Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

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Drug Interactions (Last updated February 12, 2013; last reviewed February 12, 2013)

Potential drug-drug and/or drug-food interactions should be taken into consideration when selecting an antiretroviral (ARV) regimen. A thorough review of concomitant medications can help in designing a regimen that minimizes undesirable interactions. In addition, the potential for drug interactions should be assessed when any new drug (including over-the-counter agents), is added to an existing ARV combination. Most drug interactions with ARV drugs are mediated through inhibition or induction of hepatic drug metabolism.[1] The mechanisms of drug interactions with each ARV drug class are briefly summarized below. Tables 14–16c list significant drug interactions with different ARV agents and recommendations on contraindications, dose modifications, and alternative agents.

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

All NNRTIs are metabolized in the liver by cytochrome P450 (CYP) 3A isoenzymes. In addition, efavirenz (EFV) and nevirapine (NVP) are substrates of CYP2B6 enzymes, and etravirine (ETR) is a substrate of CYP2C9 and 2C19 enzymes. Concomitantly administered drugs that induce or inhibit these enzymes can alter NNRTI drug concentrations, resulting in virologic failure or adverse effects. All NNRTIs, except rilpivirine (RPV), induce or inhibit CYP isoenzymes. EFV acts as a mixed inducer and inhibitor, but like NVP, it primarily induces CYP3A and 2B6 enzymes. ETR also induces CYP3A but inhibits CYP2C9 and 2C19 enzymes. The inducing effects of NNRTIs can result in sub-therapeutic concentrations of concomitantly administered drugs that are metabolized by CYP enzymes. Examples of such interacting medications include azole antifungals, rifamycins, benzodiazepines, hepatitis C virus (HCV) protease inhibitors, HMG-CoA reductase inhibitors (statins), and methadone. See Table 15b for dosing recommendations.

Protease Inhibitors (PIs)

All PIs are metabolized in the liver by CYP3A isoenzymes; consequently their metabolic rates may be altered in the presence of CYP inducers or inhibitors. Co-administration of PIs with ritonavir (RTV), a potent CYP3A inhibitor, intentionally increases PI exposure (see Pharmacokinetic Enhancing below). Co-administration of PIs with a potent CYP3A inducer may lead to suboptimal drug concentrations and reduced therapeutic effects of the PI. These drug combinations should be avoided if alternative agents can be used. If this is not possible, close monitoring of plasma HIV RNA, with or without ARV dosage adjustment and therapeutic drug monitoring (TDM), may be warranted. For example, the rifamycins (i.e., rifampin and, to a lesser extent, rifabutin) are CYP3A4 inducers that can significantly reduce plasma concentrations of most PIs.[2, 3] Rifabutin is a less potent CYP3A4 inducer than rifampin. Therefore, despite wider experience with rifampin use, rifabutin is generally considered a reasonable alternative to rifampin for the treatment of tuberculosis when used with a PI-based regimen.[4, 5] Table 15a lists dosage recommendations for concomitant use of rifamycins and other CYP3A4 inducers with PIs.

Some PIs may also induce or inhibit CYP isoenzymes, P-glycoprotein, or other transporters in the gut and elsewhere. Tipranavir (TPV), for example, is a potent inducer of CYP3A4 and P-glycoprotein. The net effect of ritonavir-boosted tipranavir (TPV/r) on CYP3A *in vivo*, however, appears to be enzyme inhibition. Thus, concentrations of drugs that are substrates for only CYP3A are most likely to be increased if the drugs are given with TPV/r. The net effect of TPV/r on a drug that is a substrate of both CYP3A and P-glycoprotein (P-gp) cannot be confidently predicted. Significant decreases in saquinavir (SQV), amprenavir (APV), and lopinavir (LPV) concentrations have been observed *in vivo* when the PIs were given with TPV/r.

The use of a CYP3A substrate that has a narrow margin of safety in the presence of a potent CYP3A inhibitor, such as the PIs, may lead to markedly prolonged elimination half-life ($t_{1/2}$) and toxic drug

accumulation. Avoidance of concomitant use or dose reduction of the affected drug, with close monitoring for dose-related toxicities, may be warranted.

The list of drugs that may have significant interactions with PIs is extensive and is continuously expanding. Some examples of these drugs include lipid-lowering agents (e.g., statins), benzodiazepines, calcium channel blockers, immunosuppressants (e.g., cyclosporine, tacrolimus), anticonvulsants, rifamycins, erectile dysfunction agents (e.g., sildenafil), ergot derivatives, azole antifungals, macrolides, oral contraceptives, methadone, and HCV protease inhibitors. Herbal products, such as St. John's wort, can also cause interactions that risk adverse clinical effects. See Table 15a for dosage recommendations.

Integrase Strand Transfer Inhibitors (INSTIs)

Raltegravir (RAL) is primarily eliminated by glucuronidation mediated by the uridine diphosphate (UDP)-glucuronosyltransferase (UGT) 1A1 enzymes. Strong inducers of UGT1A1 enzymes (e.g., rifampin) can significantly reduce the concentration of RAL.[6] See Table 15e for dosage recommendations. Raltegravir does not appear to affect CYP or UGT enzymes or P-glycoprotein-mediated transport.

Elvitegravir (EVG) is available only as a fixed dose combination with cobicistat (COBI), tenofovir (TDF), and emtricitabine (FTC). EVG is metabolized largely by CYP3A enzymes but also undergoes glucuronidation by UGT 1A1/3 enzymes. Co-administration of EVG with COBI, a CYP3A inhibitor, increases EVG exposure (see Pharmacokinetic Enhancing below). Drugs that induce or inhibit CYP3A enzymes can alter concentrations of EVG. The co-formulation of EVG/COBI/TDF/FTC should not be co-administered with other ARVs because of potential drug interactions that may alter drug levels of EVG, COBI, or the concomitant drug. Examples of interacting drugs include those listed above for NNRTIs and PIs. See Table 15e for dosage recommendations.

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

Unlike PIs, NNRTIs, EVG, and maraviroc (MVC), NRTIs do not undergo hepatic transformation through the CYP metabolic pathway. Significant pharmacodynamic interactions of NRTIs and other drugs, such as additive bone marrow suppressive effects of zidovudine (ZDV) and ganciclovir, have been reported. Pharmacokinetic (PK) interactions have also been reported; for example, atazanavir (ATV) concentration can be reduced when it is co-administered with TDF.[7] However, the mechanisms underlying some of these interactions are still unclear. Table 15c lists significant interactions with NRTIs.

CCR5 Antagonist

MVC is a substrate of CYP3A enzymes and P-glycoprotein. As a consequence, the concentrations of MVC can be significantly increased in the presence of strong CYP3A inhibitors (such as RTV and other PIs, except for TPV/r) and are reduced when MVC is used with CYP3A inducers (such as EFV or rifampin). Dose adjustment is necessary when MVC is used in combination with these agents (see Table 16b or Appendix B, Table 6 for dosage recommendations). MVC is neither an inducer nor an inhibitor of the CYP3A system and does not alter the PKs of the drugs evaluated in interaction studies to date.

Fusion Inhibitor

The fusion inhibitor enfuvirtide (T20) is a 36-amino-acid peptide that does not enter human cells. It is expected to undergo catabolism to its constituent amino acids with subsequent recycling of the amino acids in the body pool. No clinically significant drug-drug interaction with T20 has been identified to date.

Pharmacokinetic (PK) Enhancing

PK enhancing is a strategy used in ARV treatment to increase the exposure of an ARV by concomitantly administering a drug that inhibits the specific drug metabolizing enzymes for which the ARV is a substrate.

Currently two agents are used in clinical practice as PK enhancers: RTV and COBI.

RTV is an HIV PI that is primarily used in clinical practice at a lower than approved dose (100 to 400 mg per day) as a PK enhancer for other PIs because of its inhibitory effects on CYP450, predominately CYP3A4 and P-glycoprotein (P-gp). RTV increases the trough concentration (C_{min}) and prolongs the half-life of the active PIs.[8] The higher C_{min} allows for a greater C_{min}: inhibitory concentration ratio, which reduces the risk that drug resistance will develop as a result of suboptimal drug exposure. The longer half-life of the PI allows for less frequent dosing, which may enhance medication adherence. Because RTV is a potent inhibitor, it may result in complex drug-drug interactions when used with PIs and with other ARVs or non ARVs. Tables 15a and 16a–c list interactions between RTV-containing PI regimens and other medications, as well as comments on the clinical management of these interactions.

COBI is a specific, potent CYP3A inhibitor that has a weak to no effect on other CYP450 isoforms. COBI has no ARV activity. The high water solubility of COBI allows for its co-formulation with other agents.[9] COBI is currently available only as part of a fixed dose combination of EVG/COBI/TDF/FTC. COBI is used to increase the plasma concentrations of EVG, an INSTI. Like RTV, COBI has a complex drug-drug interaction profile. COBI also is an inhibitor of P-gp-mediated transport, which appears to be the mechanism by which COBI increases the systemic exposure to TDF. Table 15e lists interactions with COBI identified in PK studies conducted to date, projected interactions, and drugs that should not be co-administered with COBI.

When using RTV- or COBI-containing regimens, clinicians should be vigilant in assessing the potential for adverse drug-drug interactions. This is especially important when prescribing CYP3A substrates for which no PK data are available.

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Table 14. Drugs That Should Not Be Used With Antiretroviral Agents (Last updated February 12, 2013; last reviewed February 12, 2013) (page 1 of 2)

This table only lists drugs that should not be co-administered at any dose and regardless of ritonavir (RTV) boosting. See Tables 15 and 16 for more detailed pharmacokinetic (PK) interaction data.

Drug Categories										
Antiretroviral Agents[a,b]	**Cardiac Agents**	**Lipid-Lowering Agents**	**Antimyco-bacterials**	**Gastro-intestinal Drugs**	**Neuro-leptics**	**Psycho-tropics**	**Ergot Derivatives (vasoconstrictors)**	**Herbs**	**Anti-retroviral Agents**	**Others**
ATV +/– RTV	amiodarone dronedarone	lovastatin simvastatin	rifampin rifapentine[c]	cisapride[e]	pimozide	midazolam[f] triazolam	dihydroergotamine ergonovine ergotamine methylergonovine	St. John's wort	ETR NVP	alfuzosin irinotecan salmeterol sildenafil for PAH
DRV/r	amiodarone dronedarone	lovastatin simvastatin	rifampin rifapentine[c]	cisapride[e]	pimozide	midazolam[f] triazolam	dihydroergotamine ergonovine ergotamine methylergonovine	St. John's wort	none	alfuzosin salmeterol sildenafil for PAH
FPV +/– RTV	amiodarone dronedarone flecainide propafenone	lovastatin simvastatin	rifampin rifapentine[c]	cisapride[e]	pimozide	midazolam[f] triazolam	dihydroergotamine ergonovine ergotamine methylergonovine	St. John's wort	ETR	alfuzosin salmeterol sildenafil for PAH
LPV/r	amiodarone dronedarone	lovastatin simvastatin	rifampin[d] rifapentine[c]	cisapride[e]	pimozide	midazolam[f] triazolam	dihydroergotamine ergonovine ergotamine methylergonovine	St. John's wort	none	alfuzosin salmeterol sildenafil for PAH
SQV/r	amiodarone dronedarone dofetilide flecainide lidocaine propafenone quinidine	lovastatin simvastatin	rifampin[d] rifapentine[c]	cisapride[e]	pimozide	midazolam[f] triazolam trazodone	dihydroergotamine ergonovine ergotamine methylergonovine	St. John's wort garlic supple-ments	none	alfuzosin salmeterol sildenafil for PAH
TPV/r	amiodarone dronedarone flecainide propafenone quinidine	lovastatin simvastatin	rifampin rifapentine[c]	cisapride[e]	pimozide	midazolam[f] triazolam	dihydroergotamine ergonovine ergotamine methylergonovine	St. John's wort	ETR	alfuzosin salmeterol sildenafil for PAH
EFV	none	none	rifapentine[c]	cisapride[e]	pimozide	midazolam[f] triazolam	dihydroergotamine ergonovine ergotamine methylergonovine	St. John's wort	other NNRTIs	none
ETR	none	none	rifampin rifapentine[c]	none	none	none	none	St John's wort	unboosted PIs ATV/r, FPV/r, or TPV/r other NNRTIs	carbamazepine phenobarbital phenytoin clopidogrel

Table 14. Drugs That Should Not Be Used With Antiretroviral Agents (Last updated February 12, 2013; last reviewed February 12, 2013) (page 2 of 2)

Drug Categories										
Antiretroviral Agents[a,b]	**Cardiac Agents**	**Lipid-Lowering Agents**	**Antimyco-bacterials**	**Gastro-intestinal Drugs**	**Neuro-leptics**	**Psycho-tropics**	**Ergot Derivatives (vasoconstrictors)**	**Herbs**	**Anti-retroviral Agents**	**Others**
NVP	none	none	rifapentine[c]	none	none	none	none	St. John's wort	ATV +/– RTV other NNRTIs	ketoconazole
RPV	none	none	rifabutin rifampin rifapentine[c]	proton pump inhibitors	none	none	none	St. John's wort	other NNRTIs	carbamazepine oxcarbazepine phenobarbital phenytoin
MVC	none	none	rifapentine[c]	none	none	none	none	St. John's wort	none	none
EVG/COBI/ TDF/FTC	none	lovastatin simvastatin	rifabutin rifampin rifapentine[c]	cisapride[e]	pimozide	midazolam[f] triazolam	dihydroergotamine ergotamine methylergonovine	St. John's wort	All other ARVs	alfuzosin sildenafil for PAH

[a] DLV, IDV, NFV, and RTV (as sole PI) are not included in this table. Refer to the appropriate FDA package insert for information regarding DLV-, IDV-, NFV-, and RTV (as sole PI)-related drug interactions.

[b] Certain listed drugs are contraindicated on the basis of theoretical considerations. Thus, drugs with narrow therapeutic indices and suspected metabolic involvement with CYP450 3A, 2D6, or unknown pathways are included in this table. Actual interactions may or may not occur in patients.

[c] HIV-infected patients treated with rifapentine have a higher rate of tuberculosis (TB) relapse than those treated with other rifamycin-based regimens. Therefore an alternative agent to rifapentine is recommended.

[d] A high rate of Grade 4 serum transaminase elevation was seen when a higher dose of RTV was added to LPV/r or SQV or when double-dose LPV/r was used with rifampin to compensate for rifampin's induction effect and therefore, these dosing strategies should not be used.

[e] The manufacturer of cisapride has a limited-access protocol for patients who meet specific clinical eligibility criteria.

[f] Use of oral midazolam is contraindicated. Parenteral midazolam can be used with caution as a single dose and can be given in a monitored situation for procedural sedation.

Suggested alternatives to:

- **Lovastatin, simvastatin:** Fluvastatin, pitavastatin, and pravastatin (except for pravastatin with DRV/r) have the least potential for drug-drug interactions (see Table 15a). Use atorvastatin and rosuvastatin with caution; start with the lowest possible dose and titrate based on tolerance and lipid-lowering efficacy.
- **Rifampin:** Rifabutin (with dosage adjustment, see Tables 15a and 15b)
- **Midazolam, triazolam:** temazepam, lorazepam, oxazepam

Key to Abbreviations: ATV +/- RTV = atazanavir +/- ritonavir, ATV/r = atazanavir/ritonavir, COBI = cobicistat, CYP = cytochrome P, DLV = delavirdine, DRV/r = darunavir/ritonavir, EFV = efavirenz, ETR = etravirine, EVG = elvitegravir, FDA = Food and Drug Administration, FPV +/- RTV = fosamprenavir +/- ritonavir, FPV/r = fosamprenavir/ritonavir, IDV = indinavir, LPV/r = lopinavir/ritonavir, MVC = maraviroc, NFV = nelfinavir, NNRTI = non-nucleoside reverse transcriptase inhibitor, NVP = nevirapine, PAH = pulmonary arterial hypertension, PI = protease inhibitor, PK = pharmacokinetic, RPV = rilpivirine, RTV = ritonavir, SQV = saquinavir, SQV/r = saquinavir/ritonavir, TB = tuberculosis, TPV/r = tipranavir/ritonavir

Table 15a. Drug Interactions between Protease Inhibitors (PI)* and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 1 of 10)

This table provides information relating to pharmacokinetic (PK) interactions between PIs and non-antiretroviral (ARV) drugs. When information is available, interactions with boosted and unboosted PIs are listed separately. For interactions between ARV agents and for dosing recommendations, refer to Table 16a.

* Nelfinavir (NFV) and indinavir (IDV) are not included in this table. Please refer to the NFV and IDV FDA package inserts for information regarding drug interactions with these PIs.

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	ATV, ATV/r	When given simultaneously, ↓ ATV expected	Give ATV at least 2 hours before or 1 hour after antacids or buffered medications.
	FPV	APV AUC ↓ 18%; no significant change in APV C_{min}	Give FPV simultaneously with (or at least 2 hours before or 1 hour after) antacids.
	TPV/r	TPV AUC ↓ 27%	Give TPV at least 2 hours before or 1 hour after antacids.
H2 Receptor Antagonists	**RTV-boosted PIs**		
	ATV/r	↓ ATV	H2 receptor antagonist dose should not exceed a dose equivalent to famotidine 40 mg BID in ART-naive patients or 20 mg BID in ART-experienced patients. Give ATV 300 mg + RTV 100 mg simultaneously with and/or ≥10 hours after the H2 receptor antagonist. If using TDF and H2 receptor antagonist in ART-experienced patients, use ATV 400 mg + RTV 100 mg.
	DRV/r, LPV/r	No significant effect	No dosage adjustment necessary.
	PIs without RTV		
	ATV	↓ ATV	H2 receptor antagonist single dose should not exceed a dose equivalent of famotidine 20 mg or total daily dose equivalent of famotidine 20 mg BID in ART-naive patients. Give ATV at least 2 hours before and at least 10 hours after the H2 receptor antagonist.
	FPV	APV AUC ↓ 30%; no significant change in APV C_{min}	If concomitant use is necessary, give FPV at least 2 hours before H2 receptor antagonist. Consider boosting FPV with RTV.
Proton Pump Inhibitors (PPIs)	ATV	↓ ATV	**PPIs are not recommended in patients receiving unboosted ATV.** In these patients, consider alternative acid-reducing agents, RTV boosting, or alternative PIs.
	ATV/r	↓ ATV	PPIs should not exceed a dose equivalent to omeprazole 20 mg daily in PI-naive patients. PPIs should be administered at least 12 hours before ATV/r. **PPIs are not recommended in PI-experienced patients.**
	DRV/r, TPV/r	↓ omeprazole PI: no significant effect	May need to increase omeprazole dose when using TPV/r.
	FPV, FPV/r, LPV/r	No significant effect	No dosage adjustment necessary.
	SQV/r	SQV AUC ↑ 82%	Monitor for SQV toxicities.

Table 15a. Drug Interactions between Protease Inhibitors (PI)* and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 2 of 10)

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticoagulants			
Warfarin	ATV, ATV/r, DRV/r, FPV, FPV/r, LPV/r, SQV/r, TPV/r	↑ or ↓ warfarin possible DRV/r ↓ S-warfarin AUC 21%	Monitor INR closely when stopping or starting PI and adjust warfarin dose accordingly.
Rivaroxaban	All PIs	↑ rivaroxaban	Avoid concomitant use. Co-administration is expected to result in increased exposure of rivaroxaban which may lead to risk of increased bleeding.
Anticonvulsants			
Carbamazepine	**RTV-boosted PIs**		
	ATV/r, FPV/r, LPV/r, SQV/r, TPV/r	↑ carbamazepine possible TPV/r ↑ carbamazepine AUC 26% May ↓ PI levels substantially	Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response. **Do not co-administer with LPV/r once daily.**
	DRV/r	carbamazepine AUC ↑ 45% DRV: no significant change	Monitor anticonvulsant level and adjust dose accordingly.
	PIs without RTV		
	ATV, FPV	May ↓ PI levels substantially	Monitor anticonvulsant level and virologic response. Consider alternative anticonvulsant, RTV boosting for ATV and FPV, and/or monitoring PI level.
Lamotrigine	LPV/r	lamotrigine AUC ↓ 50% LPV: no significant change	A dose increase of lamotrigine may be needed and therapeutic concentration monitoring for lamotrigine may be indicated; particularly during dosage adjustment or consider alternative anticonvulsant. A similar interaction is possible with other RTV-boosted PIs.
Phenobarbital	All PIs	May ↓ PI levels substantially	Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response. **Do not co-administer with LPV/r once daily.**
Phenytoin	**RTV-boosted PIs**		
	ATV/r, DRV/r, SQV/r, TPV/r	↓ phenytoin possible ↓ PI possible	Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response.
	FPV/r	phenytoin AUC ↓ 22% APV AUC ↑ 20%	Monitor phenytoin level and adjust dose accordingly. No change in FPV/r dose recommended.
	LPV/r	phenytoin AUC ↓ 31% LPV/r AUC ↓ 33%	Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response. **Do not co-administer with LPV/r once daily.**
	PIs without RTV		
	ATV, FPV	May ↓ PI levels substantially	Consider alternative anticonvulsant, RTV boosting for ATV and FPV, and/or monitoring PI level. Monitor anticonvulsant level and virologic response.
Valproic Acid (VPA)	LPV/r	↓ or ⇔ VPA possible LPV AUC ↑ 75%	Monitor VPA levels and virologic response. Monitor for LPV-related toxicities.

Table 15a. Drug Interactions between Protease Inhibitors (PI)* and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 3 of 10)

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants			
Bupropion	LPV/r	bupropion AUC ↓ 57%	Titrate bupropion dose based on clinical response.
	TPV/r	bupropion AUC ↓ 46%	
Paroxetine	DRV/r	paroxetine AUC ↓ 39%	Titrate paroxetine dose based on clinical response.
	FPV/r	paroxetine AUC ↓ 55%	
Sertraline	DRV/r	sertraline AUC ↓ 49%	Titrate sertraline dose based on clinical response.
Trazodone	ATV/r, ATV, DRV/r, FPV/r, FPV, LPV/r, TPV/r	RTV 200 mg BID (for 2 days) ↑ trazodone AUC 240%	Use lowest dose of trazodone and monitor for CNS and cardiovascular adverse effects.
	SQV/r	↑ trazodone expected	**Contraindicated. Do not co-administer.**
Tricyclic Antidepressants (TCAs) (Amitriptyline, Desipramine, Imipramine, Nortriptyline)	All RTV-boosted PIs	↑ TCA expected	Use lowest possible TCA dose and titrate based on clinical assessment and/or drug levels.
Antifungals			
Fluconazole	**RTV-boosted PIs**		
	ATV/r	No significant effect	No dosage adjustment necessary.
	SQV/r	No data with RTV boosting SQV (1200 mg TID) AUC ↑ 50%	No dosage adjustment necessary.
	TPV/r	TPV AUC ↑ 50%	Fluconazole >200 mg daily is not recommended. If high-dose fluconazole is indicated, consider alternative PI or another class of ARV drug.
Itraconazole	**RTV-boosted PIs**		
	ATV/r, DRV/r, FPV/r, TPV/r	↑ itraconazole possible ↑ PI possible	Consider monitoring itraconazole level to guide dosage adjustments. High doses (>200 mg/day) are not recommended unless dose is guided by itraconazole levels.
	LPV/r	↑ itraconazole	Consider monitoring itraconazole level to guide dosage adjustments. High doses (>200 mg/day) are not recommended unless dose is guided by itraconazole levels
	SQV/r	Bidirectional interaction has been observed	Dose not established, but decreased itraconazole dosage may be warranted. Consider monitoring itraconazole level.
	PIs without RTV		
	ATV, FPV	↑ itraconazole possible ↑ PI possible	Consider monitoring itraconazole level to guide dosage adjustments.

Table 15a. Drug Interactions between Protease Inhibitors (PI)* and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 4 of 10)

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antifungals, continued			
Posaconazole	ATV/r	ATV AUC ↑ 146%	Monitor for adverse effects of ATV.
	ATV	ATV AUC ↑ 268%	Monitor for adverse effects of ATV.
	FPV	FPV (1400 mg BID) ↓ posaconazole AUC 23%; (compared with FPV/RTV 700 mg/100 mg) APV AUC ↓ 65%	**Do not co-administer.**
Voriconazole	**RTV-boosted PIs**		
	All RTV-boosted PIs	RTV 400 mg BID ↓ voriconazole AUC 82% RTV 100 mg BID ↓ voriconazole AUC 39%	**Do not co-administer** voriconazole and RTV unless benefit outweighs risk. If administered, consider monitoring voriconazole level and adjust dose accordingly.
	PIs without RTV		
	ATV, FPV	↑ voriconazole possible ↑ PI possible	Monitor for toxicities.
Antimycobacterials			
Clarithromycin	ATV/r, ATV	clarithromycin AUC ↑ 94%	May cause QTc prolongation. Reduce clarithromycin dose by 50%. Consider alternative therapy (e.g., azithromycin).
	DRV/r, FPV/r, LPV/r, SQV/r, TPV/r	DRV/r ↑ clarithromycin AUC 57% FPV/r ↑ clarithromycin possible LPV/r ↑ clarithromycin expected RTV 500 mg BID ↑ clarithromycin 77% SQV unboosted ↑ clarithromycin 45% TPV/r ↑ clarithromycin 19% clarithromycin ↑ unboosted SQV 177% clarithromycin ↑ TPV 66%	Monitor for clarithromycin-related toxicities or consider alternative macrolide (e.g., azithromycin). Reduce clarithromycin dose by 50% in patients with CrCl 30–60 mL/min. Reduce clarithromycin dose by 75% in patients with CrCl <30 mL/min.
	FPV	APV AUC ↑ 18%	No dosage adjustment necessary.
Rifabutin	**RTV-boosted PIs**		
	ATV/r	rifabutin (150 mg once daily) AUC ↑ 110% and metabolite AUC ↑ 2,101% compared with rifabutin (300 mg daily) administered alone	Rifabutin 150 mg once daily or 300 mg three times a week. Monitor for antimycobacterial activity and consider therapeutic drug monitoring. PK data reported in this table are results from healthy volunteer studies. Lower rifabutin exposure has been reported in HIV-infected patients than in the healthy study participants.
	DRV/r	rifabutin (150 mg every other day) AUC not significantly changed and metabolite AUC ↑ 881% compared with rifabutin (300 mg once daily) administered alone	
	FPV/r	rifabutin (150 mg every other day) and metabolite AUC ↑ 64% compared with rifabutin (300 mg once daily) administered alone	
	LPV/r	rifabutin (150 mg once daily) and metabolite AUC ↑ 473% compared with rifabutin (300 mg daily) administered alone	
	SQV/r	↑ rifabutin with unboosted SQV	
	TPV/r	rifabutin (150 mg x 1 dose) and metabolite AUC ↑ 333%	

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimycobacterials, continued			
Rifabutin, continued	**PIs without RTV**		
	ATV, FPV	↑ rifabutin AUC expected	Rifabutin 150 mg daily or 300 mg three times a week
Rifampin	All PIs	↓ PI conc. by >75%	**Do not co-administer rifampin and PIs.** Additional RTV does not overcome this interaction and increases hepatotoxicity.
Rifapentine	All PIs	↓ PI expected	**Do not co-administer rifapentine and PIs.**
Benzodiazepines			
Alprazolam **Diazepam**	All PIs	↑ benzodiazepine possible RTV (200 mg BID for 2 days) ↑ alprazolam half-life 222% and AUC 248%	Consider alternative benzodiazepines such as lorazepam, oxazepam, or temazepam.
Lorazepam **Oxazepam** **Temazepam**	All PIs	No data	These benzodiazepines are metabolized via non-CYP450 pathways; there is less interaction potential than with other benzodiazepines.
Midazolam	All PIs	↑ midazolam expected SQV/r ↑ midazolam (oral) AUC 1,144% and C_{max} 327%	**Do not co-administer oral midazolam and PIs.** Parenteral midazolam can be used with caution when given as a single dose in a monitored situation for procedural sedation.
Triazolam	All PIs	↑ triazolam expected RTV (200 mg BID) ↑ triazolam half-life 1,200% and AUC 2,000%	**Do not co-administer triazolam and PIs.**
Cardiac Medications			
Bosentan	All PIs	LPV/r ↑ bosentan 48-fold (day 4) and 5-fold (day 10) ↓ ATV expected	**Do not co-administer bosentan and ATV without RTV.** In patients on a PI (other than unboosted ATV) >10 days: Start bosentan at 62.5 mg once daily or every other day. In patients on bosentan who require a PI (other than unboosted ATV): Stop bosentan ≥36 hours before PI initiation and restart 10 days after PI initiation at 62.5 mg once daily or every other day.
Digoxin	RTV, SQV/r	RTV (200 mg BID) ↑ digoxin AUC 29% and half-life 43% SQV/r ↑ digoxin AUC 49%	Use with caution. Monitor digoxin levels. Digoxin dose may need to be decreased.
Dihydropyridine Calcium Channel Blockers (CCBs)	All PIs	↑ dihydropyridine possible	Use with caution. Titrate CCB dose and monitor closely. ECG monitoring is recommended when CCB used with ATV.
Diltiazem	ATV/r, ATV	diltiazem AUC ↑ 125%	Decrease diltiazem dose by 50%. ECG monitoring is recommended.
	DRV/r, FPV/r, FPV LPV/r, SQV/r, TPV/r	↑ diltiazem possible	Use with caution. Adjust diltiazem according to clinical response and toxicities.

Table 15a. Drug Interactions between Protease Inhibitors (PI)* and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 6 of 10)

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Corticosteroids			
Budesonide (systemic)	All PIs	↓ PI levels possible ↑ glucocorticoids	Use with caution. Co-administration can result in adrenal insufficiency, including Cushing's syndrome. **Do not co-administer unless potential benefits of systemic budesonide outweigh the risks of systemic corticosteroid adverse effects.**
Budesonide (inhaled or intranasal)	All RTV-boosted PIs	↑ glucocorticoids	Use with caution. Co-administration can result in adrenal insufficiency, including Cushing's syndrome. **Do not co-administer unless potential benefits of inhaled or intranasal budesonide outweigh the risks of systemic corticosteroid adverse effects.**
Dexamethasone	All PIs	↓ PI levels possible	Use systemic dexamethasone with caution or consider alternative corticosteroid for long-term use.
Fluticasone (inhaled or intranasal)	All RTV-boosted PIs	RTV 100 mg BID ↑ fluticasone AUC 350-fold and ↑ C_{max} 25-fold	Co-administration can result in adrenal insufficiency, including Cushing's syndrome. **Do not co-administer unless potential benefits of inhaled fluticasone outweigh the risks of systemic corticosteroid adverse effects.**
Prednisone	LPV/r	↑ prednisolone AUC 31% ↓ lopinavir	Use with caution. Co-administration can result in adrenal insufficiency, including Cushing's syndrome. **Do not co-administer unless potential benefits of prednisone outweigh the risks of systemic corticosteroid adverse effects.**
Hepatitis C NS3/4A Protease Inhibitors			
Boceprevir	ATV/r	ATV AUC ↓ 35%, C_{min} ↓ 49% RTV AUC ↓ 36% boceprevir AUC ⇔	**Co-administration is not recommended.**
	DRV/r	DRV AUC ↓ 44%, C_{min} ↓ 59% RTV AUC ↓ 26% boceprevir AUC ↓ 32%, C_{min} ↓ 35%	**Co-administration is not recommended.**
	LPV/r	LPV AUC ↓ 34%, C_{min} ↓ 43% RTV AUC ↓ 22% boceprevir AUC ↓ 45%, C_{min} ↓ 57%	**Co-administration is not recommended.**
Telaprevir	ATV/r	telaprevir AUC ↓ 20%	No dose adjustment necessary.
	DRV/r	telaprevir AUC ↓ 35% DRV AUC ↓ 40%	**Co-administration is not recommended.**
	FPV/r	telaprevir AUC ↓ 32% APV AUC ↓ 47%	**Co-administration is not recommended.**
	LPV/r	telaprevir AUC ↓ 54% LPV: no significant change	**Co-administration is not recommended.**

Table 15a. Drug Interactions between Protease Inhibitors (PI)* and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 7 of 10)

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Herbal Products			
St. John's Wort	All PIs	↓ PI expected	**Do not co-administer.**
Hormonal Contraceptives			
Hormonal Contraceptives	**RTV-boosted PIs**		
	ATV/r	ethinyl estradiol AUC ↓ 19% and C_{min} ↓ 37% norgestimate ↑ 85%	Oral contraceptive should contain at least 35 mcg of ethinyl estradiol. Oral contraceptives containing progestins other than norethindrone or norgestimate have not been studied.[a]
	DRV/r	ethinyl estradiol AUC ↓ 44% norethindrone AUC ↓ 14%	Use alternative or additional contraceptive method.
	FPV/r	ethinyl estradiol AUC ↓ 37% norethindrone AUC ↓ 34%	Use alternative or additional contraceptive method.
	LPV/r	ethinyl estradiol AUC ↓ 42% norethindrone AUC ↓ 17%	Use alternative or additional contraceptive method.
	SQV/r	↓ ethinyl estradiol	Use alternative or additional contraceptive method.
	TPV/r	ethinyl estradiol AUC ↓ 48% norethindrone: no significant change	Use alternative or additional contraceptive method.
	PIs without RTV		
	ATV	ethinyl estradiol AUC ↑ 48% norethindrone AUC ↑ 110%	Use oral contraceptive that contains no more than 30 mcg of ethinyl estradiol or use alternative contraceptive method. Oral contraceptives containing less than 25 mcg of ethinyl estradiol or progestins other than norethindrone or norgestimate have not been studied.[b]
	FPV	With APV: ↑ ethinyl estradiol and ↑ norethindrone C_{min}; APV C_{min} ↓ 20%	Use alternative contraceptive method.
HMG-CoA Reductase Inhibitors			
Atorvastatin	ATV/r, ATV	↑ atorvastatin possible	Titrate atorvastatin dose carefully and use lowest dose necessary.
	DRV/r FPV/r, FPV, SQV/r	DRV/r + atorvastatin 10 mg similar to atorvastatin 40 mg administered alone; FPV +/– RTV ↑ atorvastatin AUC 130%–153%; SQV/r ↑ atorvastatin AUC 79%	Titrate atorvastatin dose carefully and use the lowest necessary dose. Do not exceed 20 mg atorvastatin daily.
	LPV/r	LPV/r ↑ atorvastatin AUC 488%	Use with caution and use the lowest atorvastatin dose necessary.
	TPV/r	↑ atorvastatin AUC 836%	**Do not co-administer.**
Lovastatin	All PIs	Significant ↑ lovastatin expected	**Contraindicated. Do not co-administer.**
Pitavastatin	All PIs	ATV ↑ pitavastatin AUC 31% and C_{max} ↑ 60% ATV: no significant effect LPV/r ↓ pitavastatin AUC 20% LPV: no significant effect	No dose adjustment necessary.

Table 15a. Drug Interactions between Protease Inhibitors (PI)* and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 8 of 10)

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
HMG-CoA Reductase Inhibitors, continued			
Pravastatin	DRV/r	pravastatin AUC ↑ 81%	Use lowest possible starting dose of pravastatin with careful monitoring.
	LPV/r	pravastatin AUC ↑ 33%	No dose adjustment necessary.
	SQV/r	pravastatin AUC ↓ 47%–50%	No dose adjustment necessary.
Rosuvastatin	ATV/r, LPV/r	ATV/r ↑ rosuvastatin AUC 3-fold and C_{max} ↑ 7-fold LPV/r ↑ rosuvastatin AUC 108% and C_{max} ↑ 366%	Titrate rosuvastatin dose carefully and use the lowest necessary dose. Do not exceed 10 mg rosuvastatin daily.
	DRV/r	rosuvastatin AUC ↑ 48% and C_{max} ↑ 139%	Titrate rosuvastatin dose carefully and use the lowest necessary dose while monitoring for toxicities.
	FPV +/- RTV	No significant effect on rosuvastatin	No dosage adjustment necessary.
	SQV/r	No data available	Titrate rosuvastatin dose carefully and use the lowest necessary dose while monitoring for toxicities.
	TPV/r	rosuvastatin AUC ↑ 26% and C_{max} ↑ 123%	No dosage adjustment necessary.
Simvastatin	All PIs	Significant ↑ simvastatin level; SQV/r 400 mg/400 mg BID ↑ simvastatin AUC 3,059%	**Contraindicated. Do not co-administer.**
Immunosuppressants			
Cyclosporine Sirolimus Tacrolimus	All PIs	↑ immunosuppressant possible	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for toxicities. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.
Narcotics/Treatment for Opioid Dependence			
Buprenorphine	ATV	buprenorphine AUC ↑ 93% norbuprenorphine[c] AUC ↑ 76% ↓ ATV possible	**Do not co-administer buprenorphine with unboosted ATV.**
	ATV/r	buprenorphine AUC ↑ 66% norbuprenorphine[c] AUC ↑ 105%	Monitor for sedation. Buprenorphine dose reduction may be necessary.
	DRV/r	buprenorphine: no significant effect norbuprenorphine[c] AUC ↑ 46% and C_{min} ↑ 71%	No dosage adjustment necessary. Clinical monitoring is recommended.
	FPV/r	buprenorphine: no significant effect norbuprenorphine[c] AUC ↓ 15%	No dosage adjustment necessary. Clinical monitoring is recommended.
	LPV/r	No significant effect	No dosage adjustment necessary.
	TPV/r	buprenorphine: no significant effect norbuprenorphine[c] AUC, C_{max}, and C_{min} ↓ 80% TPV C_{min} ↓ 19%–40%	Consider monitoring TPV level.

Table 15a. Drug Interactions between Protease Inhibitors (PI)* and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 9 of 10)

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Narcotics/Treatment for Opioid Dependence, continued			
Oxycodone	LPV/r	oxycodone AUC ↑ 2.6 fold	Monitor for opioid-related adverse effects. Oxycodone dose reduction may be necessary.
Methadone	**RTV-boosted PIs**		
	ATV/r, DRV/r, FPV/r, LPV/r, SQV/r, TPV/r	ATV/r, DRV/r, FPV/r ↓ R-methadone[d] AUC 16%–18%; LPV/r ↓ methadone AUC 26%–53%; SQV/r 1000/100 mg BID ↓ R-methadone[d] AUC 19%; TPV/r ↓ R-methadone[d] AUC 48%	Opioid withdrawal unlikely but may occur. Dosage adjustment of methadone is not usually required, but monitor for opioid withdrawal and increase methadone dose as clinically indicated.
	PIs without RTV		
	ATV	No significant effect	No dosage adjustment necessary.
	FPV	No data with unboosted FPV APV ↓ R-methadone[d] C_{min} 21%, AUC no significant change	Monitor and titrate methadone as clinically indicated. The interaction with FPV is presumed to be similar.
Phosphodiesterase Type 5 (PDE5) Inhibitors			
Avanafil	ATV, ATV/r, DRV/r, FPV/r, SQV/r, LPV/r	RTV (600 mg BID x 5 days) ↑ avanafil AUC 13-fold, C_{max} 2.4-fold	**Co-administration is not recommended.**
	FPV	No data	Avanafil dose should not exceed 50 mg once every 24 hours.
Sildenafil	All PIs	DRV/r + sildenafil 25 mg similar to sildenafil 100 mg alone; RTV 500 mg BID ↑ sildenafil AUC 1,000%; SQV unboosted ↑ sildenafil AUC 210%	For treatment of erectile dysfunction Start with sildenafil 25 mg every 48 hours and monitor for adverse effects of sildenafil. For treatment of PAH **Contraindicated**
Tadalafil	All PIs	RTV 200 mg BID ↑ tadalafil AUC 124%; TPV/r (1st dose) ↑ tadalafil AUC 133%; TPV/r steady state: no significant effect	For treatment of erectile dysfunction Start with tadalafil 5-mg dose and do not exceed a single dose of 10 mg every 72 hours. Monitor for adverse effects of tadalafil. For treatment of PAH *In patients on a PI >7 days:* Start with tadalafil 20 mg once daily and increase to 40 mg once daily based on tolerability. *In patients on tadalafil who require a PI:* Stop tadalafil ≥24 hours prior to PI initiation, restart 7 days after PI initiation at 20 mg once daily, and increase to 40 mg once daily based on tolerability. For treatment of benign prostatic hyperplasia Maximum recommended daily dose is 2.5 mg per day

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Phosphodiesterase Type 5 (PDE5) Inhibitors, continued			
Vardenafil	All PIs	RTV 600 mg BID ↑ vardenafil AUC 49-fold	Start with vardenafil 2.5 mg every 72 hours and monitor for adverse effects of vardenafil.
Miscellaneous Interactions			
Colchicine	All PIs	RTV 100 mg BID ↑ colchicine AUC 296%, C_{max} 184% With all PIs: significant ↑ in colchicine AUC expected	For treatment of gout flares Colchicine 0.6 mg x 1 dose, followed by 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. *With FPV without RTV:* 1.2 mg x 1 dose and no repeat dose for at least 3 days For prophylaxis of gout flares Colchicine 0.3 mg once daily or every other day *With FPV without RTV:* colchicine 0.3 mg BID or 0.6 mg once daily or 0.3 mg once daily For treatment of familial Mediterranean fever Do not exceed colchicine 0.6 mg once daily or 0.3 mg BID. *With FPV without RTV:* Do not exceed 1.2 mg once daily or 0.6 mg BID. **Do not co-administer in patients with hepatic or renal impairment.**
Salmeterol	All PIs	↑ salmeterol possible	**Do not co-administer** because of potential increased risk of salmeterol-associated cardiovascular events.
Atovaquone/ proguanil	ATV/r, LPV/r	ATV/r ↓ atovaquone AUC 46% and ↓ proguanil AUC 41% LPV/r ↓ atovaquone AUC 74% and ↓ proguanil AUC 38%	No dosage recommendation. Consider alternative drug for malaria prophylaxis, if possible.

[a] The following products contain at least 35 mcg of ethinyl estradiol combined with norethindrone or norgestimate (generic formulation may also be available): Ovcon 35, 50; Femcon Fe; Brevicon; Modicon; Ortho-Novum 1/35, 10/11, 7/7/7; Norinyl 1/35; Tri-Norinyl; Ortho-Cyclen; Ortho Tri-Cyclen.

[b] The following products contain no more than 30 mcg of ethinyl estradiol combined with norethindrone or norgestimate (generic formulation may also be available): Loestrin 1/20, 1.5/30; Loestrin Fe 1/20, 1.5/30; Loestrin 24 Fe; Ortho Tri-Cyclen Lo.

[c] Norbuprenorphine is an active metabolite of buprenorphine.

[d] R-methadone is the active form of methadone.

Acronyms: APV = amprenavir, ART = antiretroviral therapy, ARV = antiretroviral, ATV = atazanavir, ATV/r = atazanavir + ritonavir, AUC = area under the curve, BID = twice daily, CCB = calcium channel blocker, C_{max} = maximum plasma concentration, C_{min} = minimum plasma concentration, CNS = central nervous system, CrCl = creatinine clearance, CYP = cytochrome P, DRV = darunavir, DRV/r = darunavir + ritonavir, ECG = electrocardiogram, FDA = Food and Drug Administration, FPV = fosamprenavir (FPV is a pro-drug of APV), FPV/r = fosamprenavir + ritonavir, IDV = indinavir, INR = international normalized ratio, LPV = lopinavir, LPV/r = lopinavir + ritonavir, NFV = nelfinavir, PAH = pulmonary arterial hypertension, PDE5 = phosphodiesterase type 5, PI = protease inhibitor, PK = pharmacokinetic, PPI = proton pump inhibitor, RTV = ritonavir, SQV = saquinavir, SQV/r = saquinavir + ritonavir, TCA = tricyclic antidepressant, TDF = tenofovir disoproxil fumarate, TID = three times a day, TPV = tipranavir, TPV/r = tipranavir + ritonavir, VPA = valproic acid

Table 15b. Drug Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors* and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 1 of 7)

This table provides information relating to pharmacokinetic (PK) interactions between non-nucleoside reverse transcriptase inhibitors (NNRTIs) and non-antiretroviral (ARV) drugs. For interactions between ARV agents and for dosing recommendations, refer to Table 16b.

* Delavirdine (DLV) is not included in this table. Please refer to the DLV Food and Drug Administration package insert for information regarding drug interactions.

Concomitant Drug Class/Name	NNRTI[a]	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	RPV	↓ RPV expected when given simultaneously	Give antacids at least 2 hours before or at least 4 hours after RPV.
H2-Receptor Antagonists	RPV	↓ RPV	Give H2-receptor antagonists at least 12 hours before or at least 4 hours after RPV.
Proton Pump Inhibitors (PPI)	RPV	↓ RPV	**Contraindicated. Do not co-administer.**
Anticoagulants/Antiplatelets			
Warfarin	EFV, NVP	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
	ETR	↑ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
Clopidogrel	ETR	↓ activation of clopidogrel possible	ETR may prevent metabolism of clopidogrel (inactive) to its active metabolite. Avoid co-administration, if possible.
Anticonvulsants			
Carbamazepine Phenobarbital Phenytoin	EFV	carbamazepine + EFV: carbamazepine AUC ↓ 27% and EFV AUC ↓ 36% phenytoin + EFV: ↓ EFV and ↓ phenytoin possible	Monitor anticonvulsant and EFV levels or, if possible, use alternative anticonvulsant to those listed.
	ETR	↓ anticonvulsant and ETR possible	**Do not co-administer.** Consider alternative anticonvulsant.
	NVP	↓ anticonvulsant and NVP possible	Monitor anticonvulsant and NVP levels and virologic responses or consider alternative anticonvulsant.
	RPV	↓ RPV possible	**Contraindicated. Do not co-administer.** Consider alternative anticonvulsant.
Antidepressants			
Bupropion	EFV	bupropion AUC ↓ 55%	Titrate bupropion dose based on clinical response.
Paroxetine	EFV, ETR	No significant effect	No dosage adjustment necessary.
Sertraline	EFV	sertraline AUC ↓ 39%	Titrate sertraline dose based on clinical response.

Table 15b. Drug Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors* and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 2 of 7)

Concomitant Drug Class/Name	NNRTI[a]	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antifungals			
Fluconazole	EFV	No significant effect	No dosage adjustment necessary.
	ETR	ETR AUC ↑ 86%	No dosage adjustment necessary. Use with caution.
	NVP	NVP AUC ↑ 110%	Increased risk of hepatotoxicity possible with this combination. Monitor NVP toxicity or use alternative ARV agent.
	RPV	↑ RPV possible	No dosage adjustment necessary. Clinically monitor for breakthrough fungal infection (RPV 150 mg/day reduces ketoconazole exposure; no data on interaction with fluconazole).
Itraconazole	EFV	itraconazole and OH-itraconazole AUC, C_{max}, and C_{min} ↓ 35%–44%	Failure to achieve therapeutic itraconazole concentrations has been reported. Avoid this combination if possible. If co-administered, closely monitor itraconazole concentration and adjust dose accordingly.
	ETR	↓ itraconazole possible ↑ ETR possible	Dose adjustments for itraconazole may be necessary. Monitor itraconazole level and antifungal response.
	NVP	↓ itraconazole possible ↑ NVP possible	Avoid combination if possible. If co-administered, monitor itraconazole concentration and adjust dose accordingly.
	RPV	↑ RPV possible	No dosage adjustment necessary. Clinically monitor for breakthrough fungal infection. (RPV 150 mg/day reduces ketoconazole exposure; no data on interaction with itraconazole.)
Posaconazole	EFV	posaconazole AUC ↓ 50% ↔ EFV	Avoid concomitant use unless the benefit outweighs the risk. If co-administered, monitor posaconazole concentration and adjust dose accordingly.
	ETR	↑ ETR possible	No dosage adjustment necessary.
	RPV	↑ RPV possible	No dosage adjustment necessary. Clinically monitor for breakthrough fungal infection. (RPV 150 mg/day reduces ketoconazole exposure; no data on interaction with posaconazole.)

Table 15b. Drug Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors* and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 3 of 7)

Concomitant Drug Class/Name	NNRTI[a]	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antifungals, continued			
Voriconazole	EFV	voriconazole AUC ↓ 77% EFV AUC ↑ 44%	**Contraindicated at standard doses.** Dose: voriconazole 400 mg BID, EFV 300 mg daily.
	ETR	voriconazole AUC ↑ 14% ETR AUC ↑ 36%	No dosage adjustment necessary; use with caution. Consider monitoring voriconazole level.
	NVP	↓ voriconazole possible ↑ NVP possible	Monitor for toxicity and antifungal response and/or voriconazole level.
	RPV	↑ RPV possible	No dosage adjustment necessary. Clinically monitor for breakthrough fungal infection (RPV 150 mg/day reduces ketoconazole exposure; no data on interaction with voriconazole).
Antimycobacterials			
Clarithromycin	EFV	clarithromycin AUC ↓ 39%	Monitor for effectiveness or consider alternative agent, such as azithromycin, for MAC prophylaxis and treatment.
	ETR	clarithromycin AUC ↓ 39% ETR AUC ↑ 42%	Consider alternative agent, such as azithromycin, for MAC prophylaxis and treatment.
	NVP	clarithromycin AUC ↓ 31%	Monitor for effectiveness or use alternative agent, such as azithromycin, for MAC prophylaxis and treatment.
	RPV	↔ clarithromycin expected ↑ RPV possible	Consider alternative macrolide, such as azithromycin, for MAC prophylaxis and treatment.
Rifabutin	EFV	rifabutin ↓ 38%	Dose: rifabutin 450–600 mg once daily or 600 mg three times a week if EFV is not co-administered with a PI.
	ETR	rifabutin and metabolite AUC ↓ 17% ETR AUC ↓ 37%	**If ETR is used with an RTV-boosted PI, rifabutin should not be co-administered.** Dose: rifabutin 300 mg once daily **if** ETR is not co-administered with an RTV-boosted PI.
	NVP	rifabutin AUC ↑ 17% and metabolite AUC ↑ 24% NVP C_{min} ↓ 16%	No dosage adjustment necessary. Use with caution.
	RPV	RPV AUC ↓ 46%	**Contraindicated. Do not co-administer.**
Rifampin	EFV	EFV AUC ↓ 26%	Maintain EFV dose at 600 mg once daily and monitor for virologic response. Consider therapeutic drug monitoring. Some clinicians suggest EFV 800 mg dose in patients who weigh more than 60 kg.
	ETR	Significant ↓ ETR possible	**Do not co-administer.**
	NVP	NVP ↓ 20%–58%	**Do not co-administer.**
	RPV	RPV AUC ↓ 80%	**Contraindicated. Do not co-administer.**

Table 15b. Drug Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors* and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 4 of 7)

Concomitant Drug Class/Name	NNRTI[a]	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimycobacterials, continued			
Rifapentine	EFV, ETR, NVP, RPV	↓ NNRTI expected	**Do not co-administer.**
Benzodiazepines			
Alprazolam	EFV, ETR, NVP, RPV	No data	Monitor for therapeutic effectiveness of alprazolam.
Diazepam	ETR	↑ diazepam possible	Decreased dose of diazepam may be necessary.
Lorazepam	EFV	lorazepam C_{max} ↑ 16%, AUC ↔	No dosage adjustment necessary.
Midazolam	EFV	Significant ↑ midazolam expected	**Do not co-administer with oral midazolam.** Parenteral midazolam can be used with caution as a single dose and can be given in a monitored situation for procedural sedation.
Triazolam	EFV	Significant ↑ triazolam expected	**Do not co-administer.**
Cardiac Medications			
Dihydropyridine calcium channel blockers (CCBs)	EFV, NVP	↓ CCBs possible	Titrate CCB dose based on clinical response.
Diltiazem Verapamil	EFV	diltiazem AUC ↓ 69% ↓ verapamil possible	Titrate diltiazem or verapamil dose based on clinical response.
	NVP	↓ diltiazem or verapamil possible	
Corticosteroids			
Dexamethasone	EFV, ETR, NVP	↓ EFV, ETR, NVP possible	Consider alternative corticosteroid for long-term use. If dexamethasone is used with NNRTI, monitor virologic response.
	RPV	Significant ↓ RPV possible	**Contraindicated with more than a single dose of dexamethasone.**

Table 15b. Drug Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors* and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 5 of 7)

Concomitant Drug Class/Name	NNRTI[a]	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hepatitis C NS3/4A - Protease Inhibitors			
Boceprevir	EFV	EFV AUC ↑ 20% boceprevir AUC ↓ 19%, C_{min} ↓ 44%	**Co-administration is not recommended.**
	ETR	ETR AUC ↓ 23% boceprevir AUC, C_{max} ↑ 10%	No dosage adjustment necessary.
Telaprevir	EFV	EFV AUC ↔ telaprevir AUC ↓ 26%, C_{min} ↓ 47% With TDF: EFV AUC ↓ 15%–18%, telaprevir AUC ↓ 18%–20%	Increase telaprevir dose to 1125 mg q8h.
Herbal Products			
St. John's wort	EFV, ETR, NVP, RPV	↓ NNRTI	**Do not co-administer.**
Hormonal Contraceptives			
Hormonal contraceptives	EFV	ethinyl estradiol ↔ levonorgestrel AUC ↓ 83% norelgestromin AUC ↓ 64% ↓ etonogestrel (implant) possible	Use alternative or additional contraceptive methods. Norelgestromin and levonorgestrel are active metabolites of norgestimate.
	ETR	ethinyl estradiol AUC ↑ 22% norethindrone: no significant effect	No dosage adjustment necessary.
	NVP	ethinyl estradiol AUC ↓ 20% norethindrone AUC ↓ 19%	Use alternative or additional contraceptive methods.
		DMPA: no significant change	No dosage adjustment necessary.
	RPV	ethinyl estradiol AUC ↑ 14% norethindrone: no significant change	No dosage adjustment necessary.
Levonorgestrel (for emergency contraception)	EFV	levonorgestrel AUC ↓ 58%	Effectiveness of emergency post-coital contraception may be diminished.
HMG-CoA Reductase Inhibitors			
Atorvastatin	EFV, ETR	atorvastatin AUC ↓ 32%–43%	Adjust atorvastatin according to lipid responses, not to exceed the maximum recommended dose.
	RPV	atorvastatin AUC ↔ atorvastatin metabolites ↑	No dosage adjustment necessary.

Table 15b. Drug Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors* and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 6 of 7)

Concomitant Drug Class/Name	NNRTI[a]	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
HMG-CoA Reductase Inhibitors, continued			
Fluvastatin	ETR	↑ fluvastatin possible	Dose adjustments for fluvastatin may be necessary.
Lovastatin Simvastatin	EFV	simvastatin AUC ↓ 68%	Adjust simvastatin dose according to lipid responses, not to exceed the maximum recommended dose. If EFV used with RTV-boosted PI, simvastatin and lovastatin should be avoided.
	ETR, NVP	↓ lovastatin possible ↓ simvastatin possible	Adjust lovastatin or simvastatin dose according to lipid responses, not to exceed the maximum recommended dose. If ETR or NVP used with RTV-boosted PI, simvastatin and lovastatin should be avoided.
Pitavastatin	EFV, ETR, NVP, RPV	No data	No dosage recommendation.
Pravastatin Rosuvastatin	EFV	pravastatin AUC ↓ 44% rosuvatatin: no data	Adjust statin dose according to lipid responses, not to exceed the maximum recommended dose.
	ETR	No significant effect expected	No dosage adjustment necessary.
Immunosuppressants			
Cyclosporine Sirolimus Tacrolimus	EFV, ETR, NVP	↓ immunosuppressant possible	Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.
Narcotics/Treatment for Opioid Dependence			
Buprenorphine	EFV	buprenorphine AUC ↓ 50% norbuprenorphine[b] AUC ↓ 71%	No dosage adjustment recommended; monitor for withdrawal symptoms.
	ETR	buprenorphine AUC ↓ 25%	No dosage adjustment necessary.
	NVP	No significant effect	No dosage adjustment necessary.
Methadone	EFV	methadone AUC ↓ 52%	Opioid withdrawal common; increased methadone dose often necessary.
	ETR	No significant effect	No dosage adjustment necessary.
	NVP	methadone AUC ↓ 37%–51% NVP: no significant effect	Opioid withdrawal common; increased methadone dose often necessary.
	RPV	R-methadonec AUC ↓ 16%	No dosage adjustment necessary, but monitor for withdrawal symptoms.

Table 15b. Drug Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors* and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 7 of 7)

Concomitant Drug Class/Name	NNRTI[a]	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Phosphodiesterase Type 5 (PDE5) Inhibitors			
Avanafil	EFV, ETR, NVP, RPV	No data	**Co-administration is not recommended.**
Sildenafil	ETR	sildenafil AUC ↓ 57%	May need to increase sildenafil dose based on clinical effect.
	RPV	sildenafil ↔	No dosage adjustment necessary.
Tadalafil	ETR	↓ tadalafil possible	May need to increase tadalafil dose based on clinical effect.
Vardenafil	ETR	↓ vardenafil possible	May need to increase vardenafil dose based on clinical effect.
Miscellaneous Interactions			
Atovaquone/ proguanil	EFV	↓ atovaquone AUC 75% ↓ proguanil AUC 43%	No dosage recommendation. Consider alternative drug for malaria prophylaxis, if possible.

[a] Approved dose for RPV is 25 mg once daily. Most PK interaction studies were performed using 75 to 150 mg per dose.

[b] Norbuprenorphine is an active metabolite of buprenorphine.

[c] R-methadone is the active form of methadone.

Key to Abbreviations: ARV = antiretroviral, AUC = area under the curve, BID = twice daily, CCB = calcium channel blocker, C_{max} = maximum plasma concentration, C_{min} = minimum plasma concentration, DLV = delavirdine, DMPA = depot medroxyprogesterone acetate, EFV = efavirenz, ETR = etravirine, FDA = Food and Drug Administration, INR = international normalized ratio, MAC = *Mycobacterium avium* complex, NNRTI = non-nucleoside reverse transcriptase inhibitor, NVP = nevirapine, OH-clarithromycin = active metabolite of clarithromycin, PDE5 = phosphodiesterase type 5, PI = protease inhibitor, PPI = proton pump inhibitor, RPV = rilpivirine, RTV = ritonavir, TDF = tenofovir disoproxil fumarate

Table 15c. Drug Interactions between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated February 12, 2013; last reviewed February 12, 2013) (page 1 of 2)

Concomitant Drug Class/Name	NRTI	Effect on NRTI or Concomitant Drug Concentrations	Dosage Recommendations and Clinical Comments
Antivirals			
Adefovir	TDF	No data	**Do not co-administer.** Serum concentrations of TDF and/or other renally eliminated drugs may be increased.
Boceprevir	TDF	No significant PK effects	No dose adjustment necessary.
Ganciclovir **Valganciclovir**	TDF	No data	Serum concentrations of these drugs and/or TDF may be increased. Monitor for dose-related toxicities.
	ZDV	No significant PK effects	Potential increase in hematologic toxicities
Ribavirin	ddI	↑ intracellular ddI	**Contraindicated. Do not co-administer.** Fatal hepatic failure and other ddI-related toxicities have been reported with co-administration.
	ZDV	Ribavirin inhibits phosphorylation of ZDV.	Avoid co-administration if possible, or closely monitor virologic response and hematologic toxicities.
Telaprevir	TDF	TDF AUC ↑ 30%, C_{min} ↑ 6%–41%	Monitor for TDF-associated toxicity.
Integrase Inhibitor			
RAL	TDF	RAL AUC ↑ 49%, C_{max} ↑ 64%	No dosage adjustment necessary.
Narcotics/Treatment for Opioid Dependence			
Buprenorphine	3TC, ddI, TDF, ZDV	No significant effect	No dosage adjustment necessary.
Methadone	ABC	methadone clearance ↑ 22%	No dosage adjustment necessary.
	d4T	d4T AUC ↓ 23%, C_{max} ↓ 44%	No dosage adjustment necessary.
	ZDV	ZDV AUC ↑ 29%–43%	Monitor for ZDV-related adverse effects.
NRTIs			
ddI	d4T	No significant PK interaction	**Do not co-administer.** Additive toxicities of peripheral neuropathy, lactic acidosis, and pancreatitis seen with this combination.
	TDF	ddI-EC AUC and C_{max} ↑ 48%–60%	**Avoid co-administration.**
Other			
Allopurinol	ddI	ddI AUC ↑ 113% In patients with renal impairment: ddI AUC ↑ 312%	**Contraindicated.** Potential for increased ddI-associated toxicities.

Table 15c. Drug Interactions between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated February 12, 2013; last reviewed February 12, 2013) (page 2 of 2)

Concomitant Drug Class/Name	NRTI	Effect on NRTI or Concomitant Drug Concentrations	Dosage Recommendations and Clinical Comments
PIs			
ATV	ddI	With ddI-EC + ATV (with food): ddI AUC ↓ 34%; ATV no change	Administer ATV with food 2 hours before or 1 hour after ddI.
	TDF	ATV AUC ↓ 25% and C_{min} ↓ 23%–40% (higher C_{min} with RTV than without RTV) TDF AUC ↑ 24%–37%	Dose: ATV/r 300/100 mg daily co-administered with TDF 300 mg daily. Avoid concomitant use without RTV. If using TDF and H2 receptor antagonist in ART-experienced patients, use ATV/r 400 mg/100 mg daily. Monitor for TDF-associated toxicity.
	ZDV	ZDV C_{min} ↓ 30%, no change in AUC	Clinical significance unknown.
DRV/r	TDF	TDF AUC ↑ 22%, C_{max} ↑ 24%, and C_{min} ↑ 37%	Clinical significance unknown. Monitor for TDF toxicity.
LPV/r	TDF	LPV/r AUC ↓ 15% TDF AUC ↑ 34%	Clinical significance unknown. Monitor for TDF toxicity.
TPV/r	ABC	ABC AUC ↓ 35%–44%	Appropriate doses for this combination have not been established.
	ddI	ddI-EC AUC ↔ and C_{min} ↓ 34% TPV/r ↔	Separate doses by at least 2 hours.
	TDF	TDF AUC ↔ TPV/r AUC ↓ 9%–18% and C_{min} ↓ 12%–21%	No dosage adjustment necessary.
	ZDV	ZDV AUC ↓ 35% TPV/r AUC ↓ 31%–43%	Appropriate doses for this combination have not been established.

Key to Abbreviations: 3TC = lamivudine, ABC = abacavir, ART = antiretroviral, ATV = atazanavir, ATV/r = atazanavir/ritonavir, AUC = area under the curve, C_{max} = maximum plasma concentration, C_{min} = minimum plasma concentration, d4T = stavudine, ddI = didanosine, DRV/r = darunavir/ritonavir, EC = enteric coated, LPV/r = lopinavir/ritonavir, NRTI = nucleoside reverse transcriptase inhibitor, PI = protease inhibitor, PK = pharmacokinetic, RAL = raltegravir, TDF = tenofovir, TPV/r = tipranavir/ritonavir, ZDV = zidovudine

Table 15d. Drug Interactions between Integrase Inhibitors and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 1 of 6)

Raltegravir (RAL) is expected to have fewer drug interactions than elvitegravir/cobicistat (EVG/COBI) (see Drug Interactions text). In the following table, where RAL is not listed, no data currently exists and there is either no dosage recommendation or no dosage adjustment is necessary when RAL is used with the concomitant medication.

Concomitant Drug Class/Name	Integrase Inhibitor	Effect on Integrase Inhibitor or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	EVG/COBI/TDF/FTC	EVG AUC ↓ 15%–20% if given 2 hours before or after antacid; ↔ with 4-hour interval	Separate EVG/COBI/FTC/TDF and antacid administration by more than 2 hours
H2-Receptor Antagonists	EVG/COBI/TDF/FTC	No significant effect	No dosage adjustment necessary.
Proton Pump Inhibitors	EVG/COBI/TDF/FTC	No significant effect	No dosage adjustment necessary.
	RAL	RAL AUC ↑ 212%, C_{max} ↑ 315%, and C_{min} ↑ 46%	No dosage adjustment necessary.
Anticoagulants			
Warfarin	EVG/COBI/TDF/FTC	No data: but warfarin levels may be affected	Monitor INR and adjust warfarin dose accordingly.
Anticonvulsants			
Carbamazepine **Oxcarbazepine** **Phenobarbital** **Phenytoin**	EVG/COBI/TDF/FTC	↑ carbamazepine possible ↓ EVG possible ↓ COBI possible	Consider alternative anticonvulsant.
Ethosuximide	EVG/COBI/TDF/FTC	↑ ethosuximide possible	Clinically monitor for ethosuxamide toxicities.
Antidepressants			
Selective Serotonin Reuptake Inhibitors (SSRIs)	EVG/COBI/TDF/FTC	↑ SSRI possible	Initiate with lowest dose of SSRI and titrate dose carefully based on antidepressant response.
Tricyclic Antidepressants (TCAs) **Amitriptyline** **Desipramine** **Imipramine** **Nortriptyline**	EVG/COBI/TDF/FTC	Desipramine AUC ↑ 65%	Initiate with lowest dose and titrate dose of TCA carefully.
Trazodone	EVG/COBI/TDF/FTC	↑ trazodone possible	Initiate with lowest dose and titrate dose of trazodone carefully.

Table 15d. Drug Interactions between Integrase Inhibitors and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 2 of 6)

Concomitant Drug Class/Name	Integrase Inhibitor	Effect on Integrase Inhibitor or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antifungals			
Itraconazole	EVG/COBI/TDF/FTC	↑ itraconazole expected ↑ EVG and COBI possible	Consider monitoring itraconazole level to guide dosage adjustments. High doses (>200 mg/day) are not recommended unless dose is guided by itraconazole levels.
Posaconazole	EVG/COBI/TDF/FTC	↑EVG and COBI possible ↑ posaconazole possible	Monitor posaconazole concentrations with co-administration.
Voriconazole	EVG/COBI/TDF/FTC	↑ voriconazole expected ↑ EVG and COBI possible	Risk/benefit ratio should be assessed to justify use of voriconazole. If administered, consider monitoring voriconazole level. Adjust dose accordingly.
Antimycobacterials			
Clarithromycin	EVG/COBI/TDF/FTC	↑ clarithromycin possible ↑ COBI possible	CrCl ≥60 mL/min: No dose adjustment necessary CrCl 50–60 mL/min: Reduce clarithromycin dose by 50% CrCl <50 mL/min: EVG/COBI/TDF/FTC is not recommended.
Rifabutin	EVG/COBI/TDF/FTC	Rifabutin (150 mg every other day): No significant change in rifabutin AUC; For 25-O-desacetyl-rifabutin, AUC ↑ 625% compared with rifabutin (300 mg daily) administered alone EVG AUC ↓ 21%, C_{min} ↓ 67%	**Do not co-administer.**
	RAL	RAL AUC ↑ 19%, C_{max} ↑ 39%, and C_{min} ↓ 20%	No dosage adjustment necessary.
Rifampin	EVG/COBI/TDF/FTC	Significant ↓ EVG and COBI expected	**Do not co-administer.**
	RAL	RAL 400 mg: RAL AUC ↓ 40% and C_{min} ↓ 61% Rifampin with RAL 800 mg BID compared with RAL 400 mg BID alone: RAL AUC ↑ 27% and C_{min} ↓ 53%	Dose: RAL 800 mg BID Monitor closely for virologic response or consider using rifabutin as an alternative rifamycin
Rifapentine	EVG/COBI/TDF/FTC	Significant ↓ EVG and COBI expected	**Do not co-administer.**
Benzodiazepines			
Clonazepam **Clorazepate** **Diazepam** **Estazolam** **Flurazepam**	EVG/COBI/TDF/FTC	↑ benzodiazepines possible	Dose reduction of benzodiazepine may be necessary. Initiate with low dose and clinically monitor. Consider alternative benzodiazepines to diazepam, such as lorazepam, oxazepam, or temazepam.
Midazolam **Triazolam**	EVG/COBI/TDF/FTC	↑ midazolam expected ↑ triazolam expected	Do not co-administer triazolam or oral midazolam and EVG/COBI. Parenteral midazolam can be used with caution in a closely monitored setting. Consider dose reduction, especially if >1 dose is administered.

Table 15d. Drug Interactions between Integrase Inhibitors and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 3 of 6)

Concomitant Drug Class/Name	Integrase Inhibitor	Effect on Integrase Inhibitor or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cardiac Medications			
Anti-Arrhythmics (amiodarone, bepridil, digoxin, disopyramide, dronedarone, flecainide, systemic lidocaine, mexilitine, propafenone, quinidine)	EVG/COBI/TDF/FTC	↑ anti-arrhythmics possible digoxin C_{max} ↑ 41%, AUC no significant change	Use anti-arrhythmics with caution. Therapeutic drug monitoring, if available, is recommended for anti-arrhythmics.
Bosentan	EVG/COBI/TDF/FTC	↑ bosentan possible	In patients on EVG/COBI/FTC/TDF ≥10 days: start bosentan at 62.5 mg once daily or every other day based on individual tolerability. In patients on bosentan who require EVG/COBI/FTC/TDF: stop bosentan ≥36 hours before EVG/COBI/FTC/TDF initiation. After at least 10 days following initiation of EVG/COBI/FTC/TDF, resume bosentan at 62.5 mg once daily or every other day based on individual tolerability.
Beta-blockers	EVG/COBI/TDF/FTC	↑ beta-blockers possible	Adjust beta-blockers according to clinical response. Beta-blocker dose may need to be decreased. Some beta-blockers are metabolized via CYP450 pathway (e.g., metoprolol, timolol). Consider using other beta-blockers (e.g., atenolol, labetalol, nadolol, sotalol) as these agents are not metabolized by CYP450 enzymes.
Dihydropyridine and Non-Dihydropyridine Calcium Channel Blockers	EVG/COBI/TDF/FTC	↑ CCBs possible	Co-administer with caution. Monitor for CCB efficacy and toxicities.
Corticosteroids			
Dexamethasone	EVG/COBI/TDF/FTC	↓ EVG and COBI possible	Co-administer with caution, monitor HIV virologic response
Fluticasone (inhaled/intranasal)	EVG/COBI/TDF/FTC	↑ fluticasone possible	Use alternative inhaled corticosteroid, particularly for long-term use
Hepatitis C NS3/4A—Protease Inhibitors			
Boceprevir	EVG/COBI/TDF/FTC	No data	**Do not co-administer.**
	RAL	No significant effect	No dosage adjustment necessary.
Telaprevir	EVG/COBI/TDF/FTC	No data	**Do not co-administer.**
	RAL	RAL AUC ↑ 31% Telaprevir ↔	No dosage adjustment necessary.

Table 15d. Drug Interactions between Integrase Inhibitors and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 4 of 6)

Concomitant Drug Class/Name	Integrase Inhibitor	Effect on Integrase Inhibitor or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Contraceptives			
Hormonal contraceptives	RAL	No clinically significant effect	Safe to use in combination
Norgestimate/ethinyl estradiol	EVG/COBI/TDF/FTC	Norgestimate AUC, C_{max}, C_{min} ↑ > 2-fold Ethinyl estradiol AUC ↓ 25%, C_{min} ↓ 44%	The effects of increases in progestin (norgestimate) are not fully known and can include insulin resistance, dyslipidemia, acne, and venous thrombosis. Weigh the risks and benefits of the drug, and consider alternative contraceptive method.
HMG-CoA Reductase Inhibitors			
Atorvastatin	EVG/COBI/TDF/FTC	↑ atorvastatin possible	Titrate statin dose slowly and use the lowest dose possible.
Lovastatin	EVG/COBI/TDF/FTC	Significant ↑ lovastatin expected	**Contraindicated. Do not co-administer.**
Pitavastatin **Pravastatin**	EVG/COBI/TDF/FTC	No data	No dosage recommendation
Rosuvastatin	EVG/COBI/TDF/FTC	Rosuvastatin AUC ↑ 38% and C_{max} ↑ 89%	Titrate statin dose slowly and use the lowest dose possible.
Simvastatin	EVG/COBI/TDF/FTC	Significant ↑ simvastatin expected	**Contraindicated. Do not co-administer.**
Immunosuppressants			
Cyclosporine **Sirolimus** **Tacrolimus**	EVG/COBI/TDF/FTC	↑ immunosuppressant possible	Initiate with an adjusted immunosuppressant dose to account for potential increased concentrations and monitor for toxicities. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.
Narcotics/Treatment for Opioid Dependence			
Buprenorphine	EVG/COBI/TDF/FTC	Buprenorphine: AUC ↑ 35%, C_{max} ↑ 12%, C_{min} ↑ 66% Norbuprenorphine: AUC ↑ 42%, C_{max} ↑ 24%, C_{min} ↑ 57%	No dosage adjustment necessary. Clinical monitoring is recommended.
	RAL	No significant effect	No dosage adjustment necessary.
Methadone	EVG/COBI/TDF/FTC	No significant effect	No dosage adjustment necessary.
	RAL	No significant effect	No dosage adjustment necessary.
Neuroleptics			
Perphenazine **Risperidone** **Thioridazine**	EVG/COBI/TDF/FTC	↑ neuroleptic possible	Initiate neuroleptic at a low dose. Decrease in neuroleptic dose may be necessary.

Table 15d. Drug Interactions between Integrase Inhibitors and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 5 of 6)

Concomitant Drug Class/Name	Integrase Inhibitor	Effect on Integrase Inhibitor or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Phosphodiesterase Type 5 (PDE5) Inhibitors			
Avanafil	EVG/COBI/TDF/FTC	No data	**Co-administration is not recommended.**
Sildenafil	EVG/COBI/TDF/FTC	↑ sildenafil expected	For treatment of erectile dysfunction: Start with sildenafil 25 mg every 48 hours and monitor for adverse effects of sildenafil. For treatment of PAH: **Contraindicated**
Tadalafil	EVG/COBI/TDF/FTC	↑ tadalafil expected	For treatment of erectile dysfunction: Start with tadalafil 5-mg dose and do not exceed a single dose of 10 mg every 72 hours. Monitor for adverse effects of tadalafil. For treatment of PAH: *In patients on a EVG/COBI >7 days:* Start with tadalafil 20 mg once daily and increase to 40 mg once daily based on tolerability. *In patients on tadalafil who require EVG/COBI:* Stop tadalafil ≥24 hours before EVG/COBI initiation. Seven days after EVG/COBI initiation restart tadalafil at 20 mg once daily, and increase to 40 mg once daily based on tolerability.
Vardenafil	EVG/COBI/TDF/FTC	↑ vardenafil expected	Start with vardenafil 2.5 mg every 72 hours and monitor for adverse effects of vardenafil.
Sedatives/Hypnotics			
Buspirone	EVG/COBI/TDF/FTC	↑ buspirone possible	Initiate buspirone at a low dose. Dose reduction may be necessary.
Zolpidem	EVG/COBI/TDF/FTC	↑ zolpidem possible	Initiate zolpidem at a low dose. Dose reduction may be necessary.

Table 15d. Drug Interactions between Integrase Inhibitors and Other Drugs (Last updated February 12, 2013; last reviewed February 12, 2013) (page 6 of 6)

Concomitant Drug Class/Name	Integrase Inhibitor	Effect on Integrase Inhibitor or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Miscellaneous Interactions			
Colchicine	EVG/COBI/TDF/FTC	↑ colchicine expected	**Do not co-administer in patients with hepatic or renal impairment.** For treatment of gout flares: Colchicine 0.6 mg x 1 dose, followed by 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. For prophylaxis of gout flares: If original regimen was colchicine 0.6 mg BID, the regimen should be decreased to 0.3 mg once daily. If regimen was 0.6 mg once daily, the regimen should be decreased to 0.3 mg every other day. For treatment of familial Mediterranean fever: Do not exceed colchicine 0.6 mg once daily or 0.3 mg BID.
Salmeterol	EVG/COBI/TDF/FTC	↑ salmeterol possible	**Do not co-administer** because of potential increased risk of salmeterol-associated cardiovascular events.

Key to Abbreviations: AUC = area under the curve, BID = twice daily, CCB = calcium channel blocker, COBI = cobicistat, C_{max} = maximum plasma concentration, C_{min} = minimum plasma concentration, EVG = elvitegravir, PAH = pulmonary arterial hypertension, RAL = raltegravir

Table 15e. Drug Interactions between CCR5 Antagonist and Other Drugs (Last updated March 27, 2012; last reviewed February 12, 2013)

This table provides information relating to pharmacokinetic (PK) interactions between maraviroc (MVC) and non-antiretroviral (ARV) drugs. For interactions between ARV agents and for dosing recommendations, please refer to Table 16b.

Concomitant Drug Class/Name	CCR5 Antagonist	Effect on CCR5 Antagonist or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticonvulsants			
Carbamazepine **Phenobarbital** **Phenytoin**	MVC	↓ MVC possible	If used without a strong CYP3A inhibitor, use MVC 600 mg BID or an alternative antiepileptic agent.
Antifungals			
Itraconazole	MVC	↑ MVC possible	Dose: MVC 150 mg BID
Ketoconazole	MVC	MVC AUC ↑ 400%	Dose: MVC 150 mg BID
Voriconazole	MVC	↑ MVC possible	Consider dose reduction to MVC 150 mg BID
Antimycobacterials			
Clarithromycin	MVC	↑ MVC possible	Dose: MVC 150 mg BID
Rifabutin	MVC	↓ MVC possible	If used without a strong CYP3A inducer or inhibitor, use MVC 300 mg BID. If used with a strong CYP3A inhibitor, use MVC 150 mg BID.
Rifampin	MVC	MVC AUC ↓ 64%	**Co-administration is not recommended.** If co-administration is necessary, use MVC 600 mg BID. If co-administered with a strong CYP3A inhibitor, use MVC 300 mg BID.
Rifapentine	MVC	↓ MVC expected	**Do not co-administer.**
Herbal Products			
St. John's wort	MVC	↓ MVC possible	**Co-administration is not recommended.**
Hormonal Contraceptives			
Hormonal contraceptives	MVC	No significant effect on ethinyl estradiol or levonorgestrel	Safe to use in combination

Key to Abbreviations: ARV = antiretroviral, AUC = area under the curve, BID = twice daily, CYP = cytochrome P, MVC = maraviroc, PK = pharmacokinetic

Table 16a. Interactions Between Protease Inhibitors* (Last updated February 12, 2013; last reviewed February 12, 2013)

* Nelfinavir (NFV) and indinavir (IDV) are not included in this table. Refer to the NFV and IDV Food and Drug Administration package inserts for information regarding drug interactions.

Drug Affected	ATV	FPV	LPV/r	RTV	SQV	TPV
DRV	Dose: ATV 300 mg once daily + DRV 600 mg BID + RTV 100 mg BID	No data	**Should not be co-administered because doses are not established**	Dose: (DRV 600 mg + RTV 100 mg) BID or (DRV 800 mg + RTV 100 mg) once daily	**Should not be co-administered because doses are not established**	No data
FPV	Dose: Insufficient data	•	**Should not be co-administered because doses are not established**	Dose: (FPV 1400 mg + RTV [100 mg or 200 mg]) once daily or (FPV 700 mg + RTV 100 mg) BID	Dose: Insufficient data	**Should not be co-administered because doses are not established**
LPV/r	Dose: ATV 300 mg once daily + LPV/r 400/100 mg BID	**Should not be co-administered because doses are not established**	•	LPV is co-formulated with RTV and marketed as Kaletra.	Dose: SQV 1000 mg BID + LPV/r 400/100 mg BID	**Should not be co-administered because doses are not established**
RTV	Dose: (ATV 300 mg + RTV 100 mg) once daily	Dose: (FPV 1400 mg + RTV [100 mg or 200 mg]) once daily or (FPV 700 mg + RTV 100 mg) BID	LPV is co-formulated with RTV and marketed as Kaletra.	•	Dose: (SQV 1000 mg + RTV 100 mg) BID	Dose: (TPV 500 mg + RTV 200 mg) BID
SQV	Dose: Insufficient data	Dose: Insufficient data	Dose: SQV 1000 mg BID + LPV/r 400/100 mg BID	Dose: (SQV 1000 mg + RTV 100 mg) BID	•	**Should not be co-administered because doses are not established**

Key to Abbreviations: ATV = atazanavir, BID = twice daily, DRV = darunavir, FDA = Food and Drug Administration, FPV = fosamprenavir, IDV = indinavir, LPV/r = lopinavir/ritonavir, NFV = nelfinavir, PI = protease inhibitor, RTV = ritonavir, SQV = saquinavir, TPV = tipranavir

Table 16b. Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors* (Last updated March 27, 2012; last reviewed February 2013) (page 1 of 3)

* Delavirdine (DLV), indinavir (IDV), and nelfinavir (NFV) are not included in this table. Refer to the DLV, IDV, and NFV Food and Drug Administration package inserts for information regarding drug interactions.

		EFV	ETR	NVP	RPV[a]
ATV +/- RTV	**PK data**	With unboosted ATV ATV: AUC ↓ 74% EFV: no significant change With (ATV 300 mg + RTV 100 mg) once daily with food ATV concentrations similar to those with unboosted ATV without EFV	With unboosted ATV ETR: AUC ↑ 50%, C_{max} ↑ 47%, and C_{min} ↑ 58% ATV: AUC ↓ 17% and C_{min} ↓ 47% With (ATV 300 mg + RTV 100 mg) once daily ETR: AUC, C_{max}, and C_{min} ↑ approximately 30% ATV: AUC ↓ 14% and C_{min} ↓ 38%	With (ATV 300 mg + RTV 100 mg) once daily ATV: AUC ↓ 42% and C_{min} ↓ 72% NVP: AUC ↑ 25%	With boosted and unboosted ATV ↑ RPV possible
	Dose	**Do not co-administer with unboosted ATV.** In ART-naive patients (ATV 400 mg + RTV 100 mg) once daily **Do not co-administer in ART-experienced patients.**	**Do not co-administer with ATV +/– RTV.**	**Do not co-administer with ATV +/– RTV.**	Standard
DRV (always use with RTV)	**PK data**	With (DRV 300 mg + RTV 100 mg) BID DRV: AUC ↓ 13%, C_{min} ↓ 31% EFV: AUC ↑ 21%	ETR 100 mg BID with (DRV 600 mg + RTV 100 mg) BID DRV: no significant change ETR: AUC ↓ 37%, C_{min} ↓ 49%	With (DRV 400 mg + RTV 100 mg) BID DRV: AUC ↑ 24%[b] NVP: AUC ↑ 27% and C_{min} ↑ 47%	RPV 150 mg once daily with (DRV 800 mg + RTV 100 mg) once daily DRV: no significant change RPV: AUC ↑ 130% and C_{min} ↑ 178%
	Dose	Clinical significance unknown. Use standard doses and monitor patient closely. Consider monitoring drug levels.	Standard (ETR 200 mg BID). Safety and efficacy of this combination, despite decreased ETR concentration, have been established in a clinical trial.	Standard	Standard
EFV	**PK data**	•	↓ ETR possible	NVP: no significant change EFV: AUC ↓ 22%	↓ RPV possible
	Dose		**Do not co-administer.**	**Do not co-administer.**	**Do not co-administer.**
ETR	**PK data**	↓ ETR possible	•	↓ ETR possible	↓ RPV possible
	Dose	**Do not co-administer.**		**Do not co-administer.**	**Do not co-administer.**

Table 16b. Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors, and Protease Inhibitors* (Last updated March 27, 2012; last reviewed February 2013) (page 2 of 3)

		EFV	ETR	NVP	RPV[a]
FPV	**PK data**	With (FPV 1400 mg + RTV 200 mg) once daily APV: C_{min} ↓ 36%	With (FPV 700 mg + RTV 100 mg) BID APV: AUC ↑ 69%, C_{min} ↑ 77%	With unboosted FPV 1400 mg BID APV: AUC ↓ 33% NVP: AUC ↑ 29% With (FPV 700 mg + RTV 100 mg) BID NVP: C_{min} ↑ 22%	With boosted and unboosted FPV ↑ RPV possible
	Dose	(FPV 1400 mg + RTV 300 mg) once daily or (FPV 700 mg + RTV 100 mg) BID EFV standard	**Do not co-administer with FPV +/– RTV.**	(FPV 700 mg + RTV 100 mg) BID NVP standard	Standard
LPV/r	**PK data**	With LPV/r tablets 500/125 mg BID[c] + EFV 600 mg LPV levels similar to LPV/r 400/100 mg BID without EFV	With LPV/r tablets ETR: AUC ↓ 35% (comparable to the decrease with DRV/r) LPV: AUC↓ 13%	With LPV/r capsules LPV: AUC ↓ 27% and C_{min} ↓51%	RPV 150 mg once daily with LPV/r capsules LPV: no significant change RPV: AUC ↑ 52% and C_{min} ↑ 74%
	Dose	LPV/r tablets 500/125 mg[c] BID; LPV/r oral solution 533/133 mg BID EFV standard	Standard	LPV/r tablets 500/125 mg[c] BID; LPV/r oral solution 533/133 mg BID NVP standard	Standard
NVP	**PK data**	NVP: no significant change EFV: AUC ↓ 22%	↓ ETR possible	•	↓ RPV possible
	Dose	**Do not co-administer.**	**Do not co-administer.**		**Do not co-administer.**
RPV	**PK data**	↓ RPV possible	↓ RPV possible	↓ RPV possible	•
	Dose	**Do not co-administer.**	**Do not co-administer.**	**Do not co-administer.**	
RTV	**PK data** **Dose**	Refer to information for boosted PI.	Refer to information for boosted PI.	Refer to information for boosted PI.	Refer to information for boosted PI.
SQV (always use with RTV)	**PK data**	With SQV 1200 mg TID SQV: AUC ↓ 62% EFV: AUC ↓ 12%	With (SQV 1000 mg + RTV 100 mg) BID SQV: AUC unchanged ETR: AUC ↓ 33%, C_{min} ↓ 29% Reduced ETR levels similar to reduction with DRV/r	With 600 mg TID SQV: AUC ↓ 24% NVP: no significant change	↑ RPV possible
	Dose	(SQV 1000 mg + RTV 100 mg) BID	(SQV 1000 mg + RTV 100 mg) BID	Dose with SQV/r not established	Standard

Table 16b. Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors, and Protease Inhibitors* (Last updated March 27, 2012; last reviewed February 2013) (page 3 of 3)

		EFV	ETR	NVP	RPV[a]
TPV (always use with RTV)	**PK data**	With (TPV 500 mg + RTV 100 mg) BID TPV: AUC ↓ 31%, C_{min} ↓ 42% EFV: no significant change With (TPV 750 mg + RTV 200 mg) BID TPV: no significant change EFV: no significant change	With (TPV 500 mg + RTV 200 mg) BID ETR: AUC ↓ 76%, C_{min} ↓ 82% TPV: AUC ↑ 18%, C_{min} ↑ 24%	With (TPV 250 mg + RTV 200 mg) BID and with (TPV 750 mg + RTV 100 mg) BID NVP: no significant change TPV: no data	↑ RPV possible
	Dose	Standard	**Do not co-administer.**	Standard	Standard

[a] Approved dose for RPV is 25 mg once daily. Most PK interaction studies were performed using 75 mg to 150 mg per dose.

[b] Based on between-study comparison.

[c] Use a combination of two LPV/r 200 mg/50 mg tablets + one LPV/r 100 mg/25 mg tablet to make a total dose of LPV/r 500 mg/125 mg.

Key to Abbreviations: APV = amprenavir, ART = antiretroviral therapy, ATV = atazanavir, AUC = area under the curve, BID = twice daily, C_{max} = maximum plasma concentration, C_{min} = minimum plasma concentration, CYP = cytochrome P, DLV = delavirdine, DRV = darunavir, DRV/r = darunavir/ritonavir, EFV = efavirenz, ETR = etravirine, FDA = Food and Drug Administration, FPV = fosamprenavir, IDV = indinavir, LPV = lopinavir, LPV/r = lopinavir/ritonavir, MVC = maraviroc, NFV = nelfinavir, NVP = nevirapine, PI = protease inhibitor, PK = pharmacokinetic, RAL = raltegravir, RPV = rilpivirine, RTV = ritonavir, SQV = saquinavir, SQV/r = saquinavir/ritonavir, TID = three times a day, TPV = tipranavir

Table 16c. Interactions between Integrase Inhibitors or Maraviroc and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors* (Last updated February 12, 2013; last reviewed February 12, 2013) (page 1 of 2)

* Delavirdine (DLV), indinavir (IDV), and nelfinavir (NFV) are not included in this table. Refer to the DLV, IDV, and NFV Food and Drug Administration package inserts for information regarding drug interactions.

		EVG/COBI/TDF/FTC	RAL	MVC
ATV +/- RTV	**PK Data**	↑ or ↓ EVG, COBI, ATV possible	With unboosted ATV RAL: AUC ↑ 72% With (ATV 300 mg + RTV 100 mg) once daily RAL: AUC ↑ 41%	With unboosted ATV MVC: AUC ↑ 257% With (ATV 300 mg + RTV 100 mg) once daily MVC: AUC ↑ 388%
	Dose	**Do not co-administer.**	Standard	MVC 150 mg BID with ATV +/– RTV
DRV (always use with RTV)	**PK Data**	↑ or ↓ EVG, COBI, DRV possible	With (DRV 600 mg + RTV 100 mg) BID RAL: AUC ↓ 29% and C_{min} ↑ 38%	With (DRV 600 mg + RTV 100 mg) BID MVC: AUC ↑ 305% With (DRV 600 mg + RTV 100 mg) BID + ETR MVC: AUC ↑ 210%
	Dose	**Do not co-administer.**	Standard	MVC 150 mg BID
EFV	**PK Data**	↑ or ↓ EVG, COBI, EFV possible	EFV: AUC ↓ 36%	MVC: AUC ↓ 45%
	Dose	**Do not co-administer.**	Standard	MVC 600 mg BID
EVG/COBI/TDF/FTC	**PK Data**	•	No data	↑ MVC possible
	Dose		**Do not co-administer.**	**Do not co-administer.**
ETR	**PK Data**	↑ or ↓ EVG, COBI, ETR possible	ETR: C_{min} ↓ 17% RAL: C_{min} ↓ 34%	MVC: AUC ↓ 53%, C_{max} ↓ 60%
	Dose	**Do not co-administer.**	Standard	MVC 600 mg BID in the absence of a potent CYP3A inhibitor
FPV	**PK Data**	↑ or ↓ EVG, COBI, FPV possible	No significant effect	Unknown; ↑ MVC possible
	Dose	**Do not co-administer.**	Standard	MVC 150 mg BID
LPV/r	**PK Data**	↑ or ↓ EVG, COBI, LPV possible RTV and COBI have similar effects on CYP3A.	↓ RAL ↔ LPV/r	MVC: AUC ↑ 295% With LPV/r + EFV MVC: AUC ↑ 153%
	Dose	**Do not co-administer.**	Standard	MVC 150 mg BID
NVP	**PK Data**	↑ or ↓ EVG, COBI, NVP possible	No data	MVC: AUC ↔ and C_{max} ↑ 54%
	Dose	**Do not co-administer.**	Standard	Without PI MVC 300 mg BID With PI (except TPV/r) MVC 150 mg BID

Table 16c. Interactions between Integrase Inhibitors or Maraviroc and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors* (Last updated February 12, 2013; last reviewed February 12, 2013) (page 2 of 2)

		EVG/COBI/TDF/FTC	RAL	MVC
RAL	**PK Data**	No data	•	RAL: AUC ↓ 37% MVC: AUC ↓ 21%
	Dose	**Do not co-administer.**		Standard
RPV	**PK Data**	↑ or ↓ EVG, COBI, RPV possible	No data	No data
	Dose	**Do not co-administer.**	No data	No data
RTV	**PK Data**	↑ or ↓ EVG, COBI possible RTV and COBI have similar effects on CYP3A.	With RTV 100 mg BID RAL: AUC ↓ 16%	With RTV 100 mg BID MVC: AUC ↑ 161%
	Dose	**Do not co-administer.**	Standard	MVC 150 mg BID
SQV (always use with RTV)	**PK Data**	↑ or ↓ EVG, COBI, SQV possible RTV and COBI have similar effects on CYP3A.	No data	With (SQV 1000 mg + RTV 100 mg) BID MVC: AUC ↑ 877% With (SQV 1000 mg + RTV 100 mg) BID + EFV MVC: AUC ↑ 400%
	Dose	**Do not co-administer.**	Standard	MVC 150 mg BID
TPV (always use with RTV)	**PK Data**	↑ or ↓ EVG, COBI, TPV possible RTV and COBI have similar effects on CYP3A.	With (TPV 500 mg + RTV 200 mg) BID RAL: AUC ↓ 24%	With (TPV 500 mg + RTV 200 mg) BID MVC: No significant change in AUC TPV: No data
	Dose	**Do not co-administer.**	Standard	MVC 300 mg BID

Key to Abbreviations: APV = amprenavir, ART = antiretroviral therapy, ATV = atazanavir, AUC = area under the curve, BID = twice daily, COBI = cobicistat, C_{max} = maximum plasma concentration, C_{min} = minimum plasma concentration, CYP = cytochrome P, DLV = delavirdine, DRV = darunavir, DRV/r = darunavir/ritonavir, EFV = efavirenz, EVG = elvitegravir, ETR = etravirine, FDA = Food and Drug Administration, FPV = fosamprenavir, IDV = indinavir, LPV = lopinavir, LPV/r = lopinavir/ritonavir, MVC = maraviroc, NFV = nelfinavir, NVP = nevirapine, PI = protease inhibitor, PK = pharmacokinetic, RAL = raltegravir, RPV = rilpivirine, RTV = ritonavir, SQV = saquinavir, SQV/r = saquinavir/ritonavir, TID = three times a day, TPV = tipranavir