1.9–3.8 ng/mL. (Increased risk of respiratory depression at >2 ng/mL and CNS depression at >3 ng/mL). Adequacy of analgesia should be evaluated at 72 hours. If inadequate, option is to increase dose, give 25 µg/hour patch q48h or supplement with other opiates. Equivalence with oral morphine sulfate (MS): Fentanyl patch 25: MS 45–134 mg; Fentanyl patch 100: MS 315–404 mg; Fentanyl patch 200: MS 675–764 mg; Fentanyl patch 300: MS 1034–1124 mg.

PATIENT INSTRUCTIONS: Apply to dry, non-irritated, flat surface of upper torso with firm pressure x 30 sec. Clean area with soap and water, and clip hair (don't shave) prior to application. Rotate sites. After use, fold system so it adheres to itself and flush in toilet. Other CNS depressants are additive. Warn of CNS toxicity with confusion and drowsiness, and anticholinergic effects with constipation, postural hypotension, dry mouth, urine retention.

WARNINGS: Respiratory depression, esp. with concentrations >2 ng/mL (usually ≥75 µg/hr.) in opiate naive patients and patients with chronic lung disease. CNS depression with concentrations >3 ng/mL in opiate naive patients. Tolerance with extended use. Need for higher dose in opiate experienced patients. PIs may increase Fentanyl levels.

MONITOR: Heart rate, respiratory rate, degree of sedation.

SIDE EFFECTS: Respiratory depression with hypoventilation, esp. with ≥2 ng/mL. CNS depression, esp. with ≥3 ng/mL. Anesthesia and profound respiratory depression with 10–20 ng/mL. Tolerance with chronic use.

DRUG INTERACTIONS: CNS depressants increase risk of respiratory failure; anticholinergics and antidiarrheal agents increase risk of constipation; caution or avoid use of MAO inhibitor within 14 days; naloxone antagonizes CNS depression, but may precipitate withdrawal symptoms; opioids often given to supplement rapid action, for break-through pain and between patch applications—risk of CNS depression is additive.

PREGNANCY: Category C

Fluconazole: *Diflucan* (Pfizer)

CLASS: Triazole

INDICATION: Fungal infections.

FORMS AND PRICE: Tabs: 50 mg at \$4.90, 100 mg at \$7.70, 150 mg at \$11.66, 200 mg at \$12.60; IV vials: 200 mg at \$85.50

PATIENT ASSISTANCE: 800–646–4455

REGIMENS

- *Candida*: Thrush: 50 or 100 mg/day x 14 days; esophagitis: 200 mg/day x 2 to 3 weeks; vaginitis: 150 mg x 1

- *Cryptococcus*: Non-meningeal: 200–400 mg/day. Meningitis: 400 mg/day x 8 weeks then 200 mg/day (usually follows induction with amphotericin)
- *C. immitis*: Maintenance 200 mg/day
- Renal failure: CrCl >50 mL/min.: standard; 10–50 mL/min.: Half dose; <10 mL/min.: Quarter dose
- IV: Oral bioavailability >90%, give IV if NPO

PATIENT INSTRUCTIONS: Take without regard to meals.

WARNINGS: Long term use for candidiasis risks azole-resistant *Candida*. Reversible alopecia—10% to 20% with ≥400 mg/day. Marked increase in RBT levels: Monitor for RBT toxicity with uveitis, nausea, neutropenia.

SIDE EFFECTS: GI intolerance—2% to 8%. Elevated AST/ALT to >5 x ULN—1%. Reversible alopecia with ≥400 mg/d at median time of 3 mos.

DRUG INTERACTIONS: Inhibits P450 metabolic pathway to increase levels of atovaquone, benzodiazepines, clarithromycin, opiates, warfarin, RBT and cyclosporin. RIF and RBT reduce fluconazole levels.

PREGNANCY: Category C

Flucytosine, 5-FC: *Ancobon* (ICN)

CLASS: Antifungal

INDICATIONS: Deep infection caused by *Cryptococcus* and *Candida* sp.

FORMS AND PRICE: Caps: 250 mg, 500 mg at \$2.52

REGIMENS: Use with amphotericin B or fluconazole for induction phase treatment of cryptococcal meningitis. 25 mg/kg PO q 6h (fourteen 500 mg caps/day for 70 kg person). Renal failure: CrCl 20–40 mL/min.: 0.5 dose (standard dose q12h); 10–20 mL/min.: 0.25 dose (standard dose q24h); <10 mL/min.: Not recommended.

PATIENT INSTRUCTIONS: Warn of large pill burden.

WARNINGS: Dose related neutropenia and thrombocytopenia. Need to adjust dose with renal failure that is common with amphotericin B.

MONITOR: Optional monitoring of serum levels at 2 hrs. post dose; goal is 50–100 mcg/mL. Hepatitis, GI intolerance, and marrow suppression correlate with dose and are most common with levels >100 mcg/mL.

SIDE EFFECTS: Neutropenia and thrombocytopenia, esp. with renal failure, concurrent marrow suppressing drugs. GI intolerance, rash, hepatitis, peripheral neuropathy.

PREGNANCY: Category C. Teratogenic in animals.

Fluoroquinolones

PATIENT INSTRUCTIONS: Avoid concurrent antacids or sucralfate (including buffered ddi); take antacids ≥2 to 4 hours before or ≥2 hours after FQ. Avoid during pregnancy.

■ TABLE 11–9: Comparison of Commonly Used Fluoroquinolones

	Ciprofloxacin	Levofloxacin	Gatifloxacin	Moxifloxacin
Trade Name	<i>Cipro</i>	<i>Levaquin</i>	<i>Tequin</i>	<i>Avelox</i>
Manufacturer	Bayer	Ortho-McNeil	Bristol-Myers Squibb	Bayer
Form PO mg/tab	250, 500, 750	250, 500	200, 400	400
IV formulation	+	+	+	Expected winter 2001
Cost AWP PO	\$4.51/500 mg	\$8.53/500 mg	\$7.48/400 mg	\$8.71/400 mg
Usual dose PO	500–750 mg bid	500 mg/day	400 mg/day	400 mg/day
Usual dose IV	400 bid	500 mg/day	500 mg/day	—
Dose renal failure				
■ CrCl 10–50	■ 250–500 mg q12h	■ 250 mg/day	■ 400 mg q24h–q48h	■ 400 mg/day
■ CrCl <10	■ 250–500 q18h	■ 250 qod	■ 400 qod	■ 400 mg/day
■ Hemodialysis	■ 250–500 mg/day	■ 500 q48	■ —	■ 400 mg/day
Activity				
■ <i>S. pneumoniae</i>	++	+++	+++	+++
■ <i>P. aeruginosa</i>	+++	++	++	++
TB	+++	+++	+++	+++
Anaerobes	—	+	++	++

SIDE EFFECTS: Arthropathies in weight bearing joints of immature animals; significance in humans is unclear, but this finding is the basis for FDA contraindication to use in pregnant women and persons <18 years. GI intolerance, diarrhea—*C. difficile* (unusual). Class ADRs: CNS toxicity: headache, malaise, insomnia, restlessness, dizziness, hallucinations/delirium/psychosis/coma, all rare; prolonged QT interval (rare); tendon rupture (rare); and photosensitivity (rare).

DRUG INTERACTIONS: Decreased absorption with antacids containing cations (Mg⁺⁺, Ca⁺⁺, Al⁺⁺⁺), sucralfate, buffered ddi, or medicines containing Zn⁺⁺ or Fe⁺⁺. Avoid concurrent use. Increase activity of theophylline (*Cipro*) and possibly warfarin and cyclosporin. Decrease levels of phenytoin (*Cipro*).

PREGNANCY: Category C (all fluoroquinolones). Trials in humans have not been performed, but arthropathy in immature animals has resulted in the recommendation to avoid in pregnancy.

Foscarnet: *Foscavir* (Astra)

CLASS: Antiviral

INDICATIONS: Herpes viruses: CMV, HSV, EBV, VZV, HHV–6, HHV–8, ganciclovir resistant CMV, acyclovir resistant HSV and VZV.

FORMS AND PRICE: Vials: 6000 mg at \$73/day (usual maintenance dose); 12,000 mg at \$143/day (induction).

PATIENT ASSISTANCE: 800-488-3247

REGIMENS

- CMV: Induction: 90 mg/kg IV q12h x 14 days; maintenance: 90–120 mg/day IV
- HSV and VZV: 60 mg/kg IV q12h x 3 weeks.
- Infusion guidelines: Doses of ≤ 60 mg/kg must be over 1 hr.; higher doses over 2 hrs. Patient must be hydrated. Give undiluted (24 mg/mL) by central catheter; if using peripheral vein, dilute 1:1 to 12 mg/mL with D₅W or 0.9% saline.

■ TABLE 11-10: Foscarnet Dose With Renal Failure

CrCl (mL/min./kg)	60 mg/kg dose	90 mg/kg dose	120 mg/kg dose
>1.4	60	90	120
1.3	49	78	104
0.9	35	71	94
0.5	21	57	76

PATIENT INSTRUCTIONS: Report symptoms of hypocalcemia: Perioral and extremity paresthesias and numbness. Wash genitals after urination to avoid ulceration. Maintain fluid intake.

WARNINGS: High rate of nephrotoxicity: Must hydrate patient, give foscarnet by slow infusion, reduce dose in renal failure and avoid concurrent nephrotoxic drugs. Note marrow toxicity and electrolyte imbalance. Usual peak dose for initial Rx is 90 mg/kg bid; the 120 mg/kg dose is always included in recommendations but has no evidence of superiority.

MONITOR: Renal function and CBC 2–3x/week during induction and every week during maintenance. Ca⁺⁺ (total and ionized), Mg⁺⁺, PO₄, K⁺ 2–3x/week during induction and every week during maintenance. If neurologic or cardiac Sx suggest hypocalcemia despite normal total Ca⁺⁺, measure ionized Ca⁺⁺ at end of infusion.

SIDE EFFECTS: Renal failure with creatinine >2 mg/dL in 37%, usually in week 2. Electrolyte changes: Low Ca⁺⁺—15%, PO₄—8%, Mg⁺⁺—15%, K⁺—16%. Anemia—33% of 189 patients in 5 controlled trials, but only 1 required d/c of foscarnet. Neutropenia—17% of 189 patients in 5 controlled trials, but only 2 required d/c foscarnet. Seizures (renal failure and hypocalcemia). Penile, vulvar, or oral ulcers.

DRUG INTERACTIONS: Avoid concurrent use of nephrotoxic drugs. Concurrent IV pentamidine may cause severe hypocalcemia; AZT may increase anemia.

PREGNANCY: Category C

Ganciclovir: *Cytovene*—oral, *Cytovene*—IV, *Valcyte*—oral valganciclovir (Roche); *Vitraser*—intraocular release device (Chiron Vision)

CLASS: Antiviral; valganciclovir is a prodrug.

INDICATIONS: Visceral or retinal CMV infection.

- CMV Retinitis: *Vitraser* + oral valganciclovir. IV ganciclovir induction and maintenance. IV ganciclovir induction and valganciclovir maintenance
- CMV Polyradiculopathy and encephalitis: IV ganciclovir induction and maintenance + foscarnet (response variable; quality of life with ganciclovir + foscarnet is poor)
- CMV Esophagitis: IV ganciclovir induction, then IV ganciclovir or PO valganciclovir maintenance (response usually good)
- CMV Colitis: As above (response variable)

FORMS AND PRICE: Ganciclovir caps: 250 mg at \$4.28 and 500 mg at \$8.56; Valganciclovir caps: 450 mg at \$23.97; IV vials 500 mg at \$35.68; *Vitraser* at \$600/device/6 mos.

PATIENT ASSISTANCE: *Cytovene*: 800-285-4484; *Vitraser*: 800-843-1137

ACTIVITY: Active against herpes viruses CMV, HSV1, HSV2, EBV, VZV, HHV-8. Not active against most acyclovir-resistant HSV.

REGIMENS

- IV: 5 mg/kg IV q12h x 14 to 21 days (induction); 5 mg/kg/day (maintenance)
- Oral: Valganciclovir 900 mg (2 tabs) bid x 21 days (induction); 900 mg/day (maintenance)
- Oral: Ganciclovir, 1000 mg tid
- Ganciclovir intraocular release device (*Vitraser*): q6mo

■ TABLE 11-11: Ganciclovir Dose in Renal Failure

CrCl (mL/min.)	IV*	Ganciclovir PO	Valganciclovir*
>80	5 mg/kg q12h	1000 mg tid	900 mg bid
50-79	2.5 mg/kg q12h	500 mg tid	900 mg bid
25-49	2.5 mg/kg q24h	500 mg/day	450 mg bid
<25†	1.25 mg/kg q24h	500 mg 3x/wk.	450 mg qod

*Induction doses. Maintenance doses after 3 wks. should be 1/2 induction dose

†Not recommended for CrCl <10 mL/min.

PATIENT INSTRUCTIONS: Oral ganciclovir and valganciclovir must be taken with meal—doubles absorption of pills that cost \$50/day.

WARNINGS: Neutropenia with ANC <500/mL in 25% to 40% given IV ganciclovir, also common with PO form—d/c or give G-CSF; baseline <500/mm³ is contraindication. Thrombocytopenia (<25,000/dL) in 2% to 8%; baseline platelet count <25,000/dL is contraindication. Anemia with Hgb <8 gm % in 10%. Valganciclovir has largely replaced oral ganciclovir for PO use due to better absorption (60% vs 6%) at comparable cost. Standard dose of valganciclovir (900 mg/day) actually gives levels comparable to standard IV doses. CMV resistance noted in 25% to 30% treated 12 months.

MONITOR: IV and PO forms—CBC 2–3x/wk. If given with ddl, monitor for ddl toxicity since ddl levels increase 2x.

SIDE EFFECTS: Marrow suppression, see above. Renal failure: Creatinine >2.5 mg/dL—4%; >1.5 mg/dL—73%.

DRUG INTERACTIONS: Marrow suppressing drugs: AZT, interferon, ribavirin, sulfadiazine, TMP-SMX, HU. ddl AUC increased 100%.

PREGNANCY: Category C

G-CSF or Filgrastim: *Neupogen* (Amgen)

CLASS: 20 kd glycoprotein recombinant that stimulates granulocyte precursors.

INDICATIONS: ANC <500–750/mm³ usually due to drugs (AZT, ganciclovir, interferon, TMP-SMX, HU), HIV *per se*. Chemotherapy for tumors.

FORMS AND PRICE: 300 µg/1 mL vial at \$165.30; 480 µg vials

REGIMEN: Initial 5–10 µg/kg/day SC (lean body weight); increase by 1 µg/kg q 5 to 7 days up to 10 µg/kg/day; alternatively decrease 1 µg/kg/day, give qod or d/c. If unresponsive to 10 µg/kg/day x 7 days—d/c.

PATIENT INSTRUCTIONS: Most patients self inject SC using abdomen, or upper thighs; if other person administers, use upper arms. Injection sites should be rotated. Drug should be stored at 36° to 46° F (refrigerate).

WARNINGS: Biggest mistake is “runaway G-CSF,” meaning continued administration after ANC returns to safe range and wastage due to discarding unused portion in vial. To avoid waste (and increased cost), save residual in separate syringe that is refrigerated.

MONITOR: CBC 2x/week and keep ANC >1000–2000/mm³

SIDE EFFECTS: Medullar bone pain—10% to 20%; usually controlled with acetaminophen.

DRUG INTERACTIONS: None

PREGNANCY: Category C

Gemfibrozil: *Lopid* (Parke-Davis), generic (various manufacturers)

CLASS: Fibrate

INDICATIONS: Elevated blood lipids, esp. triglyceride (may increase LDL cholesterol). Risk of pancreatitis with triglyceride levels >2000 mg/mL.

FORMS AND PRICE: Tabs: 600 mg at \$1.10

REGIMEN: 600 mg bid PO >30 min. before meal. Renal failure or hepatic failure: Reduce dose.

PATIENT INSTRUCTIONS: Take >30 min. before morning and evening meal. Combine with lifestyle changes, diet, exercise, weight loss, etc. Increased risk of myositis when given with statin.

WARNINGS: Contraindicated with gallbladder disease, primary biliary cirrhosis, hepatic failure, and renal failure. May increase LDL cholesterol. Gemfibrozil increases risk of myositis and rhabdomyolysis with concurrent statins.

MONITOR: Blood lipids: Discontinue gemfibrozil if marked increase in LDL cholesterol or if there is no decrease in triglyceride level at 3 months. Obtain CBC and LFTs at baseline, at 3 to 6 months, and then annually.

SIDE EFFECTS: Gallstones and cholecystitis. Increases LDL cholesterol. GI intolerance. Marrow suppression. Hepatotoxicity.

DRUG INTERACTIONS: Statins: increased risk of myositis and rhabdomyolysis. May increase anticoagulant effect of warfarin.

PREGNANCY: Category C

Growth Hormone: *Serostim* (Serono)

CLASS: Recombinant human growth hormone

INDICATIONS: FDA labeling: AIDS associated wasting or cachexia; sometimes used for lipodystrophy with fat redistribution.

FORMS AND PRICE: Vials: 4 mg (about 12 IU), 5 mg (16 IU), 6 mg (18 IU) at \$42/mg. Average daily cost \$252 or \$21,000/12 wk. course

PATIENT ASSISTANCE: 888-628-6673

REGIMENS: SC injection at hs with weight adjusted dose: >55 kg, 6 mg; 45-55 kg, 5 mg; 35-45 kg, 4 mg

PATIENT INSTRUCTIONS: Most self administer in abdomen or upper thighs and rotate sites. Warn of self limited muscle discomfort and swelling of hands and feet.

WARNINGS: Incredibly expensive drug that increases lean body mass about as much as resistance exercise program 3x/week. When used for lipodystrophy, concerns include possible increase in lipoatrophy and glucose intolerance.

MONITOR: Blood glucose.

SIDE EFFECTS: Fluid and sodium retention with edema, arthralgias and hypertension. Muscle discomfort—20% to 50%; swelling of hands and feet—25%, usually resolves with continued Rx. Flu-like Sx, back pain, malaise, carpal tunnel syndrome, chest pain, nausea, diarrhea

PREGNANCY: Category B

Hydroxyurea, HU: *Droxia, Hydrea* (Bristol-Myers Squibb), generic (various manufacturers)

CLASS: Antineoplastic

INDICATIONS: Augments activity of ddl, both anti-HIV activity and toxicity.

FORMS AND PRICE: Caps: 500 mg at \$1.42

REGIMENS: 500 mg bid or 1000 mg/day (with ddl)

PATIENT INSTRUCTIONS: Strictly avoid during pregnancy or in patients contemplating pregnancy.

WARNINGS: Give with ddl. Potentiates ddl antiviral activity, but also toxicity, including pancreatitis, peripheral neuropathy, and possibly lactic acidosis. Marrow suppression is dose related and reversible. Suppresses increase in CD4 cell count.

SIDE EFFECTS: Dose dependent marrow suppression with leukopenia, anemia and thrombocytopenia—5% to 7%. Leukopenia usually noted first; rapid recovery when drug is discontinued. GI intolerance, rash.

DRUG INTERACTIONS: HU may increase uric acid levels, may need dose adjustment of gout meds; drugs that suppress marrow may potentiate this side effect.

PREGNANCY: Category D (evidence of risk to fetus).

Indinavir, IDV: *Crixivan* (Merck)

CLASS: PI

INDICATIONS: Potent PI that may be combined with RTV to permit more convenient bid dosing.

FORMS AND PRICE: Caps: 200 mg, 333 mg, 400 mg at \$2.78

PATIENT ASSISTANCE: 800-850-3430

REGIMEN: 800 mg (two 400 mg tabs) q8h, fasting 1 hr. before or 2 hrs. post meal or with light snack. Renal failure: Standard dose. Hepatic failure: Consider dose reduction to 600 mg q8h. Common combination: IDV 800 mg bid + RTV 100-200 mg bid or IDV 400 mg bid + RTV 400 mg bid.

PATIENT INSTRUCTIONS: IDV (only PI) must be taken q8h (not tid). Take in fasting state (empty stomach) or with light meal/snack (toast and jelly, juice, coffee with skim milk and sugar, corn flakes with skim milk, etc.). Full meal decreases absorption by 77%. Must drink >48 oz fluids/day, preferably at time of IDV ingestion to prevent IDV calculi. Patient should be aware of risk of renal calculi and symptoms (blood in urine, acute flank pain) and sicca syndrome (dry skin, eyes, mouth). Avoid concurrent buffered ddl. Warn of lipodystrophy and fat redistribution.

PATIENT INSTRUCTIONS FOR IDV + RTV: This combination may be taken bid and without regard to meals. The admonition to ingest 48 oz fluids applies. The risk of renal calculi is substantially greater with the regimen of IDV 800 mg + RTV 100 mg bid compared to the 400/400mg bid regimen, but the former shows better GI tolerance.

WARNINGS: Monitor for nephrotoxicity with U/A⁺ serum creatinine at intervals not clearly defined. There was initial concern about IDV use in pregnancy due to increase in indirect bilirubin (third trimester) and possible renal calculi *in utero*; initial experience has not shown excess complications attributed to either complication. See drug interactions.

MONITOR: Urinalysis every 3 to 4 mos.; fasting lipids and glucose at baseline, at 3 to 4 mos. and then prn.

SIDE EFFECTS: Nephrolithiasis in 10% to 28% which correlates with peak plasma level >10 mg/L and AUC >30 mg/L hr. Nephrotoxicity with urine sediment changes and increased creatinine that may be independent of nephrolithiasis. Mucocutaneous: Paronychia, alopecia, ingrown toenails; dry skin, eyes and mouth. GI intolerance: Abdominal pain, diarrhea, vomiting, nausea, taste perversion. Class adverse reactions: Lipodystrophy.

DRUG INTERACTIONS: Contraindicated: RIF, astemizole, terfenadine, cisapride, midazolam, triazolam, ergotamine, simvastatin, lovastatin, St. John's wort. ddl—use *Videx EC* or separate dose of buffered formulation by >2 hrs. RBT—increase IDV to 1000 mg q8h plus RBT 150 mg/day or 300 mg 2x/week. Ketoconazole and itraconazole—decrease IDV dose to 600 mg q8h. Sildenafil—dose should not exceed 25 mg/48 hrs.

CAUTION: Anticonvulsants, methadone. PI/NNRTI combinations: See Tables 6–9 and 6–10, pp. 33–34.

PREGNANCY: Category C

Interferon and Pegylated Interferon: *Roferon A*, *PEGASYS* *Intron* (Roche), *Intron A*, *PEG-Intron* (Schering)

CLASS: Biological response modifiers

INDICATIONS: Hepatitis B and hepatitis C, Kaposi's sarcoma.

FORMS AND PRICE

■ TABLE 11–12: Interferon and Pegylated Interferon Forms and Prices

Product	Manufacturer	Vials (mil. units)	Cost/unit
Interferon alfa 2a (<i>Roferon</i>)	Roche	3, 6, 9, 18, and 36 mil	\$11.36/mil
Interferon alfa 2b (<i>Intron</i>)	Schering	3, 5, 10, 18, 25, and 50 mil	\$11.89/mil
Pegylated interferon alfa 2a (<i>PEGASYS</i>)	Roche	Not yet FDA approved	—
Pegylated interferon alfa 2b (<i>PegIntron</i>)	Schering	1 mL vials with 100, 160, 240, and 300 µg/mL	\$287/wk

■ TABLE 11–13: Regimen for Hepatitis C Treatment

Weight	Pegylated interferon (weekly)*		Ribavirin
	Alfa 2b	Alfa 2c	
>75 kg	1.5 µg/kg	180 µg	1000 mg/day see p. 131 or 10.6 mg/kg/day
<75 kg	1.5 µg/kg	180 µg	1200 mg/day see p. 131 or 10.6 mg/kg/day

*SC injections usually for 24 to 48 wks.

INDICATIONS: Medical indications (liver biopsy showing bridging fibrosis or moderate inflammation + necrosis) + patient acceptance + absence of contraindications + stable HIV.

PATIENT INSTRUCTIONS: Pegylated interferon requires weekly SC injections x 48 weeks. *Peg-Intron*: Reconstitute powder in 0.7 mL sterile water provided in kit. Give SC in abdomen or thigh and rotate injection sites. Probability of cure (sustained virologic response) is about 50% (more if genotype 2 or 3 and less if genotype 1). Anticipate severe side effects with flu-like Sx and depression in >30%. Pregnancy forbidden (see ribavirin).

WARNINGS: Contraindications to interferon: Current or prior psychosis, severe depression, neutropenia, thrombocytopenia, symptomatic heart disease, decompensated cirrhosis, uncontrolled seizures, organ transplantation. Relative contraindications: Autoimmune disorders, uncontrolled diabetes. Ribavirin contraindications: Pregnancy, lack of effective contraception, renal failure, anemia, hemoglobinopathy.

MAJOR TOXICITIES: Flu-like Sx (fever, fatigue, chills, headache, etc.), depression and other mental status changes, leukopenia.

MONITOR: CBC at 2 weeks and 4 weeks; CBC, LFTs, chemistry profile q 7 weeks; TSH and HCV RNA PCR every 3 months. If HCV RNA PCR not ↓ 2 logs at 12 to 24 weeks, consider discontinuation. Post therapy: HCV RNA PCR at 4,

12, and 24 weeks; negative results at 24 weeks indicates sustained virologic response or cure.

TOXICITY MONITORING: See HIV Co-Morbidities: HCV Treatment, p. 63.

- Hgb <10 gm/dL or decrease 2 gm/dL: Reduce ribavirin to 600–800 mg/day ± EPO.
- Hgb <8.5 gm/dL: d/c ribavirin and monitor, usually restart in 4 wks.
- ANC <750: Reduce interferon dose or d/c ± G-CSF.

SIDE EFFECTS (INTERFERON): In >30%: Flu-like Sx and thrombocytopenia. In 1% to 30%: Insomnia, alopecia, emotional instability, depression, diarrhea, autoimmune disease, leukopenia, taste perversion. In <1%: Polyneuropathy, suicide, diabetes, hearing loss, seizures, cardiotoxicity.

MANAGING SIDE EFFECTS

- Give PM injections of interferon
- Flu-like Sx: Acetaminophen, rofecoxib (25–50 mg/day), NSAIDS, hydration
- Psychiatric: Depression: SSRIs (venlafaxine, citalopram), trazodone, bupropion, mirtazapine. Insomnia—Rx tricyclics. Agitation—Rx olanzapine.
- Severe depression: d/c interferon
- Rash: Topical steroids
- Alopecia: Reversible, consider minoxidil
- Dry eyes and nose: Topical saline
- Pruritus: *Lac-Hydrin* lotion, antihistamine (*Atarax*, cetirizine), topical steroids
- Anemia: See ribavirin, p. 131
- ANC <750/mm³: d/c interferon ± G-CSF
- ITP <80,000/mm³: Reduce interferon dose 50%. <50,000/mm³: d/c interferon

DRUG INTERACTIONS: Avoid/caution with CNS depressants. Avoid/caution with marrow suppressants.

PREGNANCY: Category C

Isoniazid (INH): generic (Novartis)

CLASS: Antimycobacterial

INDICATIONS: Treatment of active and latent TB.

FORMS AND PRICE: Tabs: 50 mg, 100 mg, 300 mg at \$0.70; solution: 50 mg/5 mL. 300 mg vials for injection

REGIMENS

■ TABLE 11–14: INH Regimens for Prophylaxis and Treatment

	Daily	DOT	Pyridoxine (Vit B6)
Prophylaxis	300 mg	900 mg 2x/wk.	50 mg/day or 100 mg 2x/wk.
Treatment	300 mg	900 mg 2x/wk.	50 mg/day or 100 mg 2x/wk.

RENAL FAILURE: Half dose with CrCl < 10 mL/min.

PATIENT INSTRUCTIONS: Alert to Sx of hepatitis: Nausea, vomiting, jaundice, dark urine, abdominal pain; d/c INH and contact provider. Report Sx every month. Avoid alcohol abuse, social drinking is okay. ETOH increases risk of hepatitis. Report Sx of peripheral neuropathy: Paresthesias, unsteadiness (unlikely with pyridoxine). Take INH with food or antacids, but not Al⁺⁺ containing antacids.

WARNINGS: Provider should write INH scripts for one month at a time. Baseline ALT, AST and bilirubin. Repeat at 3 mos. and with hepatitis Sx. Discontinue INH if ALT/AST > 3x ULN plus symptoms or > 5x ULN and no symptoms. Pregnancy: Begin INH prophylaxis after 1st trimester if possible.

SIDE EFFECTS: Hepatitis—risk is 0.3% in young healthy adults; increases to 2.6% in the elderly. Risk also increases with heavy ETOH ingestion or chronic liver disease. Peripheral neuropathy: Prevented with 10–25 mg pyridoxine/day, which is recommended for HIV infected persons. Rash, fever, GI intolerance, psychosis, adenopathy, arthralgias, optic neuropathy, marrow suppression.

DRUG INTERACTIONS: No interactions with ART agents. Increases effect of warfarin, benzodiazepines, carbamazepine, cycloserine, ethionamide, phenytoin, and theophylline. Decreased absorption of INH with Al⁺⁺ containing antacids. Decrease levels of ketoconazole. Interaction with cheese or fish (tuna, skipjack, sardines): Red, itching, chills, hot feeling, sweating due to INH interference with tyramine metabolism.

PREGNANCY: Category C. ATS recommendation: Pregnant women with HIV and positive PPD should receive INH; delay until after 1st trimester if possible.

Itraconazole: *Sporanox* (Janssen)

CLASS: Antifungal

INDICATIONS: Fungal infections.

FORMS AND PRICE: Caps: 100 mg at \$7.39; Oral solution: 10 mg/mL at \$116.58/150 mL/bottle or \$7.73/100 mg; IV formulation: 10 mg/mL at \$176.23/250 mg

PATIENT ASSISTANCE: 800–544–2987

ACTIVITY

■ TABLE 11–15: Dose Recommendations for Itraconazole

Pathogen	Dose	Comment
<i>Aspergillus</i>	200–400 mg/day	Amphotericin B often preferred for initial treatment
Blastomycosis	200 mg/day or bid	—
<i>Candida</i>		Fluconazole preferred*
<ul style="list-style-type: none"> ■ Thrush ■ Esophagitis ■ Vaginal 	<ul style="list-style-type: none"> ■ 200 mg liquid swish and swallow ■ 200 mg/day ■ 200 mg/day x 3 or 200 mg bid x 1 	
Coccidioidomycosis	200–400 mg bid	Fluconazole preferred*
Cryptococcosis	200 mg bid	Fluconazole preferred*
Dermatophytes	100 mg/day	Baseline LFTs [†]
Histoplasmosis	200 mg bid	Itraconazole preferred
Onychomycosis	200 mg/day	Baseline LFTs [†]
<ul style="list-style-type: none"> ■ Fingernails ■ Toenails 	<ul style="list-style-type: none"> ■ 1 wk./mo. x 2 ■ 1 wk./mo. x 4 	
<i>Penicillium marneffei</i>	400 mg bid x 2 mos. Then 100 mg/day x 1 mo.	Efficacy shown, but relapses are common
Sporotrichosis	200 mg bid	—

*Fluconazole often preferred due to more predictable oral absorption, better CNS penetration with CNS infections, and fewer drug interactions

[†]Concern for use for trivial infections due to neg inotropic effect and rare cases of serious hepatitis

REGIMEN: Loading dose: 200 mg tid x 2 days for serious infections. IV: 200 mg IV bid x 4 loading dose, then 200 mg/day. Dose modification for renal failure: None. Dose modification for liver failure: No data.

PATIENT INSTRUCTIONS: Caps require food and gastric acid for absorption—take with food ± an acidic drink such as cola, seltzer water, or orange juice. Liquid formulation should be taken on an empty stomach for maximum absorption. Grapefruit juice decreases AUC 30%, avoid concurrent use. Warn regarding symptoms of hepatitis.

WARNINGS: Negative inotropic effect with decreased ejection fraction. Rare cases of hepatotoxicity: Need baseline LFTs when given for dermatophytic infection. Loading dose only for life-threatening infections. Caps and liquid are not bioequivalent. Blood levels of itraconazole recommended for cases where absorption/compliance questioned. Due to long half life of drug get level any time >2 hours post dose after steady state achieved with >5 to 7 days of ther-

apy. Desire level ≥ 1 mcg/mL. See drug interactions: Greater in number and severity than fluconazole.

RESOURCES FOR BLOOD LEVEL: Dr. J. Wheat, Indianapolis 317-630-2515 or Dr. Michael Rinaldi, San Antonio 210-567-4131. CLIA # 15 D0647154; CPT # 80299. Cost is \$60/test. Send 2-4 mL serum or plasma in frozen state. Goal is level > 1 mcg/mL.

MONITOR: LFTs in patients with baseline abnormal LFTs. Itraconazole levels if compliance or absorption questioned; goal is level > 1 μ g/mL.

SIDE EFFECTS: Negative inotropic effect with decreased cardiac output. Increased transaminase levels—4%; rare cause of liver failure. GI intolerance—3% to 10%. Rash—1% to 9%.

DRUG INTERACTIONS: Absorption of itraconazole caps decreased with H₂ blockers, omeprazole, antacids, sucralfate, buffered ddi; not problematic with liquid formulation. Contraindicated for concurrent use: Terfenadine, cisapride, astemizole, carbamazepine, triazolam, lovastatin, simvastatin, RIF, RBT, phenytoin, phenobarbital. Itraconazole increases levels of loratadine, cyclosporine, oral hypoglycemics, calcium channel blockers, digoxin, lovastatin, simvastatin. IDV levels are increased—decrease IDV dose to 600 mg q8h.

PREGNANCY: Category C

Ketoconazole: *Nizoral* (Janssen, McNeil)

CLASS: Antifungal, imidazole

INDICATIONS: Fungal infections.

FORMS AND PRICE: Tabs: 200 mg at \$3.37; 2% Cream: 15 gm, 30 gm at \$28.21, 60 gm; 2% Shampoo: 120 mL at \$20.74

PATIENT ASSISTANCE: 800-544-2987

REGIMENS

- Thrush: 200 mg PO/day x 14 days
- *Candida* esophagitis: 200-400 mg PO bid x 4 wks.
- *Candida* vaginitis: 200-400 mg/day PO x 7 days or 400 mg/day PO x 3 days
- Seborrhea: Shampoo (1%) q 3 to 4 days up to 8 wks.
- Dermatophytic infection: 2% cream apply qd x 2 to 4 wks.
- Systemic fungi: 200-400 mg/day
- Dose in renal failure: Standard
- Dose in hepatic failure: Standard

PATIENT INSTRUCTIONS: Take with food. Gastric acid promotes absorption—take antacids, buffered ddi, H₂ blockers etc. > 2 hours apart or substitute. Avoid alcohol, may produce disulfiram-like reaction. Warn about the possible hepa-

totoxicity and dose related consequences of cortisone and testosterone synthesis.

WARNINGS: Less effective than fluconazole for *Candida* esophagitis, but ketoconazole may be more cost effective (*Ann Intern Med* 1992;117:655). With gastric achlorhydria give 580 mg glutamic acid, or give 240 mL cola, ginger ale, seltzer water, orange juice (*Antimicrob Agent Chemother* 1995; 39:1671). High doses (>600 mg/day) for prolonged periods may reduce steroid production with lower testosterone levels and sexual dysfunction. Drug interactions including PIs, see below.

SIDE EFFECTS: GI intolerance. Temporary increase in transaminase; hepatic failure in 1/15,000; usually reversible. Dose-related decrease in steroid and testosterone synthesis with impotence, gynecomastia, reduced libido, menstrual abnormalities (usually with ≥ 600 mg/day for prolonged periods). Rare—headache, dizziness, asthenia, rash, marrow suppression, hypothyroidism, hallucinations, and adrenal suppression.

DRUG INTERACTIONS: Increased gastric pH reduces ketoconazole absorption—take antacids, H₂ blockers, proton pump inhibitors, buffered ddl ≥ 2 hours apart or use alternative azole. ETOH—possible disulfiram-like reaction. Increased levels of warfarin, theophylline, digoxin and cyclosporine.

■ TABLE 11–16: Drug Interactions: Ketoconazole With PIs and NNRTIs

Agent	Change	Ketoconazole	Recommendation
IDV	↑ 68%	—	IDV dose - 600 mg q 8h
APV	↑ 31%	↑ 44%	Dose changes unclear
SQV	↑ 3 x	—	—
RTV	—	↑ 3 x	Ketoconazole dose ≤ 200 mg/day
NFV	—	—	Standard dose
NVP	↑ 20%	↓ 63%	Avoid
EFV	?	?	No data

PREGNANCY: Category C

Lamivudine (3TC): *Epivir* (GlaxoSmithKline)

CLASS: NRTI

INDICATIONS: Potent and well tolerated NRTI with high frequency single mutation (RT 184) that reduces but does not eliminate anti-HIV activity.

FORMS AND PRICE: Tabs: 150 mg at \$4.47; Oral solution: 10 mg/mL at \$76.23/240 mL; *Combivir*: 150 mg 3TC/300 mg AZT at \$10.33; TZV: 150 mg 3TC/300 mg AZT/300 mg ABC at \$16.75.

PATIENT ASSISTANCE: 800–722–9294

REGIMENS: Dose for hepatitis B: 100 mg tab/day x 52 wks.; dose for HIV: 150 mg bid; possibly 300 mg/day.

■ TABLE 11-17: 3TC Dose Adjustment for Renal Failure

Renal failure	CrCl >50	30-49	15-29	5-14	<5/dialysis
HIV	150 mg bid	150 mg/day	100 mg/day	50 mg/day	25 mg/day
HBV	100 mg/day	50 mg/day	25 mg/day	15 mg/day	10 mg/day

PATIENT INSTRUCTIONS: Can be taken without regard for meals. Non-compliance or other causes of sub-optimal antiviral activity leads to rapid evolution of resistance.

WARNINGS: Need dose adjustment with renal failure. Patients with HBV coinfection may have increased ALT and HBV DNA levels when 3TC is discontinued. Use with partially suppressive antiretroviral regimen will usually cause 184 mutation with reduced 3TC anti-HIV activity (but 3TC does not induce other NRTI resistance mutations, and the 184 mutation does not eliminate 3TC activity). Frequency of hepatitis B virus resistance to 3TC is 50% to 90% in HIV infected patients given 3TC for 2 to 4 years (*Lancet* 2001;358:718).

SIDE EFFECTS: Infrequent: Headache, nausea, abdominal pain, insomnia.

DRUG INTERACTIONS: None

PREGNANCY: Category C

Lamotrigine: *Lamictal* (GlaxoSmithKline)

CLASS: Anticonvulsant

INDICATIONS: Peripheral neuropathy and seizures.

FORMS AND PRICE: Tabs: 25 mg at \$2.31, 100 mg at \$2.49, 150 mg at \$2.58, 200 mg at \$2.69

REGIMENS: 25 mg bid increasing to 300 mg/day over 6 wks. Renal failure: Plasma $T_{1/2}$ increases 25 hrs. → 43 hrs.

PATIENT INSTRUCTIONS: Take with or without food. Tabs may be chewed, swallowed or dispersed in water. Warn patient to discontinue at first sign of rash, ataxia, blurred or double vision.

WARNINGS: Rash—10% adults; severe enough to require hospitalization—0.3%, usually in first 8 weeks. Other HSRs include fever and adenopathy. $T_{1/2}$ increased with hepatic or renal failure; dose adjustments not clear.

SIDE EFFECTS: HSR: Skin rash, fever, adenopathy. Rash may include Stevens-Johnson syndrome, angioedema or TEN in up to .3%. Dose related: Ataxia,

blurred vision or diplopia. Infrequent: CNS toxicity with anxiety, confusion, depression.

DRUG INTERACTIONS: ETOH: Increased CNS depression. Decreases lamotrigine levels: Carbamazepine, phenobarbital, phenytoin, primidone.

PREGNANCY: Category C

Leucovorin, Folinic acid: *Wellcovorin*, generic (various manufacturers)

CLASS: Antidote for folic acid antagonists; reduced form of folic acid

INDICATIONS: Prevents hematologic toxicity of pyrimethamine.

FORMS AND PRICE: Tabs: 5 mg at \$2.02, 10 mg at \$5.75, 15 mg at \$8.66, 25 mg at \$19; Parenteral form: 50 mg at \$ 3.75, 100 mg at \$5.00, 350 mg at \$25.

REGIMENS:

- Toxoplasmosis Rx: Sulfadiazine 0.5–1 mg qid + pyrimethamine 25–50 mg/day + folinic acid 10–25 mg/day (maintenance after 6 week induction)
- Toxoplasmosis prophylaxis: Pyrimethamine 50 mg/week + folinic acid 25 mg/week + dapsone 50 mg/day
- Dose modification in renal or hepatic failure: None

PATIENT INSTRUCTIONS: No specific warning; side effects nil, absorption 97%, purpose is to prevent marrow suppression of pyrimethamine.

WARNINGS: Expensive, dose often unclear use parenteral form only if NPO.

SIDE EFFECTS: None

DRUG INTERACTIONS: Theoretical concern for concurrent use with TMP-SMX since leucovorin is an antidote to folic acid antagonists.

PREGNANCY: Category C

Lopinavir/Ritonavir (LPV/RTV): *Kaletra* (Abbott)

CLASS: PI

INDICATIONS: Potent and generally well tolerated. One of few regimens with equal antiviral potency in treatment naive patients with baseline VL above or below 100,000 c/mL; more effective as initial therapy than as salvage regimen.

FORMS AND PRICE: Caps: 133 mg LPV/33 mg RTV at \$3.76; PO solution: 80 mg LPV/20 mg RTV/mL at \$2.11 (\$338.54/160 mL bottle)

PATIENT ASSISTANCE: 800–659–9050

REGIMENS: 400 mg LPV/100 mg RTV (3 caps) or 5 mL bid with food.

PATIENT INSTRUCTIONS: Take with meals—improves absorption from 48% to 80%. Diarrhea is common side effect; usually responds to *Imodium* or calcium.

Warn of lipodystrophy and fat redistribution. Liquid formulation contains large amount of alcohol.

WARNINGS: See drug interactions, below

SIDE EFFECTS: Diarrhea—15% to 25%. Hepatitis. Class ADRs—lipodystrophy.

DRUG INTERACTIONS: Contraindicated for concurrent use: Astemizole, midazolam, triazolam, cisapride, pimozide, ergot, RIF. Reduce RBT dose to 150 mg qod + standard LPV/RTV dose. Levels of methadone reduced 53%—monitor for withdrawal. Atorvastatin AUC increased 6x; monitor for myopathy or use pravastatin or fluvastatin. Ketoconazole levels increased 3x. Anticonvulsants may decrease LPV levels. PI/NNRTI combinations; see Tables 6–9 and 6–10, pp. 33–34.

PREGNANCY: Category C

Megestrol: *Megace* (Bristol-Myers Squibb, Mead Johnson)

CLASS: Synthetic progestin

INDICATIONS: Promotes appetite; weight gain is primarily fat.

FORMS AND PRICE: Tabs: 20 mg at \$0.67; 40 mg at \$1.15; PO solution: 40 mg/mL at \$0.51

PATIENT ASSISTANCE: 800–272–4978

REGIMENS: Suspension (preferred) 400–800 mg (10–20 mL)/day; tabs 80 mg PO qid up to 800 mg/day.

PATIENT INSTRUCTIONS: May cause hypogonadism. Contraindicated in pregnancy.

WARNINGS: Often combined with anabolic steroids ± resistance exercise or with testosterone in men. Side effects include diabetes and adrenal insufficiency. Weight gain is primarily fat.

SIDE EFFECTS: Hypogonadism, diabetes, 5% adrenal insufficiency, diarrhea, rash, asthenia, flatulence. Uncommon: Carpel tunnel syndrome, thrombosis, nausea, vomiting, alopecia, vaginal bleeding. High dose (480–1600 mg/day): Hyperpnea, chest pressure, CHF.

DRUG INTERACTIONS: None

PREGNANCY: Category D

Metformin: *Glucophage* (Bristol-Myers Squibb)

CLASS: Antihyperglycemic

INDICATIONS: Type 2 diabetes.

FORMS AND PRICE: Tabs: 500 mg at \$0.78, 850 mg at \$1.33, 1000 mg at \$1.61; XR tabs: 500 mg at \$0.70

REGIMENS: 500 mg bid with meal, increase 500 mg/day at weekly intervals or 850 mg/day in AM with meal with increase of 850 mg q 14 days; max dose is 2550 mg/day.

PATIENT INSTRUCTIONS: Recognize Sx hypoglycemia (confusion, anxiety, tachycardia, shakiness, cold sweats, etc.) → blood glucose and Rx—glucose, non-diet soft drink. Recognize Sx hyperglycemia (polyuria, polydipsia, weight loss, blurred vision) → test glucose. Take with meals to reduce GI intolerance. Warn of Sx of lactic acidosis. Monitor blood glucose.

WARNINGS: Used as monotherapy or adjunct to sulfonylurea or insulin. Promotes lactic acidosis; use with caution with NRTIs, esp. d4T and ddI. Note: Early GI Sx = GI intolerance; GI Sx after several months, check lactic acid. Note: If add sulfonylurea or add metformin to sulfonylurea add gradually; failure to respond to maximum doses in 3 months indicates need for insulin.

MONITOR: Blood glucose by patient + q3 mos. by provider.

SIDE EFFECTS: Hypoglycemia. Promotes lactic acidosis. GI intolerance: Anorexia, diarrhea, dyspepsia, nausea, vomiting (reduced with small doses initially and when taken with food); tolerance improves with continued use.

DRUG INTERACTIONS: ETOH increases potential for lactic acidosis. Metformin levels increased by amiloride, Ca^{++} channel blocking agents, cimetidine, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, TMP, vancomycin—may require dose reduction, metformin (increase metformin concentrations up to 60%), esp. cimetidine. Agents that cause hyperglycemia or hypoglycemia.

PREGNANCY: Category B

Methadone: generic (various manufacturers)

CLASS: Opiate schedule II. Physician Rx restricted to those licensed for methadone maintenance programs and for methadone use in pain control.

INDICATIONS: Pain control; detoxification and maintenance for opioid addiction.

FORMS AND PRICE: Tabs: 5 mg, 10 mg, 40 mg at \$0.33; PO solution: 5 mg/5 mL at \$0.06/mL; Vials for IM or SC injection: 10 mg/mL at \$0.98/mL.

REGIMENS:

- Methadone maintenance: Usually 15–30 mg initial dose up to 40 mg/day with usual maintenance dose of 40–100 mg/day; most states limit maximum daily dose to 80–120 mg/day
- Pain control: 2.5–10 mg PO, SC or IM q3h–q4h or 5–20 mg PO q4h–q8h for severe chronic pain in terminal illness

PATIENT INSTRUCTIONS: Report withdrawal Sx when combined with PI or NNRTI or other drug that reduces methadone levels—Sx include weakness,

anxiety, anorexia, insomnia, abdominal pain, headache, sweating and hot-cold flashes.

WARNINGS: Narcotic withdrawal with many HAART regimens (see below). Main concerns are EFV and NVP.

SIDE EFFECTS: Acute toxicity with coma, stupor, respiratory depression, flaccid mm, cold skin, bradycardia, hypotension. Rx is respiratory support + gastric lavage ± naloxone (naloxone may precipitate withdrawal reaction). Tolerance/physical dependence.

DRUG INTERACTIONS

■ TABLE 11–18: Methadone Drug Interactions

Drug	Effect on Methadone	Effect on Co-admin. Drug	Comment
ABC	↓	↓ peak	Dose adjustment?
APV	↓	?	No dose change
AZT	None	↑40%	No AZT dose change, monitor for toxicity
ddl*	None	AUC ? 60%	May need ↑ ddl dose
d4T	None	↓ 20%	No dose change
DLV	↑	?	Dose adjustment?
EFV	↓↓ 48%	?	Dose adjustment?
Fluconazole	↑ 30%	None	No dose change
IDV	?	?	Not studied
LPV	↓	?	Dose adjustment?
NFV	↓	None	Need ↑ methadone
NVP	↓↓ 46%	None	Need ↑ methadone
Phenytoin	↓↓	None	Need ↑ methadone
RIF	↓↓	None	Need ↑ methadone
RBT	↓	None	Need ↑ methadone
RTV	↓	None	No dose change
SQV (FTV)	↓ 8%	None	No dose change

*Effect on *Videx EC* is not known

PREGNANCY: Category C

Nelfinavir, (NFV): *Viracept* (Agouron)

CLASS: PI

INDICATIONS: Compared with other PIs, NFV is commonly used as single PI, is well tolerated, usually has good PI options if salvage is necessary, and has least boost when combined with RTV.

FORMS AND PRICE: Tabs: 250 mg at \$2.33; PO powder: 50 mg/gm at \$0.43 gm

PATIENT ASSISTANCE: 888-777-6637

REGIMENS: 750 mg PO tid with meals or 1250 mg PO bid with meals. Renal failure and hepatic failure: Standard dose.

PATIENT INSTRUCTIONS: Take with meals, increases absorption 2–3x. Warn of diarrhea which usually responds to fiber supplements, *Imodium* (2 mg q loose stool, up to 16 mg/day) or to calcium (500 mg bid). Need alternative to oral birth control meds. Warn of lipodystrophy and fat redistribution.

WARNINGS: None

SIDE EFFECTS: Secretory diarrhea in 10% to 30%. Class ADRs: Lipodystrophy.

DRUG INTERACTIONS: Contraindicated: Simvastatin, lovastatin, RIF, astemizole, terfenadine, cisapride, midazolam, triazolam, ergot, St. John's Wort. RBT: Increase NFV to 1000 mg tid and decrease RBT to 150 mg/day or 300 mg 2x/week. Ethinyl estradiol: Use alternative method of birth control. Methadone: Standard doses, watch for withdrawal. Sildenafil: Limit sildenafil to 25 mg/48 hours. PI/NNRTI combinations: See Tables 6–9 and 6–10, pp. 33–34.

PREGNANCY: Category B

Nevirapine, (NVP): *Viramune* (Boehringer Ingelheim)

CLASS: NNRTI

INDICATIONS: Potent NNRTI with relatively few drug interactions.

FORMS AND PRICE: Tabs: 200 mg at \$5.31; Suspension 240 mL/50 mg/mL at \$69.05

REGIMENS: 200 mg/day PO x 14 days, then 200 mg PO bid

PATIENT INSTRUCTIONS: NVP may be taken without regard to food. Patients should be warned of rash reaction and symptoms of clinical hepatitis, especially during the first 12 weeks of therapy (similar to INH warning).

WARNINGS: Hepatitis reported in up to 16%, most in first 12 weeks. Discontinue if clinical signs of hepatitis occur. Hepatotoxicity usually occurs in first 12 weeks of therapy and may be asymptomatic. Nevertheless, cases have been reported during 12–52 weeks of therapy. Rash reaction—17%, most in first 12

weeks. Discontinue NVP if rash is accompanied by fever, blisters, mucous membrane involvement, conjunctivitis, edema, arthralgias or Stevens-Johnson syndrome.

MONITOR: LFTs at baseline and at intervals during the first 3 to 12 months. Usual recommendation is to monitor LFTs every 2 to 4 weeks during first 12 weeks and d/c if ALT increases to $>5x$ ULN; it is unclear that this recommendation is justified, effective, or different from other NNRTIs. If asymptomatic and LFTs return to baseline, consider re-challenge. Hepatotoxicity is not frequent or severe with pre-existing liver disease, including chronic HCV/HBV infection.

SIDE EFFECTS: Rash and hepatotoxicity, see above.

DRUG INTERACTIONS: Contraindicated for concurrent use: RIF, ketoconazole, and St. John's Wort. Estradiol: Use alternative method of birth control. Methadone: Monitor for methadone withdrawal; may need increase in methadone dose. RBT: No dose change. PI combinations: See Table 6–10, p. 34.

PREGNANCY: Category C

Nortriptyline: *Aventyl* (Eli Lilly), *Pamelor* (Novartis), generic (various manufacturers)

CLASS: Tricyclic antidepressant

INDICATIONS: Depression; peripheral neuropathy.

FORMS AND PRICE: Caps: 10 mg, 25 mg, 50 mg at \$1.52; PO suspension: 10 mg/5 mL at \$55.52/16 oz.

REGIMENS:

- Depression: 25 mg hs, increase by 25 mg q 3 days until 75 mg, then wait 5 days and get level with goal of 100–150 ng/dL
- Peripheral neuropathy: 10–25 mg hs, increase q 2 to 3 wks. to maximum of 75 mg hs

PATIENT INSTRUCTIONS: Warn of anticholinergic side effects: Dry mouth, blurred vision, constipation, urinary retention, orthostatic hypotension. Sedation may interfere with safe driving, operating heavy machinery, etc. Avoid in pregnancy, esp. first trimester. Caution with or avoid other CNS depressants including ETOH.

WARNINGS: Other CNS depressants are additive including ETOH, antihistamines; Parkinsonian syndrome; possible utility of nortriptyline levels.

MONITOR: Tricyclic levels may be indicated with suspected toxicity, failure to respond, questionable compliance; optimal time is before >8 hours after a dose.

SIDE EFFECTS: Anticholinergic (see patient warning). Sedation. Tremor or Parkinsonian syndrome. Hypotension. Sexual dysfunction.

DRUG INTERACTIONS: Contraindicated for concurrent use: MAO inhibitors, adrenergic neuronal blocking agents, clonidine, excessive ETOH, fenfluramine, cimetidine. Quinidine and fluconazole increase nortriptyline levels.

PREGNANCY: Category C

Nystatin: *Mycostatin* (Bristol-Myers Squibb), generic (various manufacturers)

CLASS: Polyene related to amphotericin B

INDICATIONS: Mucosal candidiasis.

FORMS AND PRICE: Lozenges: 200,000 units at \$1.03; Ointment and cream: 100,000 units/15 gm at \$2.64; PO suspension, 100,000 units/mL: 60 mL at \$6.25 480 mL; PO tabs: 500,000 units at \$0.64; Vaginal tabs 100,000 units at \$0.47.

REGIMENS

- Thrush: 5 mL suspension gargled 4x/day x 14 days
- Vaginitis: 100,000 units tab intravaginally 1–2x/day x 14 days

PATIENT INSTRUCTIONS: Warn about bitter taste and possible GI side effects.

SIDE EFFECTS: Transient nausea, vomiting, diarrhea.

DRUG INTERACTIONS: None

PREGNANCY: Category C

Oxandrolone: *Anavar* (Searle), *Oxandrin* (BTG)

CLASS: Anabolic steroid

INDICATIONS: Wasting.

FORMS AND PRICE: Tabs: 2.5 mg at \$3.75

PATIENT ASSISTANCE: 800–741–2698

REGIMENS: 2.5 mg 2–4x/day. Renal or hepatic failure: No dose change.

PATIENT INSTRUCTIONS: May be virilizing in women: Deep voice, acne, clitoral enlargement, hirsutism, menstrual irregularity. In men: Acne and increased or decreased potency. Avoid with pregnancy.

WARNINGS: Peliosis hepatis (blood filled cysts in liver that may be life-threatening) and cholestatic hepatitis.

MONITOR: Periodic LFTs.

SIDE EFFECTS: GI intolerance, changes in skin color, depression, insomnia, increased or decreased libido, virilization of women; rare—peliosis hepatis, cholestatic hepatitis. Long term high dose: Hepatic tumors.

DRUG INTERACTIONS: Increase activity of warfarin and oral hypoglycemics.

PREGNANCY: Category X, teratogenic.

Paromomycin: *Humatin (Monarch)*

CLASS: Aminoglycoside

INDICATIONS: Cryptosporidiosis.

FORMS AND PRICE: Caps: 250 mg at \$2.81

REGIMENS: 500 mg PO tid x 14 to 28 days or 1 gm PO bid ± azithromycin 600 mg/day PO x 4 wks., then paromomycin (alone) 1 gm bid x ≥ 8 wks.

PATIENT INSTRUCTIONS: Will not cure cryptosporidiosis.

WARNINGS: Other therapies: HAART is most important method to control cryptosporidiosis; *Imodium* and other antiperistaltic and food supplements may be important.

SIDE EFFECTS: GI intolerance. Steatorrhea and malabsorption.

DRUG INTERACTIONS: None.

PREGNANCY: Category C

Pentamidine: *NebuPent, Pentam (Fujisawa)*

CLASS: Antiprotozoan agent structurally related to stilbamidine.

INDICATIONS: Treatment and prevention of *P. carinii* pneumonia.

FORMS AND PRICE: Vials: 300 mg at \$138

PATIENT ASSISTANCE: 847-317-8604

REGIMENS

- PCP prophylaxis: 300 mg/mo. delivered by *Respirgard II* nebulizer using 300 mg in 6 mL sterile water and delivered at 6 L/min. from a 50 psi compressed air source until reservoir is dry
- PCP treatment: 3–4 mg/kg/day IV x 21 days
- Renal failure: CrCl 10–50 mL/min.: 4 mg/kg q24h–q36h; <10 mL/min.: 4 mg/kg q48h
- Infuse over 1 to 2 hrs.

PATIENT INSTRUCTIONS: Aerosol: Warn of cough and albuterol option. Systemic: Warn of diabetes, hypoglycemia and hypotension.

WARNINGS: Aerosol: Risk of transmitting TB; evaluate for TB (Sx, PPD, x-ray + sputum exam) and treat prior to aerosolized pentamidine. Systemic: highly toxic; ADRs in 70% to 75% including renal failure, prolonged hypoglycemia, diabetes, hypotension, pancreatitis (*Clin Infect Dis* 1997;24:854). Due to severity

and unpredictability of these adverse reactions, home IV therapy is usually not recommended.

MONITOR: Creatinine, CBC, glucose and K^+ qd or qod. 2 LFTs, Mg^{++} and Ca^{++} q 3 days. Monitor BP during and after infusion with patient in supine position.

SIDE EFFECTS: Aerosol: Cough and wheezing—30%, usually prevented with albuterol 2 whiffs prior to treatment. Systemic: Nephrotoxicity—25% to 50%, usually with creatinine increase in 2nd week; may cause acute renal failure. Hydrate, avoid nephrotoxic drugs and monitor creatinine. Hypotension—6%, may be lethal, warn patient; give pentamidine infusion over ≥ 60 to 120 minutes, monitor BP and keep patient supine during infusion. Hypoglycemia with blood glucose ≤ 25 mg/dL—5% to 10%, usually after 5 to 7 days; may occur post treatment and may persist days or weeks. Rx with IV glucose \pm diazoxide. Hyperglycemia—2% to 9%, may require insulin; onset may be months after pentamidine is discontinued. Leukopenia and thrombocytopenia—2% to 13%. GI intolerance: Nausea, vomiting, anorexia, metallic taste. Local reactions at injection sites.

DRUG INTERACTIONS: Avoid nephrotoxic drugs: Aminoglycosides, Amphotericin B, foscarnet. Severe but reversible decrease in Ca^{++} and Mg^{++} —foscarnet. Marrow suppressing drugs.

PREGNANCY: Category C.

Pravastatin: *Eptastatin, Pravachol* (Bristol-Myers Squibb)

CLASS: Statin

INDICATIONS: Hypercholesterolemia; preferred statin for use with PIs due to lack of drug interaction.

FORMS AND PRICE: Tabs: 10 and 20 mg at \$2.60, 40 mg at \$4.10

REGIMENS: Initial dose is 10–20 mg; increase dose at ≥ 4 wks. to maximum of 40 mg/day or maximum of 20 mg/day with hepatic disease, renal disease or in elderly patient.

PATIENT INSTRUCTIONS: Take hs without regard to food. Report Sx of myopathy: Muscle tenderness, weakness or pain, especially if accompanied by fever. Risk reduction through lifestyle changes, including weight loss, dietary changes, reduction of HBP, etc. Be aware of symptoms of hepatitis. Contraindicated in pregnancy.

WARNINGS: Myopathy: Risk possibly increased with HAART regimens; if Sx, obtain CPK.

MONITOR: Cholesterol levels every 4 wks. with dose adjustment. Creatinine kinase if symptoms of myositis. LFTs q 6 wks. x 3 mos., then 8 wks. to 1 yr., then q 6 mos.

SIDE EFFECTS: Myopathy with increased CPK. Rhabdomyolysis with renal failure reported. Hepatic injury with elevated transaminase in 1% to 2%.

DRUG INTERACTIONS: Niacin and gemfibrozil: Increased risk of myopathy. Itraconazole increases pravastatin levels. Cholestyramine and colestipol decrease pravastatin levels. PIs that appear safe for concurrent use: IDV, SQV, RTV, APV and LPV/RTV.

PREGNANCY: Category X, contraindicated in pregnancy.

Pyrazinamide (PZA): *Rifater (Aventis)*, generic (various manufacturers)

CLASS: Related to niacinamide

INDICATIONS: Tuberculosis.

FORMS AND PRICE: Tabs: 500 mg at \$1.12

REGIMENS

- Latent TB: PZA 15–20 mg/kg/day + RIF 600 mg/day x 2 mos. or PZA 15–20 mg/kg/day + RBT (dose adjusted for concurrent PI)
- Active TB—daily: 15–20 mg/kg/day up to 2 gm/day
- Active TB—DOT: 50–70 mg/kg/day up to 4 gm/day 2–3x/wk.
- Renal failure: CrCl <10 mL/min.: 12–20 mg/kg/day

PATIENT INSTRUCTIONS: Warn of polyarthralgias (in up to 40%); must be aware of symptoms of hepatitis.

WARNINGS: Hepatotoxicity—up to 15% with >3 gm/day. Severe reactions reported in small number receiving 2 month course for latent TB; incidence unknown. Use with caution in patients with gout.

MONITOR: Latent TB two month course: CBC and LFTs at baseline and at 2, 4, and 6 weeks; discontinue regimen if patient is asymptomatic with ALT >5x ULN or symptomatic with any increase in ALT.

SIDE EFFECTS: Hyperuricemia is common, but gout is rare and usually responds to uricosuric agents. Polyarthralgias, nongouty—up to 40%. Hepatotoxicity, dose related. Transient elevated ALT, jaundice or syndrome of fever, anorexia and hepatomegaly.

DRUG INTERACTIONS: None

PREGNANCY: Category C

Pyrimethamine: *Daraprim* (GlaxoSmithKline)

CLASS: Antimalarial drug structurally related to TMP; false antagonist.

INDICATIONS: Treatment and prevention of toxoplasmosis.

FORMS AND PRICE: Tabs: 25 mg at \$0.47

PATIENT ASSISTANCE: 800-722-9294

REGIMENS

- Toxoplasmosis prophylaxis: Pyrimethamine 50 mg/wk. + dapsone 50 mg/day + leucovorin 25 mg/wk. or atovaquone 1500 mg/day + pyrimethamine 25 mg/day + leucovorin 10 mg/day
- Toxoplasmosis treatment: Pyrimethamine 25–50 mg/day PO + sulfadiazine 2–4 gm/day PO (or clindamycin 300–450 mg q6h–q8h) + leucovorin 10–25 mg/day PO. Maintenance dose is ½ induction dose regimen.
- Dose modification with renal failure: None

PATIENT INSTRUCTIONS: GI tolerance improved if taken with meals.

WARNINGS: Megaloblastic anemia due to depletion of folic acid stores, prevented with folinic acid.

SIDE EFFECTS: Marrow suppression with dose related megaloblastic anemia, leukopenia, and thrombocytopenia. GI intolerance (give with meals). Dose-related ataxia, tremors, or seizures.

DRUG INTERACTIONS: Lorazepam: Hepatotoxicity.

PREGNANCY: Category C

Ribavirin: *Rebetol*–caps, *Rebetron*–ribavirin caps with interferon (Schering)

CLASS: Antiviral with activity vs HCV, RSV, Hantavirus, Lassa fever virus; FDA approved for HCV when combined with interferon and aerosol treatment of RSV in children.

INDICATIONS: HCV with biopsy evidence of fibrosis. See HIV Co-Morbidities, HCV, p. 62. Use only with interferon; ribavirin monotherapy is not effective.

FORMS AND PRICE: 200 mg caps

REGIMEN: Give 2x/day PO following any one of the 3 dosing schemes outlined below:

- 10.6 mg/kg/day
- Weight: >75 kg—600 mg; <75 kg—400 mg in A.M., 600 mg in P.M.
- Weight: <40 kg—600 mg/day; 40–65 kg—800 mg/day; 65–85 kg—1000 mg/day; 85–105 kg—1200 mg/day; >105 kg—1400 mg/day

DURATION: Genotype 1, 48 wks., but d/c if HCV RNA positive at 24 wks.; Genotype 2 or 3, consider 24 wks.; 48 wks. if advanced fibrosis.

PATIENT INSTRUCTIONS: Take ribavirin only with interferon or peginterferon. Take ribavirin with meals. Must avoid pregnancy in female patients and female partners of male patients including for 6 months post Rx. Pegylated interferon, inject SC weekly; interferon causes flu-like symptoms and mental health problems and ribavirin causes anemia.

WARNINGS: Contraindications (absolute): Pregnancy, lack of reliable contraception, severe anemia, hemoglobinopathy, severe heart disease. Relative contraindications: Old age or uncontrolled hypertension. Monitor CBC at week 2, then monthly; LFTs, chem panel q month; TSH and HCV viral load q 3 months. Major side effect of ribavirin is hemolysis with anemia in >30%. See interferon for interferon associated side effects.

SIDE EFFECTS: Hemolysis and nausea in >30%; nasal congestion, pruritus and gout.

MANAGING TOXICITY: Anemia

- Hgb ↓ ≥ 2 gm/dL or ↓ to <10 g/dL: Reduce ribavirin dose to 600–800 mg/day and/or EPO 40,000 units SC/wk.
- Hgb ↓ to <8.5 g/dL: d/c ribavirin and follow. Hgb; restart when Hgb >gm/dL

Note: If unable to restart ribavirin, continue interferon

DRUG INTERACTIONS: Caution/avoid myelosuppressants including AZT; *in vitro* antagonism between AZT and ribavirin reported, clinical significance is unknown.

PREGNANCY: Category X

Rifabutin (RBT): *Mycobutin* (Pharmacia)

CLASS: Semisynthetic derivative of rifampin.

INDICATIONS: Treatment and prevention of *M. tuberculosis* and *M. avium*.

FORMS AND PRICE: Caps: 150 mg at \$5.20

PATIENT ASSISTANCE: 800–242–7014

REGIMENS

- MAC prophylaxis: 300 mg/day* (Azithromycin or clarithromycin preferred)
- MAC treatment: 300 mg/day* + azithromycin and EMB
- TB prophylaxis and treatment: 300 mg/day*
- Dose adjustment with HAART: (see below)
- Renal failure: Standard dose

PATIENT INSTRUCTIONS: Warn that secretions (urine, tears, saliva, stool, and skin) will be discolored brown-orange; may also discolor contact lenses. High levels associated with uveitis—red, painful eye with blurred vision, photophobia or floaters. RBT may be taken with or without food.

WARNINGS: Multiple drug interactions due to induction of cytochrome p450 pathway and metabolism of RBT by this pathway; most important are PIs, NNRTIs, clarithromycin and fluconazole (see below). Dose related uveitis, refer to ophthalmologist.

SIDE EFFECTS: Discoloration of secretions. Rash—4%. GI intolerance—3%. Dose dependent uveitis, usually with doses >450 mg/day or concurrent use of clarithromycin or fluconazole. Neutropenia, arthralgias with high dose.

DRUG INTERACTIONS: RBT reduces activity of warfarin, barbiturates, benzodiazepines, B adrenergic blockers, chloramphenicol, clarithromycin, clofibrate, oral contraceptives, corticosteroids, diazepam, dapsone, digitalis, doxycycline, haloperidol, oral hypoglycemics, ketoconazole, methadone, phenytoin, quinidine, theophylline, TMP and verapamil, PIs and NNRTIs, see table below. Drugs that prolong half life of RBT: Erythromycin, clarithromycin, and azoles (esp. fluconazole).

■ TABLE 11-19: RBT Interactions With PIs and NNRTIs

Agent	ART (AUC)	RBT (AUC)	Recommendation
APV	↑↓ 14%	↑ 193%	APV standard; RBT 150 mg/day or 300 mg 2x/wk.
DLV	↓ 80%	↑ 100%	Contraindicated
EFV	NC	↓ 35%	EFV standard; RBT 450–600 mg/day or 600 mg 2x/wk.
IDV	↓ 34%	↑ 173%	IDV 1000 mg q8h, RBT 150 mg/day or 300 mg 2x/wk.
NVP	↓ 16%	↓	NVP standard; RBT 300 mg/day or 300 mg 2x/wk.
NFV	↓ 32%	↑ 200%	NFV 1000 mg tid; RBT 150 mg/day or 300 mg 2x/wk.
RTV	NC	↑ 293%	RTV standard; RBT 300 mg qod
SQV (FTV)	↓ 40%	?	Not recommended
SQV/RTV	SQV ↓ 40%	↑ 3 x	SQV/RTV standard; RBT 150 mg 2–3x/wk. or 300 mg/wk.
LPV	NC	↑ 5 x	LPV/RTV standard; RBT 150 mg qod

PREGNANCY: Category C

Rifampin (RIF): *Rifadin, Rifamate (Aventis), generic (various manufacturers)*

CLASS: Antimycobacterial.

INDICATIONS: Treatment and prevention of *M. tuberculosis*.

FORMS AND PRICE: Caps: 150 mg; 300 mg at \$1.61; 120 mg + 50 mg INH + 300 mg PZA (*Rifater*) at \$1.80/tab

REGIMENS:

- TB treatment: 600 mg/day or 600 mg 2–3x/week (+ INH, PZA + ETH or SM)
- TB prophylaxis: 600 mg/day + PZA 15–20 mg/kg/day x 2 months
- Renal or hepatic failure: Standard doses

PATIENT INSTRUCTIONS: Warn of orange-brown discoloration of secretions including urine, stool, tears, sweat, skin; may stain contact lenses. Warn of hepatitis Sx. Reduced absorption with high fat meal; take with full glass H₂O on empty stomach.

WARNINGS: See drug interactions, below. Short course treatment of latent TB (RIF + PZA x 2 mos.): Must get CBC + LFTs at baseline and at 2, 4, and 6 wks.; hepatotoxicity with death reported.

SIDE EFFECTS: GI intolerance. Hepatitis—usually cholestatic changes in first month of treatment; no increase in risk when given with INH. Hypersensitivity with pruritus + rash—3%. Flu-like illness with intermittent use. Orange-brown discolorations of secretions.

DRUG INTERACTIONS: Drug interactions due to induction of p450 metabolic pathway. RIF reduces activity of atovaquone, warfarin, barbiturates, benzodiazepines, beta-adrenergic blockers, chloramphenicol, clarithromycin, clofibrate, oral contraceptives, corticosteroids, cyclosporine, diazepam, dapsone, digitalis, doxycycline, erythromycin, haloperidol, oral hypoglycemics, ketoconazole, methadone, phenytoin, theophylline, TMP and verapamil. RIF half life is prolonged with clarithromycin, erythromycin, and azoles. The only PI/NNRTIs that can be used with RIF are RTV, RTV/SQV, and EFV; with all three, each drug in the combination is used in standard doses; EFV—consider 800 mg/day.

PREGNANCY: Category C. Dose dependent congenital malformations in animals. Case reports of neural tube defects and limb reduction in humans. Use with caution.

Ritonavir (RTV): *Norvir (Abbott)*

CLASS: PI

INDICATIONS: Potent PI, but poorly tolerated. Widely used to boost concurrent PI, especially IDV, APV, LPV, and SQV; dose may be 400 mg bid to provide RTV anti-HIV activity or 100–200 mg/day or bid where only role is to boost levels of companion PI.

FORMS AND PRICE: Soft gel caps: 100 mg at \$2.06; Liquid: 600 mg/7.5 mL at \$346/240 mL. With LPV (133 mg LPV/33 mg RTV) at \$3.76

PATIENT ASSISTANCE: 800-659-9050

REGIMENS

- Single PI: 600 mg/day; dose escalation: Days 1 and 2—300 mg bid, days 3 to 5—400 mg bid, days 6 to 13—500 mg bid, day 14 and thereafter—600 mg bid
- With SQV: RTV 400 mg/SQV 400 mg bid (FTV or INV) *or* RTV 100 mg + FTV 1600 mg/day (limited data)
- With NFV: RTV 400 mg + NFV 500–750 mg bid (limited data)
- With IDV: RTV 100–200 mg + IDV 800 mg bid *or* RTV 400 mg + IDV 400 mg bid
- With APV: RTV 100–200 mg + APV 600 mg bid *or* RTV 200 mg + APV 1200 mg/day (limited data) *or* RTV 200 mg bid + APV 1200 mg bid + EFV 600 mg hs
- With NVP: RTV + NVP: Both standard doses
- With LPV: RTV 100 mg + LPV 400 bid (*Kaletra*)

PATIENT INSTRUCTIONS: Dose related GI intolerance. Food does not alter absorption, but may improve GI tolerance. Tolerance may also be improved with dose escalation schedule, see above. Tolerance usually improves with treatment >1 month. Warn about paresthesias and GI intolerance. Warn of lipodystrophy and fat redistribution.

WARNINGS: Dose related GI intolerance makes regimens with ≥ 400 mg bid difficult for many patients.

MONITOR: Fasting glucose and blood lipids at baseline, at 3 to 4 mos., and then as needed.

SIDE EFFECTS: GI intolerance. Hepatotoxicity; possibly the most hepatotoxic of the PIs (*JAMA* 2000;238:74), taste perversion, circumoral and peripheral paresthesias. Class ADR: Lipodystrophy.

DRUG INTERACTIONS: Contraindicated for concurrent use: Amiodarone, astemizole, bepridil, cisapride, encainide, flecainide, lovastatin, midazolam, ergot, quinidine, propoxyphene, simvastatin, terfenadine, triazolam, St. John's Wort. Dose modifications: Clarithromycin AUC 77%; dose modification unclear. RBT levels increase 4x—RBT dose decrease to 150 mg qod or 150 mg 3x/week. Desipramine, dose decrease. Sildenafil, limit to 25 mg/48 hours. MDMA ("ecstasy"), potentially fatal reaction. RTV decreases levels of methadone; consider methadone dose increases. Ketoconazole increase 3x—limit to 200 mg/day. Ethinyl estradiol, use alternative birth control. Theophylline, monitor levels. Buffered ddl decreases RTV levels—take ≥ 2 hours apart (does not apply to *Videx EC*). PI/NNRTI combinations, see Tables 6–9 and 6–10, pp. 33–34.

PREGNANCY: Category B

Saquinavir (SQV), Fortovase (FTV), Invirase (INV): all forms (Roche)

CLASS: PI

INDICATION: *Fortovase* is potent PI usually combined with RTV; *Invirase* has poor bioavailability as sole PI and should be used only with RTV.

FORMS AND PRICE: FTV soft gel caps: 200 mg at \$1.23; INV hard gel caps: 200 mg at \$2.40

PATIENT ASSISTANCE: 800-282-7780

REGIMENS: FTV, as single PI: 1200 mg tid; FTV or INV with RTV: 400/400 bid or FTV 1600 mg + RTV 100 mg/day or FTV 1000 mg bid + RTV 100 mg bid

PATIENT INSTRUCTIONS: *Invirase* shows poor bioavailability and should only be used with RTV. Patients should be encouraged to switch to FTV which is better absorbed and half the price. FTV should be taken with meals when used alone; absorption is not influenced by food when SQV (*Invirase* or *Fortovase*) is combined with RTV. Main side effect is GI intolerance.

WARNINGS: Major limitation is GI intolerance.

SIDE EFFECTS: GI intolerance 20% to 30%. Headache. Hepatotoxicity. Class ADR: Lipodystrophy.

DRUG INTERACTIONS: Contraindicated for concurrent use: Terfenadine, astemizole, cisapride, triazolam, RIF, RBT, ergot, simvastatin, lovastatin, St. John's Wort. PI/NNRTI combinations, see Tables 6-9 and 6-10, p. 33-34.

PREGNANCY: Category B

Stavudine, d4T: Zerit (Bristol-Myers Squibb)

CLASS: NRTI

INDICATIONS: Potent NRTI with great tolerance in short run and increased rates of mitochondrial toxicity complications in long run.

FORMS AND PRICE: Caps: 15 mg at \$4.60, 20 mg at \$4.78, 30 mg at \$5.10, 40 mg at \$5.20. Solution: 1 mg/mL at \$57.85/200 mL.

PATIENT ASSISTANCE: 800-272-4878

REGIMENS: 40 mg bid

■ TABLE 11-20: d4T Dose Adjustment for Renal Failure:

CrCl	Weight >60 kg	Weight <60 kg
26-50 mL/min.	40 mg/day	30 mg/day
10-25 mL/min.	20 mg/day	15 mg/day
Hemodialysis	20 mg daily and post dialysis	15 mg daily and post dialysis

PATIENT INSTRUCTIONS: Take without regard to meals. Warn regarding peripheral neuropathy. Warn of lipodystrophy and fat redistribution.

WARNINGS: Avoid concurrent use with AZT. Avoid d4T and ddl combination in pregnancy. Dose modification in renal failure

SIDE EFFECTS: Peripheral neuropathy initially with paresthesias or pain in feet in 15% to 20% treated >2 years; increased frequency with d4T and ddl; must reduce dose or stop the drug. Rate of pancreatitis increased when given with ddl. Class ADRs: Lactic acidosis and fat atrophy. Macrocytosis.

DRUG INTERACTIONS: Concurrent use with AZT or ddC contraindicated. Avoid drugs that cause neuropathy: Ethionamide, EMB, INH, phenytoin, vincristine, glutethimide, gold, hydralazine, long term metronidazole.

PREGNANCY: Category C

Sulfadiazine: generic (various manufacturers)

CLASS: Sulfonamide, inhibits folic acid synthesis

INDICATIONS: Toxoplasmosis

FORMS AND PRICE: Tabs: 500 mg at \$0.55

REGIMENS: Usually 0.5–1.5 gm q4h–q6h. Renal failure: CrCl 10–50 mL/min.: 0.15–1.5 gm q8h–q12h (half dose); <10 mL/min. 0.5–1.5 gm q12h–q24h (one third dose)

PATIENT INSTRUCTIONS: Warn about dose related renal crystallization with urinary stones; need alkaline urine and/or volume of >1.5 L/day. Warn of HSR.

WARNINGS: Dose modification in renal failure.

MONITOR: Some monitor serum levels with objective of 100–150 mcg/mL.

SIDE EFFECTS: HSR: Rash, fever, serum sickness, urticaria. Crystalluria (reduced with large fluid intake and alkaline urine). Marrow suppression: Anemia, thrombocytopenia, leukopenia, anemia with G6-PD deficiency.

DRUG INTERACTIONS: Increases levels of warfarin, oral hypoglycemics and phenytoin.

PREGNANCY: Category C; avoid near term, may cause kernicterus.

Sulfamethoxazole-Trimethoprim (TMP-SMX cotrimoxazole): *Bactrim* (Roche), *Sepra* (GlaxoSmithKline), generic (various manufacturers)

CLASS: Synthetic fixed combination antimicrobial.

INDICATIONS: Treatment and prevention of *P. carinii*; treatment of common bacterial infections (sinusitis, UTIs), *Nocardia*, *S. aureus*.

FORMS AND PRICE: Tabs: Single strength (SS), 80 mg TMP/400 mg SMX at \$0.14, double strength (DS), 160 mg TMP/800 mg SMX at \$0.18; IV formulation, 10 mL 160 mg TMP + 800 mg SMX/10 mL at \$2.68.

ACTIVITY: *P. carinii*, methicillin-sensitive *S. aureus*, *Listeria*, *Toxoplasma*, *Legionella*, *H. influenzae*, *S. pneumoniae*, *Isospora*, *Cyclospora*, *Nocardia*, *Salmonella*, *E. coli*.

REGIMENS

- PCP prophylaxis: 1 DS/day or 1 SS/day (preferred) or 1 DS 3x/wk.
- PCP treatment: 5 mg/kg TMP PO or IV q8h x 21 days (usually 2 DS PO tid for 65 kg patient).
- Toxoplasmosis prophylaxis: 1 DS/day.
- *Isospora*: 1 DS PO bid or tid x 2 to 4 wks.
- Salmonellosis: 1 DS PO bid x 5 to 7 days or ≥ 14 days if relapsing.
- *Nocardia*: 4–5 DS/day x ≥ 6 mos.
- UTI prophylaxis: 1/2 SS/day.
- UTI treatment: 1–2 DS/day x 3 to 14 days.
- Dose modification in renal failure: CrCl 10–50 mL/min.: Half dose; <10 mL/min.: Avoid or reduce dose further to 1/3.

PATIENT INSTRUCTIONS: Warn of HSR with rash and fever, usually at days 7 to 14.

WARNINGS: Many or most patients with rash reaction to TMP-SMX can be treated through or rechallenged and tolerate the drug using dose escalation or lower dose.

- TABLE 11–21: **Schedule for TMP-SMX Rapid Desensitization Using Oral Solution—40 mg TMP/20 mg SMX/mL (*Clin Infect Dis* 1995; 20: 849)**

Time (hr.)	Dose (TMP-SMX)	Dilution
0	0.004/0.02 mg	1 : 10,000 (5 mL)
1	0.04/0.2 mg	1 : 1,000 (5 mL)
2	0.4/2.0 mg	1 : 100 (5 mL)
3	4/20 mg	1 : 10 (5 mL)
4	40/200 mg	5 mL
5	160/800 mg	tab

SIDE EFFECTS: Reaction rates of 30% to 50% of HIV-infected patients. Most common: Nausea, vomiting, pruritus, rash (usually pruritus, maculopapular, mor-

billiform), neutropenia, and increased transaminase. Management options: Treat through if Sx are not disabling, esp. if GI intolerance or rash. PCP prophylaxis: Drug holiday x 1 to 2 weeks and rechallenge + lower dose (but no lower than 1 SS/day or 1 DS 3x/week). Desensitize (see above). Contraindications to continued use: Erythema multiform, epidermal necrolysis, exfoliative dermatitis, Stevens-Johnson syndrome, urticaria, and Schonlein-Henoch purpura. Miscellaneous: *C. difficile* colitis; severe marrow suppression; neurotoxicity (ataxia, tremor, ankle clonus); hepatic necrosis or cholestatic jaundice; aseptic meningitis; interstitial nephritis. Hypokalemia: 20% to 50% of patients given TMP >15 mg/kg/day (*N Eng J Med* 1993;328:703).

DRUG INTERACTIONS: Increase levels of warfarin, phenytoin and procainamide.

PREGNANCY: Category C

Tenofovir (TDF): *Viread* (Gilead)

CLASS: Nucleotide

INDICATIONS: Advantages are once daily dosing, activity against most strains resistant to NRTIs, although mutations at codons 41, 74, and 210 are associated with decreased sensitivity and T69S insertions confer high level resistance.

FORMS: 300 mg tabs

REGIMEN: 300 mg/day

PATIENT INSTRUCTIONS: Absorption improved if taken with fatty meal.

WARNINGS: Caution with concurrent ddl (see below).

SIDE EFFECTS: GI intolerance.

DRUG INTERACTIONS: Increase ddl AUC 44%; monitor for ddl adverse reactions (see p. 100).

PREGNANCY: Category B

Testosterone: generic (various manufacturers)

CLASS: Androgen; controlled substance: Schedule C-III.

INDICATIONS: Clearest indication is demonstration of hypogonadism in men with 8 A.M. plasma testosterone level <300 ng/dL and/or wasting.

FORMS AND PRICE: Vials, 10 mL: 100, 200 mg/mL at \$12.71 to \$20.65 (about \$2/wk.). *Androderm* patch at \$1.95/2.5 mg/24 hr. patch. *AndroGel* at \$5.45/5 gm.

REGIMENS

- Testosterone: 100 mg 1M q wk. (replacement) with usual therapeutic doses of 100–200 mg/M q wk. or 200–400 mg q 2 wks.

- Transdermal: *Androderm* 5 mg patch/day or *Androgel* 5 mg gel/day. *Androgel* formulation permits gradual increase in dose.

PATIENT INSTRUCTIONS: Generally avoided in women who may experience virilization; absolutely contraindicated in pregnancy. Need to emphasize importance of safe sex.

WARNINGS: Transdermal systems have advantage of controlled rate of delivery, it avoids IM injections and avoids first pass hepatic metabolism, but costs more. Best justification of use is in HIV-infected men with hypogonadism: Testosterone improves quality of life and reduces depression. With wasting, weight gain is primarily lean body mass.

MONITOR: Optional: AM testosterone level with expectation of level >300 ng/dL.

SIDE EFFECTS: Androgenic effects: Acne, flushing, gynecomastia, increased lipids, priapism and edema. Less common: sleep apnea, salt retention, increased hematocrit. Women: Virilization with voice change, hirsutism, clitoral enlargement. Cholestatic hepatitis. Patches: Local reactions.

DRUG INTERACTIONS: May potentiate warfarin.

PREGNANCY: Category X

Valacyclovir: *Valtrex* (GlaxoSmithKline); see Acyclovir, p. 85

Valganciclovir: *Valcyte* (Roche)

CLASS: Antiviral

INDICATIONS: Disseminated CMV. Active against CMV, HSV, VZV, HHV-6, HHV-8.

FORMS AND PRICE: Tabs: 450 mg at \$23.75

PATIENT ASSISTANCE: 800-282-7780

REGIMENS: 900 mg (with food) bid x 3 wks., then 900 mg/day. Renal failure: CrCl >60 mL/min.: Standard; 25-59 mL/min.: Half dose; 10-24 mL/min.: 450 mg qod (induction); 450 mg 2x/wk. (maintenance) <10 mL/min.: Not recommended.

PATIENT INSTRUCTIONS: Must take with food; absorption with food is 60% compared to 6% to 9% for oral ganciclovir.

WARNINGS: Must adjust dose for renal failure. Monitor for marrow suppression: Primarily neutropenia, but also thrombocytopenia and anemia.

SIDE EFFECTS: Neutropenia. GI intolerance. Anemia and thrombocytopenia.

DRUG INTERACTIONS: Avoid marrow suppressing drugs, especially AZT.

PREGNANCY: Category C

Zalcitabine (ddC): *HIVID* (Roche)

CLASS: NRTI

INDICATIONS: NRTI that is infrequently used due to tid dosing, toxicity and limited studies verifying efficacy.

FORMS AND PRICE: Tabs: 0.375 mg at \$2.07; 0.75 mg at \$2.60

PATIENT ASSISTANCE: 800-285-4484

REGIMENS: 0.75 mg tid. Renal failure: CrCl 10-50 mL/min.: 0.75 mg bid; <10 mL/min.: 0.75 mg/day

PATIENT INSTRUCTIONS: Warn about peripheral neuropathy. Warn of lipodystrophy and fat redistribution.

WARNINGS: Peripheral neuropathy—17% to 31% of ddC recipients; pre-existing peripheral neuropathy is contraindication. Should not be combined with ddl or d4T.

SIDE EFFECTS: Peripheral neuropathy: Continued use may cause irreversible pain requiring a narcotic. Stomatitis and aphthous esophageal ulcers in 2% to 4%. Pancreatitis <1%. Rash, usually at 10 to 14 days. Class ADRs: Lactic acidosis and steatosis.

DRUG INTERACTIONS: Other drugs that cause peripheral neuropathy: ddl, d4T, EMB, cisplatin, disulfiram, ethionamide, INH, phenytoin, vincristine, glutethimide, gold, hydralazine, long-term metronidazole.

PREGNANCY: Category C

Zidovudine (AZT, ZDV): *Retrovir* (GlaxoSmithKline)

CLASS: NRTI

INDICATIONS: First antiretroviral drug; has established efficacy in preventing perinatal exposure and for healthcare worker exposure; most patients treated with it, but many are intolerant or have marrow suppression.

FORMS AND PRICE: Tabs: 100 mg at \$1.86, 300 mg at \$4.43; *Combivir*: 300 mg AZT/150 mg 3TC at \$10.33; TZV: 300 mg AZT/150 mg 3TC/300 mg ABC at \$16; IV vials, 10 mg/mL: 200 mg at \$16.74

PATIENT ASSISTANCE: 800-722-9294

REGIMENS

- Standard: 300 mg bid
- Pregnancy: Intrapartum 2 mg/kg IV over 1 hr., then 1 mg/kg/hr. until delivery
- Renal failure: CrCl <20 mL/min.: 300-400 mg/day
- Hepatic failure: 100 mg tid

PATIENT INSTRUCTIONS: Food: no effect. GI intolerance may improve with concurrent meal or smaller doses at more frequent intervals. Warn of lipodystrophy and fat redistribution.

WARNINGS: Avoid concurrent d4T (pharmacologic antagonism). Possible dose reduction with severe liver or renal failure.

MONITOR: CBC for detection of neutropenia and anemia. Some monitor compliance by following macrocytosis with expectation that the MCV will be >100 after 4 weeks.

SIDE EFFECTS: Subjective: GI intolerance, altered taste, insomnia, arthralgias, myalgias, headache—usually improves. Marrow suppression: Related to dose and duration of Rx, responds to discontinuation of drug or to cytokines (anemia: EPO; neutropenia: G-CSF). Myopathy. Macrocytosis starts within 4 weeks, may be indicator of therapy. Fingernail discoloration: Blush dark at base of nail. Myocardiopathy with reduced leftventricular function attributed to mitochondrial toxicity, supporting evidence is conflicting. Class ADRs: Lactic acidosis \pm steatosis

DRUG INTERACTIONS: Other drugs that cause marrow suppression, such as ganciclovir; others—TMP-SMX, dapsone, pyrimethamine, 5-FU, interferon, *Adriamycin*, vinblastine, vincristine, sulfadiazine, ribavirin, amphotericin B and HU.

PREGNANCY: Category C

Abbreviations

Guide to Drug Abbreviations

Abbreviation	Drug	Abbreviation	Drug
ABC	Abacavir	LPV/RTV	Lopinavir/Ritonavir
APV	Amprenavir	NFV	Nelfinavir
AZT	Zidovudine	NVP	Nevirapine
d4T	Stavudine	Pen	Penicillin
ddC	Zalcitabine	PZA	Pyrazinamide
ddI	Didanosine	RBT	Rifabutin
DLV	Delavirdine	RIF	Rifampin
EFV	Efavirenz	RTV	Ritonavir
EMB	Ethambutol	SM	Streptomycin
5-FC	Flucytosine	SMX	Sulfamethoxazole
FQ	Fluoroquinolone	SQV	Saquinavir
FTV	<i>Fortovase</i>	3TC	Lamivudine
Gent	Gentamycin	TDF	Tenofovir
HU	Hydroxyurea	TMP	Trimethoprim
IDV	Indinavir	TMP-SMX	Trimethoprim-Sulfamethoxazole
INH	Isoniazid	TZV	<i>Trizivir</i>
INV	<i>Invirase</i>	ZDV	Zidovudine
LPV	Lopinavir		

Drug Administration Abbreviations

bid	twice per day	qmo.	every month
hr., hrs.	hour, hours	qwk.	every week
min., mins.	minute, minutes	qod	every other day
mo., mos.	month, months	tid	three times per day
PO	by mouth	wk., wks.	week, weeks
qd	every day	yr., yrs.	year, years
qid	four times per day		

Abbreviations Used

Abbreviation	Term or Phrase
ACIP	Advisory Council on Immunization Practices
ACTG	AIDS Clinical Trial Group
ADRs	Adverse Drug Reaction(s)
AETC	AIDS Education Training Center
ALT	Alanine aminotransferase

Abbreviation	Term or Phrase
ANC	Absolute Neutrophil Count
ART	Antiretroviral Therapy
ASA	Aspirin
ASCUS	Atypical squamous cells of undetermined significance
AST	Aspartate aminotransferase
AUC	Area under the curve
BACOD	Bleomycin, cyclophosphamide and etoposide (chemotherapy)
c/mL	Copies per milliliter
CBC	Complete blood count
CDC	Centers for Disease Control and Prevention
CHOP	Cyclophosphamide, doxorubicin, vincristine and prednisone (chemotherapy)
CrCl	Creatinine clearance
CT	Computerized tomography
DFA	Direct fluorescent antibody
DHHS	Department of Health and Human Services (U.S.)
DOT	Directly observed therapy
DS	Double strength
DTR	Deep tendon reflex
DXA	Energy X-ray absorptiometry
EBV	Epstein Barr virus
EIA	Enzyme immunoassay
EPOCH	Etoposide, prednisone, vincristine, doxorubicin and cyclophosphamide
ERCP	Endoscopic retrograde cholangiopancreatography
HAV	Hepatitis A virus
HAART	Highly active antiretroviral therapy
HBc	Hemoglobin C
HBcAg	Hepatitis B core antigen
HBIG	Hepatitis B immune globulin
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCFA	Health Care Financing Administration (U.S.)
HCV	Hepatitis C virus
HDL	High density lipoprotein
HHV-6	Human herpes virus-6
HHV-8	Human herpes virus-8
HIVAN	HIV-associated nephropathy
HSIL	High grade squamous intraepithelial lesion
HSR	Hypersensitivity reaction
HSV	Herpes simplex virus
HSV 1	Herpes simplex virus 1
HSV 2	Herpes simplex virus 2
HTLV-1	Human T-cell lymphotropic virus-1

Abbreviation	Term or Phrase
HTLV-2	Human T-cell lymphotropic virus-2
IDSA	Infectious Diseases Society of America
IG	Immune globulin
ITP	Idiopathic thrombocytopenia purpura
IVIG	Intravenous immune globulin
KS	Kaposi's sarcoma
LDL	Low density lipoprotein
LFTs	Liver function test(s)
LP	Lumbar puncture
LSIL	Low grade squamous intraepithelial lesion
LTBI	Latent tuberculosis infection
MAC	<i>Mycobacterium avium</i> complex
MACS	Multicenter AIDS Cohort Study
MDR	Multidrug resistant
MRI	Magnetic resonance imaging
MRSA	Methicillin resistant <i>Staph aureus</i>
MSM	Men who have sex with men
MSSA	Methicillin sensitive <i>Staph aureus</i>
NCI	National Cancer Institute
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
PCP	<i>Pneumocystis carinii</i> pneumonia
PGL	Persistent generalized lymphadenopathy
PHS or USPHS	Public Health Service (U.S.)
PI	Protease inhibitor
PML	Progressive multifocal leukoencephalopathy
PPD	Purified protein derivative of tuberculin
RIBA	Recombinant Immunoblot assay
RPR	Rapid plasma reagin
RT-PCR	Reverse transcriptase polymerase chain reaction
TAMs	Thymidine analog mutations
TD	Tetanus-diphtheria
TLC	Therapeutic lifestyle change
ULN	Upper limit of normal
VDRL	Venereal disease research laboratory
VZIG	Varicella zoster immune globulin
VZV	Varicella zoster virus
WBC	White blood count

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