



Adult HIV Therapy Handbook

August 2009



Editors

Hélène H. Hardy, Pharm.D.

Paul R. Skolnik, M.D.

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This handbook is also available at <http://www.BMC.org/HIV-AIDS>

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This handbook is NOT meant to substitute for consultation with an infectious diseases or pulmonary specialist. This handbook summarizes basic principles of antiretroviral therapy (dose, frequency, adverse effects, and contraindications).

Efforts are made to ensure that the information in this handbook is accurate; however, readers are advised to check the current prescribing information provided by the manufacturer of each drug. The editors and publishers do not assume responsibility for errors, omissions, or other inadvertent outcomes resulting from the use or application of the information in this handbook to patient care or prescribing, which remain the responsibility of the provider.

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Abbreviations

Drugs				Diseases	
NRTI	nucleoside reverse transcriptase inhibitor	PI	protease inhibitor	ARS	Acute Retroviral Syndrome
NtRTI	nucleotide reverse transcriptase inhibitor	ATV	atazanavir	CMV	Cytomegalovirus
ABC	abacavir	DRV	darunavir	HBV	Hepatitis B virus
ddl	didanosine	FosAPV	fosamprenavir, same as FPV	HCV	Hepatitis C virus
ddl-EC	didanosine, enteric coated	FPV	fosamprenavir, same as FosAPV	OI	Opportunistic infection
FTC	emtricitabine	IDV	indinavir		
3TC	lamivudine	LPV/r	lopinavir + ritonavir combined		
d4T	stavudine	NFV	nelfinavir		
TDF	tenofovir	RTV	ritonavir		
AZT	zidovudine, same as ZDV	/r	ritonavir-boosted, e.g., SQV/r		
ZDV	zidovudine, same as AZT	SQV	saquinavir		
		TPV	tipranavir		
NNRTI	non-nucleoside reverse transcriptase inhibitor				
DLV	delavirdine	ENF	enfuvirtide, same as T-20		
EFV	efavirenz	T-20	enfuvirtide, same as ENF		
ETR	etravirine	MVC	maraviroc		
NVP	nevirapine	RAL	raltegravir		

Other	
ARV	Antiretroviral
ART	Antiretroviral therapy
BMC	Boston Medical Center
CHACR	Center for HIV/AIDS Care and Research
CID	Center for Infectious Diseases
ED	Emergency Department
ID	Infectious Diseases
HD	Hemodialysis
OEM	Occupational and Environmental Medicine
PEP	Post-exposure prophylaxis

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General Guidelines for Inpatient Treatment of HIV-Infected Patients at BMC

Initiating antiretroviral medications (ARVs) is not an emergency. Patients who are not in an ongoing relationship with a primary care provider should generally not have antiretroviral therapy initiated as inpatients, with priority being given to treatment of opportunistic infections or other presenting conditions. Exceptions, such as Acute Retroviral Syndrome (see page 6), or patients admitted to the Intensive Care Unit with opportunistic infections, should be discussed with the ID Consult Service or with a Center for Infectious Diseases attending physician.

If a patient on ARVs must stop an ARV for any reason, all ARVs should be stopped, in order to prevent resistance development.

In order to enhance the quality of care for patients transitioning between the Outpatient and Inpatient Services, the ID Fellow on call (beeper 8902 for the Menino Pavilion or 8903 for the East Newton Campus) should be notified of any HIV+ patient admission to or discharge from BMC.

The patient's primary care provider and, if different, HIV specialist should also be notified of a patient's hospital admission and/or discharge.

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General Guidelines for Inpatient Investigational Antiretroviral Agents at BMC

If a patient admitted to the hospital is receiving an HIV medication as part of a BMC outpatient study, the following steps should be taken by the admitting physician to ensure proper use of the study medication during the patient's hospital stay:

Contacting the HIV Clinical Research Office

1. The physician caring for the patient should contact the ID consult team and an HIV clinical research nurse (**beeper 2731**).
2. The study nurse will notify the principal investigator (PI) on the study who will determine whether it is safe for the patient to continue taking the HIV study medication.
3. If it is deemed appropriate for the patient to continue the study medication, the research nurse will contact the HIV pharmacist (**beepers 2729 and 3421**). The pharmacist will dispense the study medication, bring it to the floor, and provide information (oral or written) on appropriate storage, dosing, administration requirements, and possible side effects.

Order Entry of Study Medications

1. The physician caring for the patient should select the following in SCM order entry: Investigational Study Drug – Outpatient Continuation.
2. SCM requires the physician to enter the study drug name, dosage strength, dosage, BMC protocol title, and PI name.
3. Upon the patient's discharge from the hospital, all remaining study medication is returned by a floor nurse to the HIV pharmacist (**beepers 2729 and 3421**). The pharmacist notes all use of the medication in the study protocol drug accountability log.

4

General Guidelines for Outpatient Treatment of HIV-Infected Patients at BMC

The Center for Infectious Diseases, under the auspices of the Center for HIV/AIDS Care and Research, is the axis of adult HIV care at BMC.

In order to ensure the best patient care, it is important for the inpatient and outpatient physicians to communicate during admission, throughout a patient's hospital stay, and as the patient is discharged. Referral for ongoing HIV care should be made as described in the following table.

If patient has	newly diagnosed infection or is new to the BMC system	page beeper 4448 (4HIV) or call 617-414-5979
	established infection and has not seen an HIV specialist*	call patient's PCP to discuss referral to Center for Infectious Diseases (CID: 617-414-4290)
	established infection and has seen an HIV specialist	contact the HIV specialist

*If patient is followed by Health Care for the Homeless, call 617-414-7779 to discuss care.

Acute Retroviral Syndrome (ARS)

Symptoms of ARS appear within days to weeks of exposure; the **average incubation** period is 2 weeks, with a documented range of 4 days to 8 weeks. The **prevalence** of ARS, in published series of persons who later seroconverted, ranges from 38% to 92%. Prolonged or more severe symptoms during ARS may predict more rapid progression to AIDS.

Common symptoms and signs include rash (may be fleeting, lasting only hours or 1-2 days, often consisting of 5-10 mm non-pruritic, diffuse, erythematous maculopapular lesions, often more prominent centrally than peripherally; may include the face, palms, and soles; may be more difficult to discern on dark-skinned persons); fever; lethargy; adenopathy; pharyngitis; oral, esophageal, anal, or genital ulcerations (may be exudative); myalgia; arthralgia; diarrhea, nausea, or vomiting; hepatosplenomegaly; oral candidiasis; weight loss; headache; cognitive impairment; cranial nerve palsies; and psychosis.

Abnormal lab tests may include thrombocytopenia, leukopenia (with atypical lymphocytosis), elevated CPK, and elevated LFTs. An important **risk factor** is recent exposure—unprotected sexual contact or needle sharing. A **diagnosis** of ARS is made on the basis of a positive HIV RNA (viral load) test (usually very high) and a negative HIV antibody test. Viral load is measured with the usual in-house HIV RNA assay (2 purple-top tubes) with censoring of low values to exclude false positives.

Inpatients for whom this diagnosis is being considered should have an ID consultation to help with interpretation of the HIV RNA (viral load) test results and for possible initiation of therapy.

Outpatients suspected of having ARS should be referred to the Center for Infectious Diseases—page beeper 4448 (4HIV) or call 617-414-4290—on a semi-urgent basis for proper initiation of therapy.

Specify that the patient has acute retroviral syndrome and that s/he needs to be seen within 7 days. 6

Post-Exposure Prophylaxis (PEP)

In the event of a work-hours occupational potential exposure to HIV, the exposed employee should report to Occupational and Environmental Medicine (OEM, 8-8400) on Preston 5. If the occupational exposure is after working hours, or the potential exposure is non-occupational, the exposed person should report to the BMC Emergency Department (ED). The ED will page beeper 7845 (STIK) with any questions.

The exposed employee should obtain the source patient's name and medical record number, if possible. If obtaining this information is time consuming, the exposed employee should not delay in reporting to OEM or the ED.

The exposed employee may not obtain written consent for HIV testing or obtain a blood sample from the source patient. Another BMC caretaker must perform both of these functions.

The above procedures should be followed without delay; the goal is to administer PEP within an hour of the exposure, if possible. If the occupational exposure has happened after working hours and the exposed employee has been seen in the ED, the employee should report to OEM on the morning of the next business day (this is detailed on the ED discharge sheet). A non-occupational exposure will be referred to BMC's Center for Infectious Diseases (this is also in the ED discharge instructions).

Positive HOPE: Obstetrics/Pregnancy and HIV

SERVICES

- ✘ Preconception counseling for discordant/concordant couples with HIV desiring pregnancy, including referral for fertility evaluation in the Women's Center
- ✘ Full-service prenatal care in a multidisciplinary clinic staffed by a maternal-fetal medicine specialist, an infectious diseases physician who specializes in caring for HIV+ pregnant women, a clinical RN, and a research RN
- ✘ Case management, counseling, and social services for patients and families with social workers in the Center for HIV/AIDS Care and Research (CHACR)
- ✘ Referrals to the CHACR mental health team
- ✘ Substance abuse treatment and/or methadone maintenance referral and management
- ✘ Referral for postpartum care in the CHACR, including an ID RN for intake
- ✘ Access to clinical research programs relevant to HIV and pregnancy

REFERRAL




- ✘ For preconception counseling, call the CHACR at 617-414-4290 for an appointment with the ID specialist in perinatal HIV infection; partners are encouraged to attend
- ✘ Pregnant HIV+ patients may call the high-risk OB RN at 617-414-4165; request an appointment during a Thursday morning high-risk clinic with the specialist in maternal-fetal medicine and/or the ID specialist in perinatal HIV infection

GUIDELINES

- ✘ General guidelines for management of HIV+ pregnancy available on <http://www.aidsinfo.nih.gov/>
- ✘ Efavirenz is a Class D drug during pregnancy
- ✘ Female patients of childbearing age who are taking efavirenz should use two methods of contraception (condoms plus another) or consider an alternative antiviral medication
- ✘ Female patients may consult a family planning/GYN nurse practitioner in the CHACR
- ✘ If a woman taking efavirenz learns she is pregnant, she should immediately contact the ID specialist in perinatal HIV infection for counseling and a plan

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Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs/NtRTIs) - page 1 of 2

Generic Name (Trade Name)	Abacavir (ABC) (Ziagen®)	Didanosine (ddl) (Videx®)		Didanosine EC (ddl-EC) (Videx-EC®)		Emtricitabine (FTC) (Emtriva®)			
Form	Tab: 300 mg  Liq: 20 mg/ml (240 ml bottle)	Powder (2 g or 4 g) for oral solution dispensed in 4- and 8-ounce glass bottles		Cap (enteric coated): 125, 200, 250, 400 mg ² 		Cap: 200 mg  Liq: 10 mg/ml			
Dosing recommendations	300 mg bid or 600 mg daily (or 15 ml bid)	< 60 kg	125 mg bid or 250 mg daily	20 to < 25 kg	200 mg daily ³	200 mg daily or 240 mg (24 ml) daily			
		≥ 60 kg	200 mg bid or 400 mg daily	25 to < 60 kg	250 mg daily ³				
				≥ 60 kg	400 mg daily ³				
Food effect	Take with or without food	Take 30 min before or 2 hr after meal (food ↓ levels 55%)		Take 30 min before or 2 hr after meal (food ↓ levels 20%)		Take with or without food			
Dosing during renal impairment	Cleared renally > 80% (inactive metabolites); no need to adjust dose	CrCl	< 60 kg	≥ 60 kg	CrCl	< 60 kg	≥ 60 kg	CrCl	Dose
		≥ 60	250 mg daily or 125 mg bid	400 mg daily or 200 mg bid	≥ 60	250 mg daily	400 mg daily	30-49	200 mg cap q48h or 120 mg (12 ml) q24h soln
		30-59	150 mg daily or 75 mg bid	200 mg daily or 100 mg bid	30-59	125 mg daily	200 mg daily	15-29	200 mg cap q72h or 80 mg (8 ml) q24h soln
		10-29	100 mg daily	150 mg daily	10-29	125 mg daily	125 mg daily	< 15	200 mg cap q96h or 60 mg (6 ml) q24h soln
		< 10 HD or CAPD	75 mg daily 75 mg daily	100 mg daily 100 mg daily	< 10 HD or CAPD	do not use ⁴ do not use ⁴	125 mg daily 125 mg daily	FTC ↓ > 30% over 3-hr HD session	200 mg cap q96h or 60 mg (6 ml) q24h soln; on HD day, take after HD
Dosing during hepatic impairment	Child-Pugh Score 5-6: 200 mg (10 ml) bid ¹ ; limited clinical data; Child-Pugh Score 7-12: not recommended	No dose adjustment required		No dose adjustment required		No dose adjustment required			

HD: hemodialysis





1 Adjustment recommended in mild hepatic impairment (Child-Pugh score 5-6) 2 Generic Videx-EC formulation available in 200 mg, 250 mg, and 400 mg caps

3 TDF in combination with ddl should be avoided if possible because of possible ↓ efficacy; if TDF with ddl is necessary, a dose adjustment is required: pts < 60 kg with normal renal function should receive 200 mg ddl-EC in combination with TDF; pts > 60 kg should receive 250 mg ddl-EC with TDF and a light meal

4 EC formulation not suitable for patients < 60 kg with CrCl < 10; use ddl formulation (without EC)

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Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs/NtRTIs) - page 2 of 2

Generic Name (Trade Name)	Lamivudine (3TC) (Epivir®)	Stavudine (d4T) (Zerit®)	Tenofovir (TDF) (Viread®)	Zidovudine (AZT or ZDV) (Retrovir®)					
Form	Tab: 100 (Epivir-HBV), 150, 300 mg  Liq: 10 mg/ml (240 ml bottle)	Cap: 15, 20, 30, 40 mg  Liq: 1 mg/ml (200 ml bottle)	Tab: 300 mg 	Cap: 100 mg  Tab: 300 mg ² Liq: 10 mg/ml (240 ml bottle)					
Dosing recommendations	150 mg bid or 300 mg daily (or 15 ml bid or 30 ml daily)	≥ 60 kg: 40 mg bid (or 40 ml bid) < 60 kg: 30 mg bid (or 30 ml bid)	300 mg daily	300 mg bid (or 30 ml bid)					
Food effect	Take with or without food	Take with or without food	Take with or without food	Take with or without food					
Dosing during renal impairment	CrCl	Dose	CrCl	< 60 kg	≥ 60 kg	CrCl	Dose	CrCl	Dose
	≥ 50	150 mg (or 15 ml) bid, or 300 mg (or 30 ml) daily	≥ 50	30 mg bid (or 30 ml bid)	40 mg bid (or 40 ml bid)	≥ 50	300 mg daily	> 10	300 mg bid (or 30 ml bid)
	30-49	150 mg (or 15 ml) daily	26-49	15 mg bid (or 15 ml bid)	20 mg bid (or 20 ml bid)	30-49	300 mg q48h	< 10	100 mg tid or 300 mg daily (or 10 ml tid or 30 ml daily)
	15-29	150 mg (or 15 ml) x 1, then 100 mg (or 10 ml) daily	10-25	15 mg daily (or 15 ml daily)	20 mg daily (or 20 ml daily)	10-29	300 mg q72-96h		
	5-14	150 mg (or 15 ml) x 1, then 50 mg (or 5 ml) daily	< 10	15 mg daily (or 15 ml daily)	20 mg daily (or 20 ml daily)	< 10	300 mg q7d	HD or PD ³	100 mg tid or 300 mg daily (or 10 ml tid or 30 ml daily)
< 5	50 mg (or 5 ml) daily x 1, then 25 mg (or 2.5 ml) daily	HD	20 mg after HD, then q24h	20 mg after HD, then q24h	HD	q7d after HD			
Dosing during hepatic impairment	Dose adjustment not required ¹	Dose adjustment not required		Dose adjustment not required		Dose adjustment not required		Dose adjustment not required	

HD: hemodialysis

1 3TC has not been studied in decompensated hepatic disease






2 Zidovudine (Retrovir®) is available as a generic in 100 mg and 300 mg tablets

3 HD and peritoneal dialysis appear to have negligible effect on removal of zidovudine, whereas elimination of glucuronidated metabolite is ↑

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Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) - page 1 of 3

Generic (Trade Name)	Delavirdine (DLV) (Rescriptor®)	Efavirenz (EFV) (Sustiva®)	Etravirine (ETR) (Intelence®)	Nevirapine (NVP) (Viramune®)
Form	Tab: 100 mg Cap: 200 mg 	Cap: 50, 200 mg  Tab: 600 mg 	Tab: 100 mg 	Tab: 200 mg  Liq: 10 mg/ml suspension (240 ml bottle)
Dosing recommendations	400 mg tid 100 mg tab may be dispersed in water ≥ 3 oz; 200 mg tab should be taken intact; separate dosing with ddl or antacids by 1 hr	10- < 15 kg: 200 mg qhs; 15- < 20 kg: 250 mg qhs; 20- < 25 kg: 300 mg qhs; 25- < 32.5 kg: 350 mg qhs; 32.5- < 40 kg: 400 mg qhs; ≥ 40 kg: 600 mg qhs	200 mg po q12h May disperse in glass of water	200 mg daily x 14 days then 200 mg bid or 20 ml daily x 14 days then 20 ml bid If mild rash occurs within first 14 days of therapy, do not ↑ to bid until resolved; if mucous membranes involved or blisters occur, discontinue immediately
Food effect	Take without food	High-fat meals ↑ EFV 50%; take on empty stomach	Take with food	Take with or without food
Contraindicated concomitant medications	<ul style="list-style-type: none"> • Astemizole, terfenadine • Dihydroergotamine, ergonovine, ergotamine, methylethergonovine • Cisapride • Pimozide • Alprazolam, midazolam, triazolam • Simvastatin, lovastatin • Rifabutin, rifampin, rifapentine • FPV • Carbamazepin, phenobarbital, phenytoin 	<ul style="list-style-type: none"> • Astemizole • Bepridil • Cisapride • Midazolam • Pimozide • Triazolam • Ergot medications (e.g., ergotamine and ergonovine) • Rifapentine • St John's wort 	<ul style="list-style-type: none"> • Unboosted PIs, other NNRTIs, ATV, TPV, FPV • Rifampin, rifapentine • Carbamazepine, phenobarbital, phenytoin 	<ul style="list-style-type: none"> • Ketoconazole • Rifampin, rifapentine • St. John's wort

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) - page 2 of 3

Generic (Trade Name)	Delavirdine (DLV) (Rescriptor®)	Efavirenz (EFV) (Sustiva®)	Etravirine (ETR) (Intelence®)	Nevirapine (NVP) (Viramune®)				
Dose adjustments in combination regimens	IDV	IDV 600 mg tid	IDV	Insufficient data	IDV	Insufficient data	IDV	Insufficient data
	NFV	Insufficient data	NFV	NFV 1250 mg bid	NFV	Not recommended	NFV	NFV 1250 mg bid
	FPV	Insufficient data	FPV	FPV 1400 mg daily + RTV 300 mg daily (naïve pts ONLY) or FPV 700 mg bid + RTV 100 mg bid	FPV	Not recommended	FPV	FPV 700 mg bid + RTV 100 mg bid
	DRV	Insufficient data	DRV	DRV 600 mg bid + RTV 100 mg bid	DRV	DRV 600 mg bid + RTV 100 mg bid	DRV	DRV 600 mg bid + RTV 100 mg bid
	TPV	Insufficient data	TPV	TPV 500 mg bid + RTV 200 mg bid	TPV	Not recommended	TPV	TPV 500 mg bid + RTV 200 mg bid
	SQV	SQV 600 mg tid	SQV	SQV 1000 mg bid + RTV 100 mg bid	SQV	SQV 1000 mg bid + RTV 100 mg bid	SQV	SQV 1000 mg bid + RTV 100 mg bid
	LPV/r	Insufficient data	LPV/r	LPV/r 3 tabs (600/150 mg) bid experienced pts ONLY or LPV/r 533/133 mg (6.5 ml liq) bid	LPV/r	ETR ↑ 50-85%; LPV/r 2 tabs (400/100 mg) bid; coadminister with caution	LPV/r	LPV/r 3 tabs (600/150 mg) bid experienced pts ONLY or LPV/r 533/133 mg (6.5 ml liq) bid
	FPV		FPV	FPV 700 mg bid + RTV 100 mg bid				
ATV	Insufficient data	ATV	ATV 400 mg + RTV 100 mg daily (naïve pts ONLY); not recommended for experienced pts	ATV	Not recommended	ATV	Not recommended	

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) - page 3 of 3

Generic (Trade Name)	Delavirdine (DLV) (Rescriptor®)	Efavirenz (EFV) (Sustiva®)	Etravirine (ETR) (Intelence®)	Nevirapine (NVP) (Viramune®)
Route of metabolism	Liver CYP3A4 inhibitor	Liver Potent inducer of CYP3A4	Liver Mixed inducer of CYP3A4 and inhibitor of CYP2C9 and CYP2C19; substrate of CYP3A4, CYP2C9, and CYP2C19	Liver Mixed CYP3A4 inducer/inhibitor
Dosing during renal impairment	Not studied	Insufficient data	No dosage adjustment required	Insufficient data
Dosing during hepatic impairment	Caution if hepatic impairment	Caution if hepatic impairment	Caution when severe hepatic impairment (Child-Pugh Class C); pharmacokinetics not studied	Do not administer in pts with moderate to severe hepatic impairment (Child-Pugh Class B and C); if NVP discontinued due to hepatotoxicity, do not restart; substantially ↑ risk of symptomatic hepatic events in pts, particularly women, with ↑ CD4+ cell count (> 250 cells/mm ³ in women, > 400 cells/mm ³ in men) at therapy initiation; often associated with rash
Comments	Pts with achlorhydria should take with acidic beverage (orange or cranberry juice)	Do NOT administer during pregnancy — FDA Pregnancy Category D; false positive urine cannabinoid test observed with CEDIA DAU multi-level THC assay used for screening, monitor for CNS toxicities, rash, and AST/ALT	Pregnancy Category B	200 mg daily x 14 days to minimize risk of rash, then ↑ to 200 mg bid; monitor AST and ALT , especially during first 6 months of therapy and during pregnancy; women with CD4+ > 250 cells/mcl and men with CD4+ > 400 cells/mcl at ↑ risk for hepatotoxicity






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Coformulations



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Coformulations

Generic Name (Trade Name)	Efavirenz + Emtricitabine + Tenofovir Disoproxil Fumarate (Atripla®)	Lamivudine + Zidovudine (Combivir®)	Abacavir + Lamivudine (Epizcom®)	Abacavir + Lamivudine + Zidovudine (Trizivir®)	Emtricitabine + Tenofovir Disoproxil Fumarate (Truvada®) ²	
Form	Tab: 600/200/300 mg 	Tab: 150/300 mg 	Tab: 600/300 mg 	Tab: 300/150/300 mg 	Tab: 200/300 mg 	
Dosing recommendations	> 40 kg	1 tab qhs				
	< 40 kg	Avoid (refer to individual agent recommendations)	1 tab bid	1 tab daily	1 tab bid	
Food effect	Take on empty stomach or with light meal; high fat meal ↑ AUC 28% and ↑ C _{max} 79%	Take with or without food	Take with or without food	Take with or without food	Take with or without food	
Dosing during renal impairment	Avoid if CrCl < 50 (refer to individual agent recommendations)	Avoid combination if CrCl < 50 ¹	Avoid combination if CrCl < 50 ¹ (refer to individual agent recommendations)	Avoid combination if CrCl < 50 ¹	CrCl	
					≥ 50	1 tab q24h
					30-49	1 tab q48h
					< 30	Avoid combination (refer to individual agent recommendations)
Dosing during hepatic impairment	Use with caution if hepatic impairment	Follow recommendation for single agent in combination	Follow recommendation for single agent in combination	Follow recommendation for single agent in combination	Follow recommendation for single agent in combination	




HD: hemodialysis

¹ HD and peritoneal dialysis appear to have negligible effect on removal of zidovudine, whereas the elimination of its glucuronidated metabolite is enhanced; dose lamivudine and zidovudine separately in patients with CrCl < 50 (i.e., do not use Combivir® or Trizivir®)

² Do NOT administer during pregnancy—FDA Pregnancy Category D; false positive urine cannabinoid test observed with CEDIA DAU multi-level THC assay used for screening

Protease Inhibitors (PIs)

Protease Inhibitors (PIs) - page 1 of 9

Generic (Trade Name)	Atazanavir (ATV) (Reyataz®)	Darunavir (DRV) (Prezista®)	Fosamprenavir (FPV) (Lexiva®)
Form	Cap: 100, 150, 200, 300 mg 	Tab: 400, 600 mg 	Tab: 700 mg  Oral suspension: 50 mg/ml
Dosing recommendations	Naïve pts 400 mg daily or 300 mg daily + RTV 100 mg daily must use second option when combined with TDF—see next page	Naïve pts DRV 800 mg daily + RTV 100 mg daily	Naïve pts 1400 mg bid or FPV 1400 mg daily + RTV 100-200 mg daily or FPV 700 mg bid + RTV 100 mg bid or FPV 1400 mg + RTV 100 mg daily
	Experienced pts ATV 300 mg daily + RTV 100 mg daily	Experienced pts DRV 600 mg bid + RTV 100 mg bid	Experienced pts FPV 700 mg bid + RTV 100 mg bid
Contraindicated concomitant medications	<ul style="list-style-type: none"> • Bepiridil • Simvastatin, lovastatin • Rifampin, rifapentine • Astemizole, terfenadine • Cisapride • Pimozide • Midazolam, triazolam • DHE, ergotamine, ergonovine • St. John's wort • Other: fluticasone¹, indinavir, irinotecan, PPI (if ATV unboosted) 	<ul style="list-style-type: none"> • Simvastatin, lovastatin • Rifampin, rifapentine • Astemizole, terfenadine • Cisapride • Pimozide • Midazolam, triazolam • DHE, ergotamine, ergonovine • St. John's wort • Other: fluticasone¹, carbamazepine, phenobarbital, phenytoin 	<ul style="list-style-type: none"> • Bepiridil • Simvastatin, lovastatin • Rifampin, rifapentine • Astemizole, terfenadine • Cisapride • Pimozide • Midazolam, triazolam • DHE, ergotamine, ergonovine • St. John's wort • Other: fluticasone¹, delavirdine

¹ Fluticasone coadministered with RTV significantly ↓ serum cortisol concentrations; consider alternative steroids

Protease Inhibitors (PIs) - page 2 of 9

Generic (Trade Name)	Atazanavir (ATV) (Reyataz®)	Darunavir (DRV) (Prezista®)	Fosamprenavir (FPV) (Lexiva®)									
Dose adjustments in combination regimens	EFV	ATV 400 mg + RTV 100 mg daily (naïve pts only); not recommended for experienced pts	<table border="1"> <tr> <td>ATV</td> <td>DRV 600 mg bid + RTV 100 mg bid + ATV 300 mg daily</td> </tr> <tr> <td>EFV¹</td> <td>DRV 600 mg bid + RTV 100 mg bid</td> </tr> </table>	ATV	DRV 600 mg bid + RTV 100 mg bid + ATV 300 mg daily	EFV¹	DRV 600 mg bid + RTV 100 mg bid	<table border="1"> <tr> <td>ATV</td> <td>FPV 700 mg + RTV 100 mg bid (experienced or naïve pts) + ATV 300 mg daily (monitor ATV levels)</td> </tr> <tr> <td>EFV</td> <td>FPV 1400 mg + RTV 300 mg + EFV 600 mg daily or FPV 700 mg bid + RTV 100 mg bid + EFV 600 mg daily</td> </tr> </table>	ATV	FPV 700 mg + RTV 100 mg bid (experienced or naïve pts) + ATV 300 mg daily (monitor ATV levels)	EFV	FPV 1400 mg + RTV 300 mg + EFV 600 mg daily or FPV 700 mg bid + RTV 100 mg bid + EFV 600 mg daily
	ATV	DRV 600 mg bid + RTV 100 mg bid + ATV 300 mg daily										
	EFV¹	DRV 600 mg bid + RTV 100 mg bid										
	ATV	FPV 700 mg + RTV 100 mg bid (experienced or naïve pts) + ATV 300 mg daily (monitor ATV levels)										
EFV	FPV 1400 mg + RTV 300 mg + EFV 600 mg daily or FPV 700 mg bid + RTV 100 mg bid + EFV 600 mg daily											
ETR	Do not co-administer , even if ATV/r is used	IDV IDV 800 mg bid, AEs may require IDV 600 mg bid, standard dose DRV										
NVP	Do not co-administer	LPV/r, SQV Not recommended										
TDF	ATV 300 mg + RTV 100 mg daily	NFV, FPV, TPV No data currently available										
		NVP² DRV 600 mg bid + RTV 100 mg bid										

¹ Use standard dose EFV: EFV levels ↑ 21% and DRV levels ↓ 13%




² Use standard dose NVP: NVP levels ↑ 27% and DRV levels do not change

Protease Inhibitors (PIs) - page 3 of 9

Generic (Trade Name)	Atazanavir (ATV) (Reyataz®)	Darunavir (DRV) (Prezista®)	Fosamprenavir (FPV) (Lexiva®)	
Food effect	Take with food; light meal ↑ AUC 70%; ATV solubility ↓ as pH ↑	Take with food; ↑ AUC by ~30%	Take with or without food	
Route of metabolism	Liver; inhibitors CYP3A4 and UGT1A1; inhibition potency ATV < RTV	Liver; CYP3A4 substrate; inhibits p-glycoprotein and CYP3A4	Liver; inhibits CYP3A4; inhibition potency FPV = IDV, NFV < RTV	
Dosing during renal impairment	No change; not dialyzed	No change; not dialyzed	No change; not dialyzed	
Dosing during hepatic impairment	Reduce dose to 300 mg daily for pts with moderate hepatic insufficiency (Child-Pugh Score 7-9); do not use in pts with severe hepatic insufficiency (Child-Pugh Score > 9); ATV/r not recommended in pts with hepatic impairment (~10% ↑ LFT to > 5x ULN in pts with hepatitis B or C coinfection)	Mild hepatic impairment—no adjustment necessary; not recommended in severe hepatic impairment	Child-Pugh Score	
			5-6	700 mg bid (no RTV) (naïve pts) or 700 mg bid + 100 mg RTV daily (naïve or PI-experienced pts)
			7-9	700 mg bid (no RTV) (naïve pts) or 450 mg bid + 100 mg RTV daily (naïve or PI-experienced pts)
			10-12	Use with caution; 350 mg bid (no RTV) (naïve pts); no data on FPV/r in pts with severe hepatic impairment

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Protease Inhibitors (PIs) - page 4 of 9

Generic (Trade Name)	Indinavir (IDV) (Crixivan®)	Lopinavir/Ritonavir (LPV/r) (Kaletra®)	Nelfinavir (NFV) (Viracept®)
Form	Cap: 100, 200, 333, 400 mg 	Tab: 200/50 mg, 100/25 mg  Liq: 80/20 mg/ml (mint flavor; 42% alcohol)	Tab: 250, 625 mg  Liq: 50 mg/g oral powder ²
Dosing recommendations	800 mg tid (no RTV) or 800 mg bid + 100-200 mg RTV bid or 400 mg bid + 400 mg RTV bid	Naïve pts 2 tabs bid (400/100 mg bid) or 5 ml bid or 4 tabs daily (800/200 mg daily) or 10 ml daily Experienced pts 2 tabs bid (400/100 mg bid) or 5 ml bid	1250 mg po bid 5 x 250 mg tab bid or 2 x 625 mg tab bid; tablets (both strengths) may be dissolved in small amount of water if pt unable to swallow whole
Contraindicated concomitant medications	<ul style="list-style-type: none"> • Simvastatin, lovastatin • Rifampin, rifapentine • Astemizole, terfenadine • Cisapride • Pimozide • Midazolam, triazolam • DHE, ergotamine, ergonovine • St. John's wort • Other: atazanavir 	<ul style="list-style-type: none"> • Flecainide, propafenone • Simvastatin, lovastatin • Rifampin, rifapentine • Astemizole, terfenadine • Cisapride • Pimozide • Midazolam, triazolam • DHE, ergotamine, ergonovine • St. John's wort • Other: fluticasone¹ 	<ul style="list-style-type: none"> • Simvastatin, lovastatin • Rifampin, rifapentine • Astemizole, terfenadine • Cisapride • Pimozide • Midazolam, triazolam • DHE, ergotamine, ergonovine • St. John's wort

¹ Fluticasone coadministered with RTV significantly ↓ serum cortisol concentrations; consider alternative steroids

² Mix oral powder in small amount water, soy milk, or dietary supplement (1 scoop = 50 mg); acidic juices cause bitter taste

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Protease Inhibitors (PIs) - page 5 of 9

Generic (Trade Name)	Indinavir (IDV) (Crixivan®)		Lopinavir/Ritonavir (LPV/r) (Kaletra®)		Nelfinavir (NFV) (Viracept®)	
Dose adjustments in combination regimens	NFV	Optimal dosing not established	FPV bid	LPV/r 500/125 mg q12h (two 200/50 mg tabs + one 100/25 mg tab) or 533/133 mg q12h (6.5 ml liq)	IDV	IDV 1200 mg bid (IDV food restrictions apply) + NFV 1250 mg bid
	NVP, EFV	Optimal dosing not established	FPV once daily, EFV	LPV/r once daily should not be co-administered with FPV once daily or EFV		
			IDV	IDV 600 mg bid		
LPV/r	IDV 600 mg bid	EFV	LPV/r 3 tabs bid (600/150 mg bid) for experienced pts; EFV standard dose			





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Protease Inhibitors (PIs) - page 6 of 9

Generic (Trade Name)	Indinavir (IDV) (Crixivan®)		Lopinavir/Ritonavir (LPV/r) (Kaletra®)		Nelfinavir (NFV) (Viracept®)	
Food effect	Take 1 hr before or 2 hrs after meals; may take with skim milk or low-fat snack		Tab: Take with or without food; food ↑ AUC tabs ~27% Liq: Take with food; food ↑ AUC liq 80%		Take with food; food ↑ NFV 2-3x	
Route of metabolism	Liver; CYP3A4 inhibitor < RTV		Liver; potent CYP3A4 inhibitor		Liver; CYP3A4 inhibitor < RTV	
Dosing during renal impairment	No change; not dialyzed		No change; not dialyzed		No change	
Dosing during hepatic impairment	Child-Pugh Score		Not studied; use caution		Mild hepatic impairment; can use without dose adjustment Moderate to severe hepatic impairment; do not use	
	7-9	600 mg tid				
	> 9	Avoid				

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Protease Inhibitors (PIs) - page 7 of 9

Generic (Trade Name)	Ritonavir (RTV) (Norvir®)	Saquinavir (SQV) (Invirase®; INV)	Tipranavir (TPV) (Aptivus®)
Form	Cap: 100 mg 	Cap (hard gel): 200 mg 	Cap (soft gel): 250 mg 
	Liq: 80 mg/ml (peppermint, caramel flavors)	Tab: 500 mg 	
Dosing recommendations	Rarely used: 600 mg bid (6 caps bid or 7.5 ml bid) 100 mg once daily to 200 mg bid; used in PI combination therapy to ↑ other PI	1000 mg bid + RTV 100 mg bid (must be co-administered with RTV)	500 mg bid + RTV 200 mg bid (must be co-administered with RTV)
Contraindicated concomitant medications	<ul style="list-style-type: none"> • Bepridil • Amiodarone, flecainide, propafenone, quinidine • Simvastatin, lovastatin • Rifampin, rifapentine • Astemizole, terfenadine • Cisapride • Pimozide • Midazolam, triazolam • DHE, ergotamine, ergonovine • St. John's wort • Other: voriconazole (with ≥ RTV 400 mg bid), fluticasone¹, alfuozin 	<ul style="list-style-type: none"> • Simvastatin, lovastatin • Rifampin, rifapentine • Astemizole, terfenadine • Cisapride • Pimozide • Midazolam, triazolam • DHE, ergotamine, ergonovine • St. John's wort, garlic supplement • Other: fluticasone¹ 	<ul style="list-style-type: none"> • Bepridil • Amiodarone, flecainide, propafenone, quinidine • Simvastatin, lovastatin • Rifampin, rifapentine • Astemizole, terfenadine • Cisapride • Pimozide • Midazolam, triazolam • DHE, ergotamine, ergonovine • St. John's wort • Other: fluticasone¹

¹ Fluticasone coadministered with RTV significantly ↓ serum cortisol concentrations; consider alternative steroids

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Protease Inhibitors (PIs) - page 8 of 9

Generic (Trade Name)	Ritonavir (RTV) (Norvir®)	Saquinavir (SQV) (Invirase®; INV)	Tipranavir (TPV) (Aptivus®)
Dose adjustments in combination regimens	INV	SQV 1000 mg + RTV 100 mg bid	FPV, LPV/r, SQV, ATV Do not coadminister; ↓ APV, LPV/r, SQV, and ATV Do not coadminister
	IDV	RTV 100-200 mg + IDV 800 mg bid or RTV 400 mg + IDV 400 mg bid	
	FPV	RTV 100 mg or 200 mg + FPV 1400 mg daily (naïve) or RTV 100 mg + FPV 700 mg bid (naïve or experienced)	
	ATV	RTV 100 mg + ATV 300 mg daily (naïve and experienced)	
	DRV	RTV 100 mg + DRV 800 mg once daily (naïve) or RTV 100 mg bid + DRV 600 mg bid (PI-experienced)	
	TPV	RTV 200 mg + TPV 500 mg bid	
		LPV/r	SQV 1000 mg bid (no additional RTV) + LPV standard dose
		NFV, IDV, ATV, EFV, NVP	Dosing recommendations not established
		ETR	May coadminister without dose adjustments

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Protease Inhibitors (PIs) - page 9 of 9

Generic (Trade Name)	Ritonavir (RTV) (Norvir®)	Saquinavir (SQV) ¹ (Invirase®; INV)	Tipranavir (TPV) (Aptivus®)
Food effect	Take with food--may improve tolerability; food ↑ RTV 15%	Take within 2 hrs after meal	Take with food; high fat meal ↑ TPV up to 30%; oral solution contains 116 IU/ml vitamin E; avoid vitamin E supplement > standard daily multivitamin
Route of metabolism	Liver; inhibits CYP3A4 > CYP2D6	Liver; inhibits CYP3A4 < RTV	Liver; TPV/r inhibits CYP3A4
Dosing during renal impairment	No change; not dialyzed	No change; not dialyzed	No change; not dialyzed
Dosing during hepatic impairment	Use with caution; no specific dosing recommendations	Use with caution; no specific dosing recommendations	Child Pugh Score A: no dose adjustment necessary; Child Pugh Score B or higher: avoid

¹ Fortovase (FTV) 200 mg cap discontinued in 2006

Fusion Inhibitors

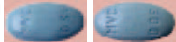


Fusion Inhibitors

Generic Name (Trade Name)	Enfuvirtide (T-20, ENF) (Fuzeon®)
Form	Injection: 90 mg/ml
Dosing recommendations	90 mg bid injected subcutaneously in upper arm, anterior thigh, or abdomen; rotate site of each injection to minimize injection site reaction; do not inject near areas where large nerves course close to skin, such as elbow, knee, or groin
Food effect	None
Route of metabolism	Hydrolyzed to form deaminated metabolite (2.5-15% of parent drug AUC detected in plasma up to 12 hrs after 90 mg SC injection of T-20)
Dosing during renal impairment	ENF clearance not affected in pts with CrCl > 35 ml/min; no data available on pts with CrCl < 35 ml/min
Dosing during hepatic impairment	Not studied
Comments	May store unconstituted ENF at room temperature; reconstitution can take up to 45 min; once reconstituted with 1.1 ml sterile water, must be refrigerated; inject only after drug reaches room temperature at site different from previous injection and site with no reaction from earlier dose

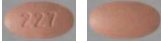
Entry Inhibitors

Entry Inhibitors

Generic Name (Trade Name)	Maraviroc (MVC) (Selzentry®)
Form	Tab: 150, 300 mg 
Dosing recommendations	<ul style="list-style-type: none"> • 150 mg bid in combination with CYP3A4 inhibitors, including any RTV-boosted PI (except TPV/r), delavirdine, ketoconazole, itraconazole, clarithromycin, and other strong CYP3A4 inhibitors (e.g., nefazodone, telithromycin); this dosage holds with or without concomitant CYP3A4 inducers • 300 mg bid in combination with other concomitant medications, including unboosted PIs, TPV/r, nevirapine, all NRTIs, enfuvirtide, and rifabutin • 600 mg bid in combination with CYP3A4 inducers (without a CYP3A4 inhibitor), including efavirenz, rifampin, carbamazepine, phenobarbital, and phenytoin; use 150 mg bid dose if there is a concomitant CYP3A4 inhibitor
Contraindicated concomitant medications	<ul style="list-style-type: none"> • St. John's Wort (hypericum perforatum): may ↓ MVC • Rifapentine
Food Effect	Take with or without food
Dosing during renal impairment	Renal clearance 25%; in pts with creatinine clearance < 50 ml/min, CYP3A4 inhibitor may ↑ MVC; if administered, monitor for adverse effects
Dosing during hepatic impairment	Metabolism of MVC, and hence plasma concentration levels, may be affected by inhibitors or inducers of CYP3A4 and CYP2D6, and by drugs influencing P-gp; administer with caution to pts with compromised hepatic function; can ↑ liver function abnormalities during combination antiretroviral therapy in pts with pre-existing Z liver dysfunction, including chronic active hepatitis— monitor per standard practice
Comments	<p>Potential side effects (reported): Cough, fever, upper respiratory tract infections, rash, musculoskeletal symptoms, abdominal pain, and dizziness;</p> <p>administer with caution to pts with history of postural hypotension or on medication known to ↓ blood pressure; FDA Pregnancy Category B</p> <p>“Black Box” Warning: hepatotoxicity may be preceded by systemic allergic reaction (e.g., pruritic rash, eosinophilia, or elevated IgE); tablets are coated with soya lecithin—may cause reaction in pts with allergy or hypersensitivity to soya lecithin, soya, or peanuts</p>

Integrase Inhibitors

Integrase Inhibitors

Generic Name (Trade Name)	Raltegravir (RAL) (Isentress®)	
Form	Tab (film-coated): 400 mg	
Dosing recommendations	400 mg bid	
Contraindicated concomitant medications	Phenobarbital, phenytoin, rifampin	
Food effect	Take with or without food	
Dosing during renal impairment	No clinically significant pharmacokinetic differences between subjects with severe renal impairment and healthy subjects observed during clinical studies; no dose adjustment necessary; administer with caution	
Dosing during hepatic impairment	No dose adjustment necessary for pts with mild to moderate hepatic impairment; administer with caution ; eliminated mainly via UGT1A1-mediated glucuronidation—drug-drug interactions may occur when co-administered with strong inhibitors or inducers of this pathway (e.g., rifampin); neither induces nor inhibits CYP450; does not inhibit P-glycoprotein-mediated transport	
Comments	Potential side effects (reported): Nausea, headache, diarrhea, pyrexia (> 10%); Grade 2-4 creatine kinase laboratory abnormalities observed in study subjects; myopathy and rhabdomyolysis have been reported; FDA Pregnancy Category C	

Adverse Reactions and Related “Black Box” Warnings for Antiretroviral Agents

Adverse Reactions and Related “Black Box” Warnings for Antiretroviral Agents - page 1 of 5

	Drug	Adverse Reactions
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)	CLASS side effects	Lactic acidosis, hepatic steatosis, peripheral fat wasting (particularly with stavudine and zidovudine)
	Abacavir (ABC)	Hypersensitivity reactions (5-9%); fever; nausea/vomiting (up to 40%); diarrhea; abdominal pain; appetite loss; sore throat; cough; shortness of breath; rash; presence of HLA-B*5701 allele correlates with high risk of hypersensitivity reaction; HLA-B*5701 screening test should be considered prior to initiation of abacavir “Black Box” Warning: Fatal hypersensitivity reactions; lactic acidosis; severe hepatomegaly with steatosis
	Didanosine (ddl)	Pancreatitis (up to 40%); dry mouth; peripheral neuropathy (9-15%); GI intolerance “Black Box” Warning: Fatal lactic acidosis when combined with stavudine in pregnancy; fatal and nonfatal pancreatitis; hepatomegaly with steatosis
	Emtricitabine (FTC)	Headache, diarrhea, and nausea (5%); rash, skin discoloration (hyperpigmentation on palms and/or soles) “Black Box” Warning: Lactic acidosis; severe hepatomegaly with steatosis reported with all nucleoside analogues; not FDA-approved for treatment of hepatitis B; severe acute exacerbations of hepatitis B reported in pts who discontinued emtricitabine
	Lamivudine (3TC)	Well tolerated; rare hepatitis “Black Box” Warning: Fatal lactic acidosis and severe hepatomegaly with steatosis; severe acute exacerbations of hepatitis B reported in pts who discontinued lamivudine
	Stavudine (d4T)	Peripheral neuropathy (15-21%); GI intolerance; hepatitis “Black Box” Warning: Fatal lactic acidosis when combined with didanosine in pregnancy; fatal and nonfatal pancreatitis; hepatomegaly with steatosis
	Zidovudine (AZT or ZDV)	“Black Box” Warning: Hematologic toxicity—anemia and leukopenia; bone marrow suppression (common if advanced symptomatic HIV disease); nausea, vomiting, myopathy (5-10%); fatigue (15-20%); headache

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Adverse Reactions and Related “Black Box” Warnings for Antiretroviral Agents - page 2 of 5

	Drug	Adverse Reactions
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)	CLASS side effects	Lactic acidosis, hepatic steatosis, peripheral fat wasting
	Tenofovir (TDF)	GI intolerance; diarrhea (up to 10%); colitis reported in Phase IV clinical trials; decreases in bone mineral density; renal impairment (mainly in pts with underlying renal disease) “Black Box” Warning: Lactic acidosis and steatosis; severe acute exacerbations of hepatitis B reported in pts who discontinued tenofovir
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	CLASS side effects	Rash, ↑ transaminase levels
	Delaviridine (DLV)	Hepatitis
	Efavirenz (EFV)	Dysphoria; CNS symptoms (53%); mood changes, vivid dreams, poor concentration, worsening depression; teratogenic in monkeys; retrospective reports of neural tube defects, especially with first trimester exposure to efavirenz; false-positive urine cannabinoid screening test
	Etravirine (ETR)	Nausea (13.9%); rash (16.9%); fatigue; headache; liver function test elevations
	Nevirapine (NVP)	Hepatitis (greatest risk during first 6 wks of therapy); often rash; rhabdomyolysis observed in some pts experiencing skin and/or liver reactions associated with nevirapine use “Black Box” Warning: Hepatotoxicity, including fulminant and cholestatic hepatitis and hepatic necrosis; severe life-threatening skin reaction (Stevens-Johnson syndrome); should not be re-started after severe hepatic skin or hypersensitivity reaction; women with CD4 counts > 250 at ↑ risk for hepatotoxicity (12 fold), including pregnant women

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Adverse Reactions and Related “Black Box” Warnings for Antiretroviral Agents - page 3 of 5

	Drug ¹	Adverse Reactions
Protease Inhibitors <i>(cont. next page)</i>	CLASS side effects	Lipodystrophy (fat wasting, fat accumulation), hyperlipidemia, diabetes mellitus, increased bleeding in patients with hemophilia type A and B
	Atazanavir (ATV)	Jaundice/scleral icterus (dose-related, up to 10% in pts on 400 mg daily); GI intolerance (5-15%); fatigue; back pain; headache; rash (10%); cardiac conduction abnormalities (PR interval prolongation may occur); post-marketing reports of nephrolithiasis Lab: ↑ indirect bilirubinemia; mild ↑ in transaminases
	Darunavir (DRV)	GI intolerance (nausea, vomiting, diarrhea, abdominal pain) > 5%; headache; hyperglycemia (1-13%); hyperlipidemia (1-10%); hypercholesterolemia (3.5-4.4%); hypertriglyceridemia (2-12%); hepatitis; rash (10%); use with caution in pts with sulfonamide allergy as darunavir contains sulfonamide moiety; fever; Stevens-Johnson syndrome (rare, < 0.1%) Lab: ↑ transaminase enzymes (12.5%)
	Fosamprenavir (FPV)	Skin rash (19%); use with caution in pts with sulfonamide allergy as fosamprenavir contains sulfonamide moiety; diarrhea; nausea; vomiting; headache; hyperglycemia; lipodystrophy; lipid abnormalities Lab: ↑ transaminase levels
	Indinavir (IDV)	Nephrolithiasis (12%); GI intolerance; nausea; headache; asthenia; blurred vision; dizziness; rash; metallic taste; thrombocytopenia; alopecia; dry skin; nail changes; hyperbilirubinemia Lab: ↑ indirect bilirubinemia (14%)
	Lopinavir (LPV)	Adverse reactions with frequency > 5%: diarrhea, nausea, abdominal pain, asthenia, vomiting, headache, and dyspepsia Lab: ↑ transaminase levels (up to 11%) and lipids

¹ Amprenavir formulations have been discontinued

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Adverse Reactions and Related “Black Box” Warnings for Antiretroviral Agents - page 4 of 5

	Drug	Adverse Reactions
Protease Inhibitors <i>(cont.)</i>	Nelfinavir (NFV)	Diarrhea (20-30%); hyperglycemia; thrombocytopenia (2%) Lab: ↑ transaminase levels
	Ritonavir (RTV)	GI intolerance (> 10%); nausea (2.7-15.5%); vomiting; diarrhea (15.6-23.8%); perioral paresthesia (1-10%); hepatitis (hepatotoxicity 4-25%); pancreatitis; asthenia (3.4-7.1%); taste changes (> 10%); hypercholesterolemia (2-26%); coadministration with certain non-sedating antihistamines, sedative hypnotics, antiarrhythmics, or ergot alkaloids may result in potentially serious and/or life-threatening adverse events Lab: Triglycerides ↑ (> 10%); transaminase ↓ (1-10%); ↑ CPK and uric acid
	Saquinavir (SQV)	GI intolerance (1-10%); nausea; diarrhea; headache; hyperglycemia (1-10%); hyperlipidemia (1-10%); hypercholesterolemia (1-10%); rash (1-10%); weakness (1-10%); paresthesia (1-10%); fever; Stevens-Johnson syndrome (< 1%) Lab: ↑ transaminase enzymes (altered AST, ALT < 1%); ↑ CPK (1-10%)
	Tipranavir (TPV)	GI intolerance (nausea/vomiting/diarrhea ≥ 2%); pyrexia; fatigue; headache; rash Lab: ↑ ALT and/or AST 24.4% (grade 2-4, week 48 data); hypertriglyceridemia (6-25%)
		“Black Box” Warning: Reports of clinical hepatitis and hepatic decompensation, including some fatalities; extra vigilance warranted in pts with chronic hepatitis B or C co-infection (increased risk of hepatotoxicity); use with caution in pts with mild hepatic impairment (Child Pugh Class A)–may ↑ tipranavir concentrations; reports of fatal and non-fatal intracranial hemorrhage associated with TPV/r; use with caution in pts at risk of increased bleeding (trauma, surgery, etc.) or pts taking medications known to increase risk of bleeding (e.g., anticoagulants) or high doses of vitamin E; rash; use with caution in pts with sulfonamide allergy as tipranavir contains sulfonamide moiety

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Adverse Reactions and Related “Black Box” Warnings for Antiretroviral Agents - page 5 of 5

	Drug	Adverse Reactions
Fusion Inhibitors	Enfuvirtide (T-20 or ENF)	Injection site reactions: pain/discomfort (96%), induration (90%), erythema (91%), nodules and cysts (80%), pruritus (65%), ecchymosis (52%); diarrhea (31.7%); nausea (22.8%); fatigue (20.2%); pneumonia (2.7%)
Entry Inhibitors	Maraviroc (MVC)	“Black Box” Warning: Hepatotoxicity, may be preceded by systemic allergic reaction such as pruritic rash, eosinophilia, or elevated IgE; additional side effects reported: abdominal pain (8.2%), constipation (5.4%), pyrexia (12%), cough (12.7%), postural hypotension (8.2%); tablet coating contains soya lecithin, which can cause hypersensitivity reaction in pts with soy allergy
Integrase Inhibitors	Raltegravir (RAL)	Diarrhea (16.6%); nausea (9.9%); headache (9.7%); pyrexia (4.9%); serum creatine kinase elevations (~2%); myopathy; rhabdomyolysis; post-marketing reports: depression (including suicidal ideation and suicidal behaviors), anxiety, and paranoia; and skin/subcutaneous tissue disorders (rash, Stevens-Johnson Syndrome)

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Antiretroviral Combinations that Should NOT Be Used at Any Time - page 1 of 2

Double NRTI combinations	Rationale
Emtricitabine (FTC) + Lamivudine (3TC)	Similar resistance profile; no added benefit
Stavudine (d4T) + Didanosine (ddl)	Additive toxicity (peripheral neuropathy, lactic acidosis, hyperlactatemia); in pregnancy, cases of lactic acidosis with hepatic steatosis with or without pancreatitis
Stavudine (d4T) + Zidovudine (AZT) or ZDV	In vitro antagonism
Tenofovir (TDF) + Didanosine (ddl) + NNRTI	High rate of early virologic failure; rapid selection of resistant mutations; potential for immunologic non-response
Triple NRTI combinations	Rationale
Abacavir (ABC) + Tenofovir (TDF) + Lamivudine (3TC) (or Emtricitabine (FTC))	High rate of virologic failure and resistance
Abacavir (ABC) + Didanosine (ddl) + Lamivudine (3TC) (or Emtricitabine (FTC))	High rate of virologic failure and resistance
Double NNRTI combinations	Rationale
Efavirenz (EFV) + Nevirapine (NVP) or Etravirine (ETR)	Higher incidence of clinical adverse events; EFV and NVP may ↓ ETR

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Antiretroviral
Combs
Not to Use

Antiretroviral Combinations that Should NOT Be Used at Any Time - page 2 of 2

Specific NNRTI + PI combinations	Rationale
Etravirine (ETR) + un-RTV-boosted PI	ETR may induce metabolism of these PIs and lead to subtherapeutic PI levels
Etravirine (ETR) + Atazanavir/ritonavir (ATV/r) or Fosamprenavir/ritonavir (FPV/r)	ETR ↓ C _{min} ATV/r 40%; ↑ C _{min} FPV/r 77%
Etravirine (ETR) + Tipranavir/ritonavir (TPV/r)	TPV/r ↓ ETR AVC 76%
Double PI combinations	Rationale
Atazanavir (ATV) + Indinavir (IDV)	Potential additive hyperbilirubinemia
Tipranavir (TPV) + Lopinavir/ritonavir (LPV/r)	↓ C _{min} LPV/r 52%
Tipranavir (TPV) + Fosamprenavir/ritonavir (FPV/r)	↓ C _{min} LPV/r 56%
Tipranavir (TPV) + Saquinavir/ritonavir (SQV/r)	↓ C _{min} LPV/r 80%
Fosamprenavir (FPV) + Lopinavir/ritonavir (LPV/r)	↓ C _{min} LPV/r 61%; ↓ C _{min} APV 69%
Darunavir (DRV) + Lopinavir/ritonavir (LPV/r)	↓ C _{min} DRV 40-50%
Darunavir (DRV) + Saquinavir/ritonavir (SQV/r)	↓ C _{min} DRV 40%

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Drug Interactions - page 1 of 12

Concomitant Drug		ARV	Effect on ARV or Concomitant Drug	Dosing Recommendations and Clinical Comments
Class	Name			
Antivirals	Ganciclovir (GCV) Valganciclovir	ddl	ddl AUC ↑ 50-111%; GCV AUC ↓ 21% when ddl administered 2 hrs prior to oral GCV; no change in IV GCV concentration	Appropriate combination doses not yet established; monitor for ddl-associated toxicities
	Ribavirin	ddl	↑ intracellular ddl	Coadministration not recommended; may cause serious ddl-related toxicities
		ZDV	Ribavirin inhibits phosphorylation of ZDV	Avoid coadministration or closely monitor virologic response and hematologic toxicities
Acid Reducers <i>(cont. next page)</i>	Antacids	ATV/r	↓ ATV	ATV ≥ 2 hrs before or 1 hr after antacids or buffered medications
		FPV	APV AUC ↓ 18%; C _{min} : no significant change	Simultaneously or ≥ 2 hrs before or 1 hr after antacids
		TPV/r	TPV ↓ ~30%	TPV ≥ 2 hrs before or 1 hr after antacid

See also page 2 for abbreviations; **NRTI** nucleoside reverse transcriptase inhibitor, **NiRTI** nucleotide reverse transcriptase inhibitor; **ABC** abacavir, **ddl** didanosine, **ddl-EC** didanosine enteric coated, **FTC** emtricitabine, **3TC** lamivudine, **d4T** stavudine, **TDF** tenofovir, **AZT** or **ZDV** zidovudine; **NNRTI** non-nucleoside reverse transcriptase inhibitor; **DLV** delavirdine, **EFV** efavirenz, **ETR** etravirine, **NVP** nevirapine; **PI** protease inhibitor; **ATV** atazanavir, **DRV** darunavir, **FPV** or **FosAPV** fosamprenavir, **IDV** indinavir, **LPV/r** lopinavir + ritonavir (one pill), **NFV** nelfinavir, **RTV** ritonavir, **r** boosted with ritonavir, **SQV** saquinavir, **TPV** tipranavir; other inhibitors: **T-20** or **ENF** enfuvirtide, **MVC** maraviroc, **RAL** raltegravir

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Drug Interactions - page 2 of 12

Concomitant Drug		ARV	Effect on ARV or Concomitant Drug	Dosing Recommendations and Clinical Comments
Class	Name			
Acid Reducers (cont.)	H2 Receptor Antagonists	ATV/r	↓ATV	Treatment-naïve pts: H2 receptor antagonist dose ≤ famotidine 40 mg bid equivalent; give ATV 300 mg + RTV 100 mg simultaneously and/or > 10 hrs after H2 receptor antagonist Treatment-experienced pts: H2 receptor antagonist dose ≤ famotidine 20 mg bid equivalent; if TDF used with H2 receptor antagonist, give ATV 400 mg + RTV 100 mg
		ATV	↓ATV	H2 receptor antagonist single dose ≤ famotidine 20 mg equivalent or total daily dose ≤ famotidine 20 mg bid equivalent in treatment-naïve pts; ATV > 2 hrs before and/or > 10 hrs after H2 receptor antagonist
		FPV	APV AUC ↓ 30%; C _{min} unchanged	Separate administration by 10 hrs; consider boosting with RTV
	Proton Pump Inhibitors (PPIs)	ATV	↓ATV	PPIs not recommended in pts receiving unboosted ATV; consider alternative acid-reducer, ritonavir-booster, or other PPI(s)
		ATV/r	↓ATV	PPI dose ≤ omeprazole 20 mg daily equivalent for treatment-naïve pts; give PPI > 12 hrs before ATV/r; PPIs not recommended for treatment-experienced pts
		NFV	NFV AUC ↓ 36%; M8 AUC ↓ 92%	Do not coadminister
		SQV/r	SQV AUC ↑ 82%	Avoid co-administration or monitor SQV levels and for SQV toxicities

See also page 2 for abbreviations; **NRTI** nucleoside reverse transcriptase inhibitor, **NiRTI** nucleotide reverse transcriptase inhibitor: ABC abacavir, ddl didanosine, ddl-EC didanosine enteric coated, FTC emtricitabine, 3TC lamivudine, d4T stavudine, TDF tenofovir, AZT or ZDV zidovudine; **NNRTI** non-nucleoside reverse transcriptase inhibitor: DLV delavirdine, EFV efavirenz, ETR etravirine, NVP nevirapine; **PI** protease inhibitor: ATV atazanavir, DRV darunavir, FPV or FosAPV fosamprenavir, IDV indinavir, LPV/r lopinavir + ritonavir (one pill), NFV nelfinavir, RTV ritonavir, /r boosted with ritonavir, SQV saquinavir, TPV tipranavir; other inhibitors: T-20 or ENF enfuvirtide, MVC maraviroc, RAL raltegravir

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Drug Interactions - page 3 of 12

Concomitant Drug		ARV	Effect on ARV or Concomitant Drug	Dosing Recommendations and Clinical Comments
Class	Name			
Anti-convulsants	Carbamazepine Phenobarbital Phenytoin	DLV	DLV C _{min} ↓ 90%	Contraindicated – do not coadminister
		EFV	Carbamazepine + EFV: AUCs ↓ 27% and 36% respectively; EFV + phenytoin: ↓ EFV	Monitor anticonvulsant; use alternative if possible
		ETR	Potential ↓ ETR and anticonvulsant	Do not coadminister; use alternative anticonvulsant
		ATV/r, DRV/r, IDV/r, LPV/r, SQV/r, TPV/r	↑ carbamazepine; ↓ PI	Consider alternative anticonvulsant or monitor levels of both
		FPV/r	↓ phenytoin; ↑ APV	Monitor anticonvulsant and adjust accordingly; FPV/r no change
		LPV/r	↓ phenytoin; ↓ phenobarbital; ↓ LPV/r; may ↓ other PIs	Consider alternative anticonvulsant or monitor levels of both
		ATV, FPV, NFV	May substantially ↓ PIs; NFV ↓ phenytoin	Monitor anticonvulsant and virologic response; consider alternative anticonvulsant, RTV boosting for ATV and FPV, and/or monitoring PI
		IDV	↓ IDV	Consider alternative anticonvulsant, RTV boosting, and/or monitoring IDV
MVC	Possible ↓ MVC	See dosing recommendations on page 30 or use alternative antiepileptic		

See also page 2 for abbreviations; **NRTI** nucleoside reverse transcriptase inhibitor, **NiRTI** nucleotide reverse transcriptase inhibitor: ABC abacavir, ddl didanosine, ddl-EC didanosine enteric coated, FTC emtricitabine, 3TC lamivudine, d4T stavudine, TDF tenofovir, AZT or ZDV zidovudine; **NNRTI** non-nucleoside reverse transcriptase inhibitor: DLV delavirdine, EFV efavirenz, ETR etravirine, NVP nevirapine; **PI** protease inhibitor: ATV atazanavir, DRV darunavir, FPV or FosAPV fosamprenavir, IDV indinavir, LPV/r lopinavir + ritonavir (one pill), NFV nelfinavir, RTV ritonavir, /r boosted with ritonavir, SQV saquinavir, TPV tipranavir; other inhibitors: T-20 or ENF enfuvirtide, MVC maraviroc, RAL raltegravir

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Drug Interactions - page 4 of 12

Concomitant Drug		ARV	Effect on ARV or Concomitant Drug	Dosing Recommendations and Clinical Comments	
Class	Name				
Anti-fungals (cont. next page)	Fluconazole	TPV/r	TPV AUC ↑ 50%, C _{max} ↑ 32%, C _{min} ↑ 69%	Fluconazole > 200 mg daily not recommended	
	Fluconazole Posaconazole	MVC	No data	No dose adjustment recommended	
	Itraconazole	DLV, NVP		No data; potential bi-directional interactions	Monitor NNRTI and itraconazole levels
		EFV		Itraconazole and OH-itraconazole AUC, C _{max} , and C _{min} ↓ 35–44%	Monitor itraconazole level—dose adjustment may be necessary
		ETR		↑ ETR; ↓ itraconazole	Monitor itraconazole—dose adjustment may be necessary
		ATV/r, DRV/r, FPV/r, IDV/r, TPV/r		Potential bi-directional inhibition	Monitor itraconazole level to guide adjustments; high dose (> 200 mg/day) not recommended
		LPV/r		↑ itraconazole	≤ 200 mg itraconazole daily or monitor itraconazole level
		SQV/r		Bi-directional interaction	Dose not established, but ↓ itraconazole may be warranted; consider monitoring itraconazole level
		ATV, FPV, NFV		Potential bi-directional inhibition	Consider monitoring itraconazole level to guide adjustments
		IDV		↑ IDV: IDV 600 mg q8h + itraconazole 200 mg bid; AUC similar to IDV 800 mg q8h	IDV 600 mg q8h (without RTV) and ≤ 200 mg itraconazole bid; dosing IDV/r and itraconazole not established
MVC		Possible ↑ MVC	↓ MVC to 150 mg bid		

See also page 2 for abbreviations; NRTI nucleoside reverse transcriptase inhibitor, NNRTI nucleotide reverse transcriptase inhibitor: ABC abacavir, ddl didanosine, ddl-EC didanosine enteric coated, FTC emtricitabine, 3TC lamivudine, d4T stavudine, TDF tenofovir, AZT or ZDV zidovudine; NNRTI non-nucleoside reverse transcriptase inhibitor: DLV delavirdine, EFV efavirenz, ETR etravirine, NVP nevirapine; PI protease inhibitor: ATV atazanavir, DRV darunavir, FPV or FosAPV fosamprenavir, IDV indinavir, LPV/r lopinavir + ritonavir (one pill), NFV nelfinavir, RTV ritonavir, /r boosted with ritonavir, SQV saquinavir, TPV tipranavir; other inhibitors: T-20 or ENF enfuvirtide, MVC maraviroc, RAL raltegravir

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Drug Interactions - page 5 of 12

Concomitant Drug		ARV	Effect on ARV or Concomitant Drug	Dosing Recommendations and Clinical Comments
Class	Name			
Anti-fungals (cont.)	Posaconazole	EFV	Posaconazole AUC ↓ 50%, C _{max} ↓ 45%; EFV C _{max} ↑ 13%	Consider alternative antifungal if possible or monitor posaconazole level if available
		EFV	EFV ↑ 44%; voriconazole ↓ 77%	Contraindicated at standard doses ; dose: voriconazole 400 mg bid, EFV 300 mg daily
	Voriconazole	ETR	↑ ETR and voriconazole	Monitor voriconazole—dose adjustment may be necessary
		NVP	Potential induction of voriconazole metabolism and inhibition of NVP metabolism	Monitor for toxicity and antifungal outcome
		ATV/r, DRV/r, FPV/r, IDV/r, LPV/r, SQV/r, TPV/r	Voriconazole AUC ↓ 39% with RTV 100 mg bid	Voriconazole + RTV 100 mg once daily or bid not recommended unless benefit outweighs risk; if used, monitor voriconazole level
MVC	Possible ↑ MVC	Consider ↓ MVC to 150 mg bid		
Anti-mycobacterials (cont. next page)	Clarithromycin	DLV	Clarithromycin ↑ 100%; DLV ↑ 44%	Clarithromycin ↓ 50% in pts with CrCl 30–60 ml/min; 75% in pts with CrCl < 30 ml/min
		EFV	Clarithromycin ↓ 39%	Monitor; consider alternative, such as azithromycin, for MAC prophylaxis and treatment
		ETR	ETR AUC ↑ 42%; clarithromycin AUC ↓ 39%; C _{min} ↓ 53%; OH-clarithromycin AUC ↑ 21%	Consider alternative, e.g., azithromycin, for MAC prophylaxis and treatment
		NVP	NVP ↑ 26%; clarithromycin ↓ 30%	Monitor efficacy or use alternative agent
		MVC	Possible ↑ MVC	↓ MVC to 150 mg bid
		ATV/r	Clarithromycin AUC ↑ 94%	May cause QTc prolongation; ↓ clarithromycin dose by 50%; consider alternative therapy
		DRV/r, IDV/r, LPV/r, SQV/r, TPV/r	Clarithromycin ↑ > 50%	↓ clarithromycin 50% in pts with CrCl 30–60 ml/min; 75% in pts with CrCl < 30 ml/min; clarithromycin ↑ SQV 177% and ↑ TPV 66%— avoid co-administration

See also page 2 for abbreviations; NRTI nucleoside reverse transcriptase inhibitor, NNRTI nucleotide reverse transcriptase inhibitor: ABC abacavir, ddl didanosine, ddl-EC didanosine enteric coated, FTC emtricitabine, 3TC lamivudine, d4T stavudine, TDF tenofovir, AZT or ZDV zidovudine; NNRTI non-nucleoside reverse transcriptase inhibitor: DLV delavirdine, EFV efavirenz, ETR etravirine, NVP nevirapine; PI protease inhibitor: ATV atazanavir, DRV darunavir, FPV or FosAPV fosamprenavir, IDV indinavir, LPV/r lopinavir + ritonavir (one pill), NFV nelfinavir, RTV ritonavir, /r boosted with ritonavir, SQV saquinavir, TPV tipranavir; other inhibitors: T-20 or ENF enfuvirtide, MVC maraviroc, RAL raltegravir

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Drug Interactions - page 6 of 12

Concomitant Drug		ARV	Effect on ARV or Concomitant Drug	Dosing Recommendations and Clinical Comments
Class	Name			
Anti-mycobacterials (cont.)	Rifabutin	EFV	Rifabutin ↓ 35%	Rifabutin 450–600 mg once daily or 600 mg 3x/wk if EFV not coadministered with PI
		ETR	ETR AUC ↓ 37%, C _{min} ↓ 35%; rifabutin AUC ↓ 17%, C _{min} ↓ 24%; 25-O-desacetylrifabutin AUC ↓ 17%, C _{min} ↓ 22%	In absence of RTV-boosted PI, dose rifabutin 300 mg once daily in combination with standard dose of ETR; in presence of RTV-boosted PI (e.g., LPV/r), dose rifabutin 150 mg qod or 3x/wk in combination with standard dose of ETR; consider therapeutic drug monitoring and adjust dose accordingly
		NVP	↓ NVP; ↑ rifabutin	No dose adjustment necessary
		MVC	Possible ↓ MVC	MVC 300 mg bid when used without strong CYP3A inducer or inhibitor; MVC 150 mg bid when used with strong CYP3A inhibitor (e.g., ritonavir)
		ATV/r, FPV/r, DRV/r, IDV/r, LPV/r, SQV/r, TPV/r	Rifabutin ↑ > 250%	Rifabutin 150 mg qod or 3x/wk; consider therapeutic drug monitoring and adjust accordingly
		ATV, FPV, IDV, NFV	↑ rifabutin > 200%; ↓ most PIs > 30%	Rifabutin 150 mg daily or 300 mg 3x/wk
	Rifampin	DLV	DLV ↓ 96%	Contraindicated – do not coadminister
		EFV	EFV ↓ 25%	Monitor viral response; maintain EFV 600 mg once daily, some clinicians suggest EFV 800 mg once daily for pts > 60 kg
		ETR	Potential significant ↓ ETR	Do not coadminister
		NVP	↓ NVP 20-58%	Do not coadminister
RAL		RAL ↓ > 50%	Coadministration not recommended ; consult HIV Pharmacist if unsure; substitute rifabutin	
	All PIs	PI ↓ > 75%	Do not coadminister	

See also page 2 for abbreviations; NRTI nucleoside reverse transcriptase inhibitor, NNRTI nucleotide reverse transcriptase inhibitor: ABC abacavir, ddI didanosine, ddI-EC didanosine enteric coated, FTC emtricitabine, 3TC lamivudine, d4T stavudine, TDF tenofovir, AZT or ZDV zidovudine; NNRTI non-nucleoside reverse transcriptase inhibitor: DLV delavirdine, EFV efavirenz, ETR etravirine, NVP nevirapine; PI protease inhibitor: ATV atazanavir, DRV darunavir, FPV or FosAPV fosamprenavir, IDV indinavir, LPV/r lopinavir + ritonavir (one pill), NFV nelfinavir, RTV ritonavir, /r boosted with ritonavir, SQV saquinavir, TPV tipranavir; other inhibitors: T-20 or ENF enfuvirtide, MVC maraviroc, RAL raltegravir

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Drug Interactions - page 7 of 12

Concomitant Drug		ARV	Effect on ARV or Concomitant Drug	Dosing Recommendations and Clinical Comments
Class	Name			
Benzodiazepines	Alprazolam	DLV	May ↑ alprazolam	Do not coadminister ; consider alternative, e.g., lorazepam, oxazepam, or temazepam
		EFV	↓ EFV 25%	Monitor viral response; maintain EFV 600 mg once daily, some clinicians suggest EFV 800 mg once daily for pts > 60 kg
		ETR	Potential significant ↓ ETR	Do not coadminister
		NVP	↑ NVP 20-58%	Do not coadminister
	Alprazolam Diazepam	All PIs	May ↑ benzodiazepine; RTV 200 mg bid x 2 days ↑ alprazolam half-life 200% and AUC 248%	Consider alternative benzodiazepine, e.g., lorazepam, oxazepam, or temazepam
	Diazepam	DLV	May ↑ diazepam	Consider alternative, e.g., lorazepam, oxazepam, or temazepam
		ETR	↑ diazepam	May need to ↓ diazepam
	Lorazepam	EFV	Lorazepam C _{max} ↑ 16%, AUC: no significant effect	No dose adjustment necessary
	Midazolam	DLV, EFV	May ↑ midazolam	Do not coadminister with oral midazolam; parenteral midazolam may be used with caution as single dose or in monitored situation for procedural sedation
		All PIs	↑ midazolam; SQV/r ↑ midazolam (oral) AUC 1144% and C _{max} 327%	Do not coadminister oral midazolam and PIs; parenteral midazolam may be used with caution as single dose and in a monitored situation for procedural sedation
Triazolam	DLV, EFV	May ↑ triazolam	Do not coadminister	
	All PIs	RTV 200 mg bid ↑ triazolam AUC 20x; other PIs may significantly ↑ triazolam	Do not coadminister	

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Drug Interactions - page 8 of 12

Concomitant Drug		ARV	Effect on ARV or Concomitant Drug	Dosing Recommendations and Clinical Comments
Class	Name			
Calcium Channel Blockers	Dihydropyridine	ATV/r	No data	Caution ; consider dose titration and ECG monitoring
		IDV/r	↑ amlodipine	Monitor closely
		LPV/r, SQV/r	↑ dihydropyridine	Caution ; clinical monitoring recommended
	Diltiazem	ATV/r	↑ diltiazem AUC 125%	↓ diltiazem dose by 50%; monitor ECG
		DRV/r, FPV/r, IDV/r, LPV/r, NFV, TPV/r	Potential ↑ diltiazem	Caution ; clinical monitoring recommended
		SQV/r	↑ diltiazem	Caution ; clinical monitoring recommended
HMG-CoA Reductase Inhibitors (cont. next page)	Atorvastatin	DLV	May inhibit atorvastatin metabolism	Use lowest possible dose and monitor for toxicity; consider other HMG-CoA reductase inhibitors with less potential for interaction
		EFV	Atorvastatin AUC ↓ 37-43%	Adjust atorvastatin according to lipid responses, not to exceed maximum recommended dose of 80 mg daily
		ETR	Atorvastatin AUC ↓ 37%	Standard dose; adjust according to response
		NVP	May induce atorvastatin metabolism	Standard dose; adjust according to response
		All PIs	↑ atorvastatin > 50% with unboosted PI, > 100% with RTV-boosted PI	Use lowest possible starting dose (10 mg) with careful monitoring and increases

See also page 2 for abbreviations; **NRTI** nucleoside reverse transcriptase inhibitor, **NtRTI** nucleotide reverse transcriptase inhibitor; **ABC** abacavir, **ddl** didanosine, **ddl-EC** didanosine enteric coated, **FTC** emtricitabine, **3TC** lamivudine, **d4T** stavudine, **TDF** tenofovir, **AZT** or **ZDV** zidovudine; **NNRTI** non-nucleoside reverse transcriptase inhibitor; **DLV** delavirdine, **EFV** efavirenz, **ETR** etravirine, **NVP** nevirapine; **PI** protease inhibitor; **ATV** atazanavir, **DRV** darunavir, **FPV** or **FosAPV** fosamprenavir, **IDV** indinavir, **LPV/r** lopinavir + ritonavir (one pill), **NFV** nelfinavir, **RTV** ritonavir, **/r** boosted with ritonavir, **SQV** saquinavir, **TPV** tipranavir; other inhibitors: **T-20** or **ENF** enfuvirtide, **MVC** maraviroc, **RAL** raltegravir

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Drug Interactions - page 9 of 12

Concomitant Drug		ARV	Effect on ARV or Concomitant Drug	Dosing Recommendations and Clinical Comments
Class	Name			
HMG-CoA Reductase Inhibitors (cont.)	Fluvastatin	ETR	↑ fluvastatin	May need to adjust fluvastatin
	Lovastatin	All PIs	Significant ↑ lovastatin	Contraindicated – do not coadminister
	Lovastatin Simvastatin	DLV	Potential large ↑ statin	Avoid concomitant use
		EFV	Simvastatin AUC ↓ 68%	Adjust simvastatin according to lipid responses, not to exceed maximum recommended dose of 80 mg daily; if RTV-boosted PI, avoid both simvastatin and lovastatin
		ETR	↓ lovastatin and simvastatin 30-40%	Adjust lovastatin or simvastatin according to lipid responses, not to exceed maximum recommended daily dose (lovastatin 80 mg, simvastatin 80 mg); with RTV-boosted PI, avoid both simvastatin and lovastatin
	Pravastatin	DRV/r	Pravastatin AUC ↑ 81%, up to 500% in some pts	Use lowest possible starting dose with careful monitoring
	Pravastatin Rosuvastatin	DLV, NVP	No data	Use lowest possible starting dose with careful monitoring
		EFV	Pravastatin AUC ↓ 44%	Adjust pravastatin according to lipid responses, not to exceed maximum recommended dose of 40 mg daily
		ETR	No effect	Standard dose

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Drug Interactions - page 10 of 12

Concomitant Drug		ARV	Effect on ARV or Concomitant Drug	Dosing Recommendations and Clinical Comments
Class	Name			
Hormonal Contraceptives		EFV	↑ ethinyl estradiol	Use alternative or additional methods; no data on other components
		ETR	↑ ethinyl estradiol; norethindrone: no effect	No dose adjustment necessary
		NVP	Ethinyl estradiol ↓ 20%	Use alternative or additional methods
		ATV/r	↓ ethinyl estradiol; ↑ progesterin	Oral contraceptive should contain ≥ 35 mcg ethinyl estradiol; oral contraceptives containing progestins other than norethindrone or norgestimate not studied
		DRV/r, FPV/r, IDV/r, LPV/r, SQV/r, TPV/r	↓ ethinyl estradiol 30-50%	Use alternative or additional method; monitor for estrogen deficiency
		ATV	↑ ethinyl estradiol AUC 48%; ↑ norethindrone AUC 110%	Oral contraceptive should contain ≤ 30 mcg ethinyl estradiol or use alternate method; oral contraceptives containing < 25 mcg ethinyl estradiol or progestins other than norethindrone or norgestimate not studied
		FPV	APV ↑ ethinyl estradiol and ↑ norethindrone; APV ↓ 20%	Use alternative method
		IDV	↑ ethinyl estradiol; ↑ norethindrone	No dose adjustment
		NFV	Ethinyl estradiol ↓ 47%; norethindrone ↓ 18%	Use alternative or additional method
		MVC	No significant affect	Safe in combination

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Drug Interactions - page 11 of 12

Concomitant Drug		ARV	Effect on ARV or Concomitant Drug	Dosing Recommendations and Clinical Comments
Class	Name			
Methadone		ABC	↓ methadone	Monitor for opiate withdrawal; titrate methadone as clinically indicated; may require ↑ methadone
		ZDV	ZDV AUC ↑ 43%	Monitor for ZDV-related adverse effects
		DLV	DLV: no effect; potential ↑ methadone	Monitor for methadone toxicity; ↓ as necessary
		EFV	Methadone ↓ 60%	Potential for opiate withdrawal; ↑ methadone as necessary
		ETR, NVP	No effect	Standard dose
		ATV/r, DRV/r, FPV/r, IDV/r, LPV/r, SQV/r, TPV/r	Methadone AUC ↓ 15-50%, depending on the boosted PI	Opiate withdrawal unlikely but may occur; no adjustment in methadone usually required but monitor for opiate withdrawal and ↑ methadone dose as clinically indicated
		FPV	↓ methadone	Monitor and titrate methadone as clinically indicated
		NFV	Methadone AUC ↓ 40%	Opiate withdrawal rarely occurs; monitor and titrate as clinically indicated; may require ↑ methadone
		RAL	No effect	Standard dose
Oral Anticoagulant		EFV, NVP	May ↑ or ↓ warfarin	Monitor INR
		ETR	↑ warfarin	Monitor INR; adjust warfarin accordingly

See also page 2 for abbreviations; **NRTI** nucleoside reverse transcriptase inhibitor, **NrRTI** nucleotide reverse transcriptase inhibitor: **ABC** abacavir, **ddl** didanosine, **ddl-EC** didanosine enteric coated, **FTC** emtricitabine, **3TC** lamivudine, **d4T** stavudine, **TDF** tenofovir, **AZT** or **ZDV** zidovudine; **NNRTI** non-nucleoside reverse transcriptase inhibitor: **DLV** delavirdine, **EFV** efavirenz, **ETR** etravirine, **NVP** nevirapine; **PI** protease inhibitor: **ATV** atazanavir, **DRV** darunavir, **FPV** or **FosAPV** fosamprenavir, **IDV** indinavir, **LPV/r** lopinavir + ritonavir (one pill), **NFV** nelfinavir, **RTV** ritonavir, **/r** boosted with ritonavir, **SQV** saquinavir, **TPV** tipranavir; other inhibitors: **T-20** or **ENF** enfuvirtide, **MVC** maraviroc, **RAL** raltegravir

This document is not intended to be complete, only the most relevant interactions are included. Please refer to the US DHHS guidelines for additional detail and information.

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Concomitant Drug		ARV	Effect on ARV or Concomitant Drug	Dosing Recommendations and Clinical Comments
Class	Name			
Phosphodiesterase Type 5 Inhibitors	Sildenafil	ETR	Sildenafil AUC ↓ 57%	Monitor; may need ↑ sildenafil, but risk of MI ↑ with > 50 mg dose sildenafil with PI
		All PIs	Sildenafil ↑ 200-1100%, e.g., DRV/r + sildenafil 25 mg similar to sildenafil 100 mg alone	Suggested max dose sildenafil = 50 mg q72hrs when given with ritonavir-boosted PI; monitor for adverse effects
	Tadalafil	All PIs	LPV/r ↑ tadalafil AUC 124%	Start tadalafil at 5 mg q72hrs; suggested max dose = 10 mg q72hrs; monitor for adverse effects
	Vardenafil	All PIs	Vardenafil ↑ 150-500%; most PIs ↓ 20-30%	Suggested max dose vardenafil = 2.5 mg q72hrs; monitor for adverse effects
Other	Desipramine	ETR	Desipramine ↑ 145%	↓ desipramine
	Dexamethasone		↓ ETR	Use systemic dexamethasone with caution or consider alternative corticosteroid for long-term use
	Grapefruit juice Vit C > 1 g/day	IDV	↓ IDV	Monitor virologic response
	Paroxetine Sertraline	DRV/r	↓ paroxetine and sertraline	Monitor antidepressant response closely; carefully titrate SSRI based on clinical assessment
	Theophylline	RTV	Theophylline ↓ 47%	Monitor theophylline
Trazodone	RTV 200 mg bid ↑ trazodone AUC 240%		Use lowest dose trazodone; monitor for CNS and CV adverse effects	

See also page 2 for abbreviations; NRTI nucleoside reverse transcriptase inhibitor, NNRTI nucleotide reverse transcriptase inhibitor: ABC abacavir, ddI didanosine, ddI-EC didanosine enteric coated, FTC emtricitabine, 3TC lamivudine, d4T stavudine, TDF tenofovir, AZT or ZDV zidovudine; NNRTI non-nucleoside reverse transcriptase inhibitor: DLV delavirdine, EFV efavirenz, ETR etravirine, NVP nevirapine; PI protease inhibitor: ATV atazanavir, DRV darunavir, FPV or FosAPV fosamprenavir, IDV indinavir, LPV/r lopinavir + ritonavir (one pill), NFV nelfinavir, RTV ritonavir, /r boosted with ritonavir, SQV saquinavir, TPV tipranavir; other inhibitors: T-20 or ENF enfuvirtide, MVC maraviroc, RAL raltegravir

This document is not intended to be complete, only the most relevant interactions are included. Please refer to the US DHHS guidelines for additional detail and information.

Prophylaxis and Treatment of Opportunistic Infections (OIs) - page 1 of 13

Candidiasis (oropharyngeal, esophageal, or vaginal)			
Dosing recommendations	Primary prophylaxis: Not recommended ; consider only under special circumstances; consult ID		
	Secondary prophylaxis: Not routinely recommended ; consider only under special circumstances; consult ID		
	Preferred	Fluconazole 100 mg po daily	
	Alternative	Itraconazole (Sporanox®) solution (10 mg/ml) 200 mg po daily on empty stomach or itraconazole 200 mg cap po daily with food ± acidic drink	
	Treatment	For resistant strains, consult ID	
	Preferred	Oropharyngeal: Fluconazole 100 mg po daily or clotrimazole troches 10 mg 5x/day or nystatin suspension 400,000-600,000 units gargled 4x/day x 7-14 days Esophageal: Fluconazole 100-400mg PO or IV daily x 7-14 days Vaginal: Terconazole vag cream (0.4-0.8%) x 7 days or suppository 80 mg x 3 days or fluconazole 150 mg po x 1 dose or miconazole vag suppository 200 mg x 3 days or cream (2%) x 7 days	
Alternative	Oropharyngeal: Itraconazole oral suspension 200 mg po daily x 7-14 days; for resistant species, consult ID specialist Esophageal: Itraconazole oral suspension 200 mg po daily x 14-21 days Vaginal: Itraconazole oral suspension 200 mg po daily x 3-7 days		
	Drug	CrCl	Dose
Dosing during renal impairment	Fluconazole	< 50	50% dose
		HD	Full dose after HD
		CAVHD/CVVHDF or CVVH	400 mg (CVVH)-800 mg (CVVHD or CVVHDF) q24h
Dosing during hepatic impairment	Fluconazole	No change	
	Itraconazole	May need to ↓ itraconazole dose; no specific guidelines available	

HD: hemodialysis

Prophylaxis and Treatment of Opportunistic Infections (OIs) - page 2 of 13

Cryptococcal Meningitis	
Dosing recommendations	Primary prophylaxis: Not routinely recommended; consult ID specialist
	Secondary prophylaxis: Chronic maintenance therapy with fluconazole 200 mg po daily until immune reconstitution, i.e., CD4+ > 200 cells/ μ L x 6 months
	Treatment ¹ : Consult ID specialist
	<p>Preferred</p> <p>Induction: Amphotericin B (Fungizone®) 0.7mg/kg IV + flucytosine (Ancobon®) 25mg/kg/day po q6h x \geq 2 wks Consolidation: Fluconazole (Diflucan®) 400 mg po daily x 8 wks</p> <p>Alternative</p> <p>Options: 1) Amphotericin B + fluconazole 400 mg IV or po daily x 2 wks, then itraconazole oral suspension 200 mg po bid x 8 wks, then itraconazole oral suspension 200 mg daily x life 2) Fluconazole 400-800 mg IV or po daily + flucytosine 25 mg/kg po q6h x 4-6 wks, then itraconazole oral suspension 200 mg po bid x 8 wks, then itraconazole oral suspension 200 mg po daily x life 3) Itraconazole (Sporanox®) 200 mg po tid x 3 days with meal + acidic drink, then 200 mg bid² 4) Fluconazole 400 mg po daily + flucytosine 100 mg/kg/day po x 6-10 wks; after 10 wks fluconazole may be \downarrow to 200 mg daily</p>

¹ Careful monitoring of cerebrospinal fluid (CSF) opening pressure through lumbar puncture, relieved by drainage of CSF to keep within normal limits, is **crucial to avoid blindness**

² Suspension of itraconazole is available (10 mg/mL) and should be taken on empty stomach; absorption significantly improved when taken with acidic beverage

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Prophylaxis and Treatment of Opportunistic Infections (OIs) - page 3 of 13

Cryptococcal Meningitis, continued			
	Drug	CrCl	Dose
Dosing during renal impairment	Amphotericin B	Consider switching to lipid amphotericin B if doubling of SrCr compared with baseline or CrCl < 50 ml/min; consult ID specialist for selection and dose of lipid amphotericin B	
		< 50	50% dose
	Fluconazole	HD	Full dose after HD
		CAVHD/CVVHDF or CVVH	400 mg (CVVH) - 800 mg (CVVHD or CVVHDF) q24h
	Flucytosine	20-40	25 mg/kg q12h
		20-10	25 mg/kg q24h
< 10		25 mg/kg q48h	
HD		25-50 mg/kg q48-72h after HD	
Itraconazole	No change; itraconazole IV not recommended if CrCl < 30 ml/min		
Dosing during hepatic impairment	Amphotericin B	No change	
	Fluconazole	No change	
	Flucytosine	No change	
	Itraconazole	May need to \downarrow itraconazole dose; no specific guidelines available	

HD: hemodialysis

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Prophylaxis and Treatment of Opportunistic Infections (OIs) - page 4 of 13

Cytomegalovirus (CMV) Retinitis and Extraocular Disease

Dosing recommendations	Primary prophylaxis: CD4+ < 50 cells/ μ L and (+) CMV antibody ¹ ; not routinely recommended; consult ID	
	Secondary prophylaxis: Lifelong maintenance therapy required unless immune reconstitution, i.e., CD4+ > 100 cells/ml x \geq 3-6 months	
	Treatment²	
	Preferred	Induction: For immediate sight-threatening lesions, ganciclovir intraocular implant (Vitrasert [®]) ³ + valganciclovir (Valcyte [®]) 900 mg po bid x 14-21 days; for small peripheral lesions, valganciclovir 900 mg po bid x 14-21 days Maintenance: Valganciclovir 900 mg po daily or ganciclovir intraocular implant (Vitrasert [®]) ³ + valganciclovir 900 mg po daily x maintenance therapy duration
Alternative	Induction: Ganciclovir 5 mg/kg IV q12h x 14-21 days, then 5mg/kg IV daily or ganciclovir 5 mg/kg IV q12h x 14-21 days, then valganciclovir 900 mg po daily or foscarnet ⁴ 60 mg/kg IV q8h or 90 mg/kg IV q12h x 14-21 days, then 90-120 mg/kg IV q24h or cidofovir (Vistide [®]) injection 5 mg/kg/wk x 2 wks + probenecid ⁵ (2 g po 3 hrs prior, 1 g po 2 hrs after, + 1 g po 8 hrs after cidofovir) Maintenance: Ganciclovir 5 mg/kg IV 5-7x/wk or foscarnet 90-120 mg/kg IV daily or cidofovir injection 3-5 mg/kg q2wks ⁵	

1 Some clinicians prefer to follow ophthalmologic examination without prophylaxis

2 For cauda equina syndrome, use combination ganciclovir and foscarnet therapy

3 Ganciclovir implants (Vitrasert[®], GCV release 1 g/h, lifespan ~8 months) have been used for maintenance therapy, but should be in combination with oral therapy; implants should be replaced q6-8 months if CD4+ count remains < 100 cells/ml

4 Foscarnet infusion requires 1.5-2 hrs per treatment; due to its potential renal toxicity, prehydrate or administer concomitantly with 1 liter normal saline; monitor for hypocalcemia, hypophosphatemia, and hypomagnesemia

5 Probenecid + prehydration ↓ incidence of nephrotoxicity associated with cidofovir

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Prophylaxis and Treatment of Opportunistic Infections (OIs) - page 5 of 13

Cytomegalovirus (CMV) Retinitis and Extraocular Disease, continued

	Drug	CrCl	Induction Dose	Maintenance Dose
Dosing during renal impairment	Cidofovir	Do not use in pts with renal impairment		
		1.0 - 1.4	70 mg/kg q12h	70-90 mg/kg q24h
	Foscarnet	0.8 - 1.0	50 mg/kg q12h	50-65 mg/kg q24h
		0.6 - 0.8	80 mg q24h	80-105 mg/kg q48h
		0.5 - 0.6	60 mg q24h	60-80 mg/kg q48h
		0.4 - 0.5	50 mg/kg q24h	50-65 mg/kg q48h
		< 0.4	Not recommended	Not recommended
		HD	60-90 mg/kg loading dose after HD	45-60 mg/kg 3x/wk after HD
	Ganciclovir	CVVH	Dose as for CrCl 10-50 ml/min	
		50 - 69	2.5 mg/kg q12h	2.5 mg/kg q24h
		25 - 49	2.5 mg/kg q24h	1.25 mg/kg q24h
		10 - 24	1.25 mg/kg q24h	0.625 mg/kg q24h
< 10 or HD		1.25 mg/kg 3x/wk after HD	0.625 mg/kg 3x/wk after HD	
Valganciclovir	40 - 59	450 mg q12h	450 mg q24h	
	25 - 39	450 mg q24h	450 mg q48h	
	10 - 24	450 mg q48h	450 mg biw	
	< 10 or HD	Not recommended, use ganciclovir	Not recommended, use ganciclovir	
Dosing during hepatic impairment	Cidofovir	No change		
	Foscarnet	No change		
	Ganciclovir	No change		
	Valganciclovir	No change		

HD: hemodialysis

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Prophylaxis and Treatment of Opportunistic Infections (OIs) - page 6 of 13

MAC/MAI Infection		
Dosing recommendations	Primary prophylaxis: CD4+ < 50 cells/mcl, may discontinue if CD4+ >100 cells/mcL x ≥ 3 mos	
	Preferred	Azithromycin (Zithromax®) 1200 mg po qwk or clarithromycin (Biaxin®) 500 mg po bid
	Alternative	Rifabutin (Mycobutin®) 300 mg po daily or azithromycin 1200 mg po daily + rifabutin 300 mg po daily
	Secondary prophylaxis: See maintenance therapy; recommended life-long suppression; may consider discontinuing if CD4+ > 100 cells/μL x ≥ 6 mos	
	Treatment	
	Preferred	Induction: Clarithromycin (Biaxin®) 500 mg po bid or azithromycin (Zithromax®) 500-600 mg po daily + ethambutol (Myambutol®) 15 mg/kg/day po ± ciprofloxacin ¹ 500-750 mg po bid (or 400 mg IV bid) ± rifabutin ¹ (Mycobutin®) 300 mg po daily ± amikacin ¹ 10-15 mg/kg/day IV Maintenance: Clarithromycin (Biaxin®) 500 mg po bid + 1 or 2 other drugs from induction regimen ¹ ; consult ID
Alternative	Induction: Rifabutin (Mycobutin®) 300 mg po daily + amikacin 10-15 mg/kg/day IV ± ciprofloxacin ¹ 500-750 mg po bid (or 400 mg IV bid)	

¹ Consider addition of third or fourth drug for pts with advanced immunosuppression (CD4+ count < 50 cells/mcl), high mycobacterial loads (> 2 log CFU/ml blood), or in the absence of effective ARV therapy

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Prophylaxis and Treatment of Opportunistic Infections (OIs) - page 7 of 13

MAC/MAI Infection, continued			
	Drug	CrCl	Dose
Dosing during renal impairment	Azithromycin	< 10	Use with caution
		30-50	250-500 mg po bid or 400 mg IV bid
	Ciprofloxacin (oral)	10 - 30	500 mg po daily or 400 mg IV daily
		< 10 or HD	250-500 mg po daily after HD, if HD
		CAVHD or CVVHDF	IV formulation: 200-400 mg IV q12h
	Clarithromycin	30-60	50% usual dose (i.e., 500 mg daily)
		< 30	250 mg daily
	Ethambutol	10-50 or CAVH or CVVH	q24-36h
< 10 or PD		q48h	
HD		15-20 mg/kg 3x/wk after HD	
Rifabutin	< 30	May consider 50% usual dose or standard dose with therapeutic drug monitoring	
Dosing during hepatic impairment	Amikacin	No change	
	Ciprofloxacin	Consider adjustment in severe hepatic dysfunction; no clear guidelines	
	Clarithromycin	No change; do not administer if both renal and hepatic function impaired	
	Ethambutol	No change	
	Rifabutin	Dose adjustment not required for mild-moderate liver dysfunction; prolonged half-life observed in severe hepatic disease	

HD: hemodialysis

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Prophylaxis and Treatment of Opportunistic Infections (OIs) - page 8 of 13

Mycobacterium Tuberculosis Infection	
Dosing recommendations	Latent tuberculosis: PPD + induration > 5 mm, or history of +PPD
	Preferred
	Isoniazid (INH®)-sensitive: Isoniazid 300 mg po daily + pyridoxine 50 mg po daily x 6 months ¹
	Isoniazid (INH®)-resistant: Consult pulmonary or ID specialist; options include rifampin (RIF, Rifadin®) 600 mg po daily or rifabutin (Mycobutin®) 300 mg po daily in combination with pyrazinamide x 6 months ¹ ; reports of fatal or severe liver injury with 2-month regimen of daily rifampin and pyrazinamide— avoid this regimen
	Alternative
	Multi-drug resistant (INH & RIF): Choice of therapy depends on susceptibility of isolates in vitro; consult ID or pulmonary specialist
Secondary prophylaxis: Chronic suppressive therapy not necessary after completion of treatment for latent TB	
Treatment	Same as for non-HIV-infected persons, with two exceptions: 1) Rifapentine should not be used ; 2) Twice weekly rifampin or rifabutin + INH should not be used in pts with CD4 < 100 cells/μl; watch for interactions between ARVs and rifamycins
Preferred	Initial phase (2 months): Isoniazid 5 mg/kg/day (max 300 mg/day, except in CNS disease - max 600 mg/day) + rifampin 10 mg/kg (max 600 mg/day) or rifabutin 300 mg po daily + pyrazinamide (PZA) 15-30 mg/kg/day (max 2000 mg/day) + ethambutol (EMB, Myambutol®) 15-20 mg/kg/day (max 1600 mg/day) Continuation phase: culture negative or positive, no cavitation after initial phase; continue x 4 months - isoniazid 5 mg/kg/day (max 300 mg, except in CNS disease, up to 600 mg) + rifampin 10 mg/kg/day (max 600 mg) or isoniazid 15 mg/kg (max 900 mg) tiw + rifampin 10 mg/kg (max 600 mg) tiw; culture positive, cavitation after induction phase; continue x 7 more months—same treatment options, longer duration
Alternative	Choice of therapy based on susceptibility of isolates, especially INH-resistant isolates; a single new drug should never be added to a failing regimen—high risk for developing resistance to new drug; consult ID or pulmonary specialist

¹ For pts with cavitary lung disease and positive culture for M. tuberculosis, after 2 months therapy extend treatment with INH and RIF for additional 3 months for total of 9 months

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Prophylaxis and Treatment of Opportunistic Infections (OIs) - page 9 of 13

Mycobacterium Tuberculosis Infection, continued			
	Drug	CrCl	Dose
Dosing during renal impairment	Ethambutol	< 30 or PD	15-20 mg/kg 3x/wk
		HD	15-20 mg/kg after HD
		CAVH or CVVH	15-20 mg/kg q24-36h
	Isoniazid	No change	
	Pyrazinamide	< 30	15-30 mg/kg 3x/wk
	Pyridoxine	No change	
	Rifabutin	< 30	50% usual dose
Dosing during hepatic impairment	Rifampin	No change	
	Ethambutol	No change	
	Isoniazid	No change	
	Pyrazinamide	Dose reduction necessary to reduce hepatotoxicity; no guidelines available	
	Pyridoxine	No change	
	Rifabutin	No change	
	Rifampin	Dose reduction necessary to reduce hepatotoxicity; no guidelines available	

HD: hemodialysis

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Prophylaxis and Treatment of Opportunistic Infections (OIs) - page 10 of 13

Pneumocystis jiroveci (carinii) Pneumonia (PCP)	
Dosing recommendations	Primary prophylaxis: CD4+ < 200 cells/ μ l, CD4% < 14, history of oropharyngeal candidiasis or other AIDS-defining illness; may be discontinued if CD4+ > 200 cells/ μ l x \geq 3 months
	Preferred TMP-SMX (Bactrim®) 1 DS po daily or 1 SS po daily ¹
	Alternative TMP-SMX 1 DS po tiw 3x/wk or dapsone 100 mg po daily ² or dapsone 50 mg po daily + pyrimethamine 50 mg po qweek + leucovorin 25 mg po qwk or atovaquone (Mepron®) 750 mg po daily (or bid) or 1500 mg daily with meal or aerosolized pentamidine 300 mg monthly via Respigard II™ nebulizer
	Secondary prophylaxis: Same as primary prophylaxis; recommended lifelong maintenance therapy; may discontinue if CD4+ > 200 cells/mcl x > 3 months
	Treatment
Preferred TMP-SMX DS (Bactrim®) 2-3 tabs po q6h or TMP-SMX DS (160/800 mg) 2 tabs po tid or TMP-SMX [15-20mg TMP and 75-100mg SMX]/kg/day po or IV divided q6h or q8h x 21 days	
Alternative Pentamidine (Pentam-300®) 3-4 mg/kg/day IV over \geq 60 min or clindamycin (Cleocin®) 600-900 mg IV or 300-450 mg po q6-8h + primaquine 15-30 mg po daily ² or atovaquone (Mepron®) 750 mg po bid x 21 days	

1 One DS tablet TMP-SMX = SMX 800 mg + TMP 160 mg; one SS tablet TMP-SMX = SMX 400 mg + TMP 80 mg = 10 ml oral suspension; oral suspension = SMX 200 mg + TMP 40 mg/5 ml; IV = SMX 80 mg + TMP 16 mg/ml; consider SS if pt cannot tolerate DS or if small body habitus

2 Ensure normal G6PD activity before treatment

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Prophylaxis and Treatment of Opportunistic Infections (OIs) - page 11 of 13

Pneumocystis jiroveci (carinii) Pneumonia (PCP), continued				
	Drug	CrCl	Treatment Dose	
Dosing during renal impairment	Atovaquone	No change; not dialyzed		
	Dapsone	No change; ensure normal G6PD activity before treatment		
	TMP-SMX	15-30	5 mg/kg TMP base q48h	5 mg/kg q6-8h x 48h, then 3.5-5 mg/kg q12h x 21 days
		< 15	5 mg/kg TMP base q72h	7-10 mg/kg/day divided q12-24h x 21 days
Dosing during hepatic impairment	Atovaquone	No change		
	Dapsone	No change; ensure normal G6PD activity before treatment		
	TMP-SMX	No change		

HD: hemodialysis

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Prophylaxis and Treatment of Opportunistic Infections (OIs) - page 12 of 13

Toxoplasmosis gondii Encephalitis	
Dosing recommendations	Primary prophylaxis: CD4+ < 100 cells/μl; may be discontinued if CD4+ > 200 cells/μl x ≥ 3 months
	Preferred TMP-SMX 1 DS po daily
	Alternative TMP-SMX 1 SS po daily (if small body habitus or DS not tolerated) or 1 DS po 3x/wk or dapsone 50 mg po daily ¹ + pyrimethamine 50 mg po qwk + leucovorin 25 mg po qwk or dapsone 200 mg po qwk ¹ + pyrimethamine 75 mg po qwk + leucovorin 25 mg po qwk or atovaquone (Mepron®) 750 mg po bid with meals +/- pyrimethamine 25 mg po daily + leucovorin 10 mg po daily
	Secondary prophylaxis: Maintenance therapy recommended; may consider discontinuing if improved signs and symptoms and MRI + CD4+ > 200 cells/μL x > 6 months
	Treatment
	Preferred Acute infection: Pyrimethamine 100-200 mg po x 1 (loading dose), then 50 mg (< 60 kg) or 75 mg (≥ 60 kg) po daily + sulfadiazine 1000 (< 60 kg) or 1500 mg (≥ 60 kg) po q6h + leucovorin 10-25 mg po daily ² x ≥ 6 wks Maintenance (lifelong suppressive therapy): Pyrimethamine 25-50 mg po daily + sulfadiazine 2-4 grams po divided into 2-4 doses daily + leucovorin 10-25 mg po daily
Alternative Acute infection: Pyrimethamine + leucovorin (see preferred regimen) + clindamycin 600 mg IV or po q6h x ≥ 6 wks or pyrimethamine + leucovorin (see preferred regimen) in combination with azithromycin 1200 mg po or TMP-SMX (5 mg/kg TMP and 25 mg SMX) IV or po bid or atovaquone 1500 mg po bid with food ± sulfadiazine or pyrimethamine + leucovorin or pyrimethamine + leucovorin (see preferred regimen) + azithromycin 900-1200 mg po daily Maintenance (lifelong suppressive therapy): Clindamycin 600 mg po q8h + pyrimethamine 25-50 mg po daily + leucovorin 10-25 mg po daily + PCP prophylaxis or atovaquone 750 mg po q6-12h +/- (pyrimethamine 25 mg po daily + leucovorin 10 mg po daily) or sulfadiazine 2-4 grams po daily	

1 Ensure normal G6PD activity before treatment

2 May increase leucovorin dose to 50 mg daily or higher based on clinical experience

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Prophylaxis and Treatment of Opportunistic Infections (OIs) - page 13 of 13

Toxoplasmosis gondii Encephalitis, continued				
	Drug	CrCl	Prophylaxis Dose	Treatment Dose
Dosing during renal impairment	TMP-SMX	15-30	5 mg/kg TMP base q48h	5 mg/kg q6-8h x 48h, then 3.5-5 mg/kg q12h
		< 15	5 mg/kg TMP base q72h	7-10 mg/kg/day divided q12h
		HD	5 mg/kg TMP base after HD	15-20 mg/kg before HD and 7-10 mg/kg after HD
	Clindamycin	No change		
	Dapsone	Cleared renally; no guidelines available; ensure normal G6PD activity before treatment		
Dosing during hepatic impairment	Leucovorin	No change		
	Pyrimethamine	No change		
	TMP-SMX	No change		
	Clindamycin	Reduce dose to 300 mg IV q8h if severe hepatic impairment		
	Dapsone	No change; ensure normal G6PD activity before treatment		
Dosing during hepatic impairment	Leucovorin	No change		
	Pyrimethamine	No change		

HD: hemodialysis

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HIV-RELATED CONTACT INFORMATION AT BOSTON MEDICAL CENTER

Post-Exposure Prophylaxis/ Sexual Assault	Non-Occupational Exposure	Report to ED; beeper 7845 (STIK)
	Occupational Exposure	Work days: report to Occupational Medicine, 617-638-8400
		After hours: report to the ED; beeper 7845 (STIK)
Center for Infectious Diseases	Appointments for established infection, acute retroviral syndrome (specify semi-urgent), or urgent needs (specify when calling)	Beeper 4448 (4HIV) or 617-414-4290
	Appointments: newly diagnosed or new to BMC system	Beeper 4448 (4HIV) or 617-414-5979
	Patient mental health crises	Beeper 6463 (MIND)
	HIV Clinical Research Office	617-414-7082
	Home Health Coordinator	617-414-8377
	Adherence Clinic or HIV Pharmacist	617-414-5401 or beeper 2729 or 617-414-4800 or beeper 3421
ID Fellow On Call	Menino Pavilion	Beeper 8902
	East Newton Campus	Beeper 8903
HIV Rapid Testing, Counseling, and Referral M-F 8:30-5:00	HIV Inpatient Testing Service (HITS) Menino Pavilion and East Newton Campus	617-414-8378 or beeper 8378 (TEST)
	HIV Outpatient Testing Service (HOTS)	617-414-6916 or beeper 4687 (HOTS)
	Information; other testing services; HIV Testing Manager	617-414-5432 or beeper 6659
Center for HIV/AIDS Care and Research	Main number and for more information; online copy of this handbook	617-414-3520; http://www.bmc.org/hiv-aids

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