

Table 22a. Drug Interactions Among Antiretrovirals and Other Drugs: PIs and Maraviroc

Page 1 of 6

(Updated **January 29, 2008**)

Drug Interactions Requiring Dose Modifications or Cautious Use		
Drugs Affected	Atazanavir (ATV)	Fosamprenavir (FPV)
ANTIFUNGALS		
Itraconazole	No data, but potential for bi-directional inhibition between itraconazole and PIs, monitor for toxicities.	No data, but potential for bi-directional inhibition between itraconazole and PIs, monitor for toxicities. Dose: Dose adjustment for patients receiving >400mg/day may be needed.
Ketoconazole	Unboosted: No dosage adjustment necessary. RTV boosted: See RTV recommendations.	No data, but presumably similar interaction as seen with APV with an increase in both APV and ketoconazole levels (APV ↑ 31%; ketoconazole ↑ 44%). Dose: Consider ketoconazole dose reduction if dose is >400mg/day. If FPV/r: Use with caution; do not exceed 200mg ketoconazole daily.
Voriconazole	RTV boosted: No data, but potential for bi-directional inhibition between voriconazole and PIs exists; monitor for toxicities. See RTV recommendations if boosted with RTV.	No data, but potential for bi-directional inhibition between voriconazole and PIs; monitor for toxicities. See RTV recommendations if boosted with RTV.
ANTI-MYCOBACTERIALS		
Clarithromycin	Levels: clarithromycin AUC ↑ 94% and may cause QTc prolongation. Clarithromycin active metabolite concentrations are significantly reduced. Dose: ↓ clarithromycin dose by 50%. Consider alternative therapy.	Presumably similar interaction and recommendation as APV. Levels: APV AUC ↑ 18%. No change in clarithromycin AUC. No dose adjustment.
Rifabutin	Levels: Rifabutin AUC ↑ 2.5-fold Dose: ↓ rifabutin dose to 150mg QOD or 3x/week [‡]	Rifabutin 150mg QOD + FPV 700/100mg BID, rifabutin unchanged. No data on FPV level. Dose: No change in FPV dose; decrease rifabutin to 150mg QD or 300mg 3x/week [‡] . If RTV-boosted FPV, reduce rifabutin dose to 150mg QOD or 3x/week [‡] .
Rifampin	Should not be coadministered.	A substantial decrease in APV AUC (≈ ↓ 82%) is expected based on the interaction with APV. Should not be coadministered.
HORMONAL CONTRACEPTIVES		
	Levels: Ethinyl estradiol AUC ↑ 48%, norethindrone AUC ↑ 110% Dose: use lowest effective dose or alternative methods.	An increase in ethinyl estradiol and norethindrone levels occurred with APV, and APV levels ↓ 20%. Do not coadminister; alternative methods of contraception are recommended.
LIPID-LOWERING AGENTS		
Atorvastatin	Atorvastatin levels have potential for large increase. Use lowest possible starting dose of atorvastatin with careful monitoring.	Atorvastatin AUC ↑ 150% - use lowest possible starting dose of atorvastatin with careful monitoring.
Pravastatin	No data.	No data.
Simvastatin Lovastatin	Levels: Potential for large increase in statin levels. Avoid concomitant use.	Levels: Potential for large increase in statin levels. Avoid concomitant use
ANTICONSULSANTS		
Carbamazepine Phenobarbital Phenytoin	Unknown, but may decrease ATV levels substantially. Monitor anticonvulsant level and virologic response. Consider using alternative anticonvulsant or monitoring ATV level and boosting with RTV if necessary.	Unknown, but may decrease APV levels substantially. Monitor anticonvulsant levels and virologic response, or consider alternative anticonvulsant. Consider monitoring APV levels and boosting with RTV if necessary.
Methadone	No change in methadone or ATV levels.	With APV, R-methadone levels ↓ 13%, and APV C _{min} ↓ 25%. The interaction with FPV is presumed to be similar. Monitor and titrate methadone if needed.

[‡] Rifabutin: At least 3x/week is recommended if CD4 cell count is <100/mm³

Table 22a. Drug Interactions Among Antiretrovirals and Other Drugs: PIs and Maraviroc

Page 2 of 6

(Updated **January 29, 2008**)

Drug Interactions Requiring Dose Modifications or Cautious Use		
Drugs Affected	Atazanavir (ATV)	Fosamprenavir (FPV)
ERECTILE DYSFUNCTION AGENTS		
Sildenafil	Sildenafil levels have potential for increase. Start with reduced dose of 25mg every 48 hours and monitor for adverse effects.	Sildenafil AUC ↑ 2- to 11-fold with APV. Use cautiously. Start with reduced dose of 25mg every 48 hours and monitor for adverse effects.
Tadalafil	Concomitant administration will result in substantial increase in tadalafil AUC and half-life (normal=17.5h). Start with a 5mg dose, and do not exceed a single dose of 10mg every 72 hours.	No data, but concomitant administration will result in substantial increase in tadalafil AUC and half-life (normal = 17.5 h). Start with a 5 mgdose, and do not exceed a single dose of 10mg every 72 hours.
Vardenafil	No data, but vardenafil AUC may be substantially increased. Start with a 2.5mg dose and do not exceed a single 2.5mg dose in 24 hours. Do not exceed 2.5mg in 72 hours if administered with RTV.	No data, but vardenafil AUC may be substantially increased. Start with a 2.5mg dose and do not exceed a single 2.5mg dose in 24 hours. Do not exceed 2.5mg in 72 hours if administered with RTV.
MISCELLANEOUS	<p>Diltiazem: AUC ↑ 125%, ↓ diltiazem dose by 50%; ECG monitoring is recommended.</p> <p>Other calcium channel blockers: caution is warranted; dose titration should be considered; ECG monitoring is recommended.</p> <p>Irinotecan: ATV inhibits UGT and may interfere with irinotecan metabolism; avoid concomitant use.</p> <p>H₂-receptor antagonists:</p> <ul style="list-style-type: none"> • Not recommended with unboosted ATV. • H₂-receptor antagonist dose should not exceed a 40mg dose equivalent of famotidine BID. ATV 300mg + RTV 100mg should be administered simultaneously with, and/or >10 hours after the H₂-receptor antagonist. • In treatment experienced patients, if TDF is used with H₂-receptor antagonists, ATV 400mg + RTV 100mg should be used. <p>Proton-Pump Inhibitors (PPI):</p> <ul style="list-style-type: none"> • PPIs are not recommended for patients receiving unboosted ATV or in treatment-experienced patients. • For treatment-naïve patients, PPI dose not exceeding a 20mg dose equivalent of omeprazole may be taken approximately 12 hours prior to ATV 300mg + RTV 100mg. <p>Antacids and buffered medications: Reduced ATV concentrations are expected with simultaneous administration; give ATV 2 hrs before or 1 hr after these medications.</p>	<p>H₂ Blockers: Coadministration of ranitidine with FPV decreases (↓) APV AUC 30%; C_{min} unchanged. Separate administration if coadministration is necessary. Monitor closely for desired virologic response. Consider boosting with RTV.</p> <p>Proton-Pump Inhibitors: No effect of esomeprazole 20mg on APV AUC, C_{max}, or C_{min}, regardless of whether FPV was given with or without ritonavir.</p>

Table 22a. Drug Interactions Among Antiretrovirals and Other Drugs: PIs and Maraviroc

Page 3 of 6

(Updated **January 29, 2008**)

Drug Interactions Requiring Dose Modifications or Cautious Use			
Drugs Affected	Darunavir + Ritonavir (DRV/RTV)[†]	Indinavir (IDV)	Lopinavir + Ritonavir (LPV/r)
ANTIFUNGALS			
Itraconazole	Level: No data. Dose: Use with caution; do not exceed 200mg itraconazole daily.	Level: IDV 600mg Q8H given with itraconazole 200mg BID: AUC similar to IDV 800mg Q8H. Dose: IDV 600mg Q8H; Itraconazole: Do not exceed 200mg BID.	Levels: Itraconazole \uparrow when administered with LPV/r. Dose: Itraconazole – consider not exceeding 200mg/day, or monitor level and toxicity.
Ketoconazole	Levels: DRV AUC \uparrow 42%. Azole AUC \uparrow 3-fold. Dose: Use with caution; do not exceed 200mg ketoconazole QD.	Levels: IDV \uparrow 68%. Dose: IDV 600mg Q8H.	Levels: LPV AUC \downarrow 13%. Azole \uparrow 3-fold. Dose: Use with caution; do not exceed 200mg ketoconazole daily.
Voriconazole	Levels: No data with DRV/r. Voriconazole AUC \downarrow 39% with RTV 100mg BID; coadministration not recommended unless benefit outweighs risk.	Levels: No significant changes in AUC of azole or IDV (healthy subjects). See RTV recommendations if boosted with RTV. Dose: Standard.	Voriconazole AUC \downarrow 39% with RTV 100mg BID; Coadministration is not recommended unless the benefit outweighs the risk.
ANTI-MYCOBACTERIALS			
Clarithromycin	Levels: Clarithromycin AUC \uparrow 57%. DRV: No significant effect. Dose: Adjust clarithromycin dose for moderate & severe renal impairment.	Levels: Clarithromycin \uparrow 53%. No dose adjustment.	Levels: \uparrow Clarithromycin AUC 77%. Dose: Adjust clarithromycin dose for moderate and severe renal impairment.
Rifabutin	Levels: No data Dose: Decrease rifabutin to 150mg QOD.	Levels: IDV \downarrow 32%. Rifabutin \uparrow 2X. Dose: \downarrow rif to 150mg/d or 300mg 3x/week. [‡] IDV 1,000mg Q8H. If RTV boosted, rif 150mg QOD or 3x/week [‡] continue current dose of boosted IDV.	Levels: Rifabutin AUC \uparrow 3-fold. 25-O-desacetyl metabolite \uparrow 47.5-fold. Dose: Decrease rifabutin dose to 150mg QOD or 3x/week [‡] ; LPV/r: Standard.
Rifampin	Levels: No data, but a significant decrease in DRV concs is expected. Should not be coadministered.	Levels: IDV (unboosted) \downarrow 89%; IDV (boosted) \downarrow 87%; Should not be coadministered.	Levels: LPV AUC \downarrow 75%. [*] Should not be coadministered.
HORMONAL CONTRACEPTIVES			
	Levels: Potential for \downarrow ethinyl estradiol from RTV. Use alternative or additional method with DRV/r.	Levels: Norethindrone \uparrow 26%. Ethinylestradiol \uparrow 24%. No dose adjustment.	Levels: Ethinyl estradiol \downarrow 42%. Use alternative or additional method.
LIPID-LOWERING AGENTS			
Atorvastatin	Statin exposure from 10mg QD with DRV/r gives similar exposure to 40mg QD alone. Use lowest possible statin starting dose w/careful monitoring.	Levels: Potential for increase in atorvastatin levels. Use lowest possible starting dose of atorvastatin with careful monitoring.	Atorvastatin AUC \uparrow 5.88-fold. Use lowest possible starting dose of atorvastatin with careful monitoring.
Pravastatin	Levels: Mean \uparrow in statin AUC was 81% with DRV/r. However, statin AUC increased by up to 5-fold in some subjects. Start at lowest dose and titrate up, monitor for toxicities.	No data.	Pravastatin AUC \uparrow 33%; no dosage adjustment necessary.
Simvastatin Lovastatin	Levels: Potential for large increase in statin levels. Avoid concomitant use.	Levels: Potential for large increase in statin levels. Avoid concomitant use.	Levels: Potential for large increase in statin levels. Avoid concomitant use.
ANTICONVULSANTS			
Carbamazepine Phenytoin	Coadministration is expected to result in significant decrease in DRV concentrations. Avoid concomitant use.	Carbamazepine markedly \downarrow IDV AUC. Consider alternative anticonvulsant, RTV boosting, and/or monitoring IDV level.	Many possible interactions: carbamazepine: \uparrow levels when co-administered with RTV. Use with caution. Monitor anticonvulsant levels. Phenytoin: \downarrow levels of LPV, RTV, and of phenytoin when given together. Avoid concomitant use or monitor LPV level.
Methadone	Levels: No data with DRV/r. However, RTV is a known inducer of methadone metabolism. Monitor closely; increase methadone as clinically indicated.	No change in methadone levels.	Methadone AUC \downarrow 53%. Opiate withdrawal may occur. Monitor and titrate dose if needed. May require \uparrow methadone dose.
ERECTILE DYSFUNCTION AGENTS			
Sildenafil	Sildenafil AUC from a 25 mg single dose given w/ DRV/r was similar to 100mg given alone. Do not exceed 25 mg q48h; monitor for adverse effects.	Sildenafil AUC \uparrow 3-fold. Use cautiously. Start with reduced dose of 25 mg every 48 hours and monitor for adverse effects.	Sildenafil AUC \uparrow 11-fold in combination with RTV. Do not exceed 25mg every 48 hours.
Tadalafil	No data, but concomitant administration is expected to result in substantial increase in tadalafil AUC and half-life (normal = 17.5h). Do not exceed a single dose of 10mg in 72h.	Concomitant administration will result in substantial increase in tadalafil AUC & half-life (normal=17.5h). Start with 5mg dose; do not exceed a single dose of 10mg q72h.	Tadalafil AUC \uparrow 124% when coadministered with RTV. Do not exceed a single dose of 10mg every 72 hours.
Vardenafil	No data, but a substantial increase in vardenafil AUC is expected. Do not exceed a single dose of 2.5 mg in 72 hours.	Vardenafil AUC \uparrow 16-fold. IDV (unboosted) AUC \downarrow 30%. Dose: Consider sildenafil instead of vardenafil if IDV unboosted. Do not exceed vardenafil 2.5mg in 72h if administered w/RTV.	No data, but vardenafil AUC may be substantially increased. Do not exceed a single 2.5mg dose in 72 hours.
Miscellaneous	Paroxetine and Sertraline AUC's \downarrow 39% and 49%, respectively. Patients initiated on DRV/r should be monitored closely for antidepressant response. Carefully titrate SSRI dose based on clinical assessment. DRV levels unchanged when DRV/r is administered with omeprazole or ranitidine.	Grapefruit juice \downarrow IDV levels by 26%. Vitamin C \geq 1 gram/day \downarrow IDV AUC by 14% and C _{min} by 32%. Amlodipine: Amlodipine AUC \uparrow 90% when coadministered with IDV/RTV. No change in IDV/RTV levels. Monitor closely.	LPV/r levels unchanged when tablets are given with omeprazole or ranitidine.

[†] Darunavir interaction studies were conducted with RTV 100mg BID and mostly with darunavir doses of 300–400mg BID instead of the FDA approved dose of DRV 600mg BID

[‡] Rifabutin: At least 3x/week is recommended if CD4 cell count is <100/mm³.

^{*} In one small study, higher doses of RTV (an additional 300mg BID) or a double dose of LPV/RTV offset rifampin-inducing activity of LPV. Of note, 28% of subjects discontinued treatment because of increases in LFTs. The safety of this combination is still under evaluation. Further studies are needed.

Table 22a. Drug Interactions Among Antiretrovirals and Other Drugs: PIs and Maraviroc

Page 4 of 6

(Updated **January 29, 2008**)

Drug Interactions Requiring Dose Modifications or Cautious Use		
Drugs Affected	Nelfinavir (NFV)	Ritonavir* (RTV)
ANTIFUNGALS		
Itraconazole	No data, but potential for bi-directional inhibition between itraconazole and PIs; monitor for toxicities.	No data, but potential for bi-directional inhibition between itraconazole and RTV; monitor for toxicities. Dose: Dose adjustment for patients receiving >400mg itraconazole may be needed, or consider monitoring itraconazole level.
Ketoconazole	No dose adjustment necessary.	Levels: ketoconazole ↑ 3X. Dose: Use with caution; do not exceed 200mg ketoconazole daily.
Voriconazole	No data, but potential for bi-directional inhibition between voriconazole and PIs exists; monitor for toxicities.	Levels: voriconazole AUC ↓ 82% when coadministered with 400mg BID of RTV, and concomitant therapy of voriconazole with RTV 400mg BID or higher is contraindicated. Voriconazole AUC ↓ 39% with RTV 100mg BID; administration of voriconazole and RTV 100mg is not recommended unless benefit outweighs risk.
ANTI-MYCOBACTERIALS		
Clarithromycin	No data.	Levels: Clarithromycin ↑ 77%. Dose: Adjust clarithromycin dose for moderate and severe renal impairment.
Rifabutin	Levels: NFV ↓ 32% if 750mg Q8H dose given; no change if 1,250mg Q12H dose used. Rifabutin ↑ 2X. Dose: ↓ rifabutin to 150mg QD or 300mg 3x/wk. ^g NFV 1,250mg BID.	Levels: Rifabutin ↑ 4X. Dose: ↓ rifabutin to 150mg QOD or dose 3x/week. ^g RTV: Maintain current dose.
Rifampin	Levels: NFV ↓ 82%. Should not be coadministered.	Levels: RTV ↓ 35%. Increased liver toxicity possible. Coadministration may lead to loss of virologic response if RTV sole PI. Alternative antimycobacterial agents, such as rifabutin, should be considered. Should not be coadministered.
HORMONAL CONTRACEPTIVES		
	Levels: Norethindrone ↓ 18%. Ethinyl estradiol ↓ 47%. Use alternative or additional method.	Levels: Ethinyl estradiol ↓ 40%. Use alternative or additional method.
LIPID-LOWERING AGENTS		
Atorvastatin	Atorvastatin AUC ↑ 74%. Use lowest possible starting dose of atorvastatin with careful monitoring.	Levels: 450% ↑ when administered with SQV/RTV combination. Use lowest possible starting dose of atorvastatin with careful monitoring.
Pravastatin	No data.	Levels: 50% ↓ when administered with SQV/RTV combination. Dose: Pravastatin dosage adjustment based on lipid response.
Simvastatin Lovastatin	Simvastatin AUC ↑ 505%. Potential for large increase in lovastatin AUC. Avoid concomitant use.	Levels: Potential for large increase in statin levels. Avoid concomitant use.
ANTICONVULSANTS		
Carbamazepine Phenobarbital Phenytoin	Unknown, but may decrease NFV levels substantially. Monitor anticonvulsant levels and virologic response. Consider alternative anticonvulsant or NFV levels.	Carbamazepine: ↑ serum levels when coadministered with RTV. Use with caution. Monitor anticonvulsant levels.
METHADONE	NFV may decrease methadone levels, but opiate withdrawal rarely occurs. Monitor and titrate dose if needed. May require ↑ methadone dose.	Methadone ↓ 37%. Monitor and titrate dose if needed. May require ↑ methadone dose.
ERECTILE DYSFUNCTION AGENTS		
Sildenafil	Sildenafil AUC ↑ 2- to 11-fold. Use cautiously. Start with reduced dose of 25mg every 48 hours; monitor for adverse effects.	Sildenafil AUC ↑ 11-fold. Use cautiously. Start with reduced dose of 25 mg every 48 hours and monitor for adverse effects.
Tadalafil	Concomitant administration will result in substantial increase in tadalafil AUC and half-life (normal = 17.5 h). Start with a 5mg dose, and do not exceed a single dose of 10mg every 72 hours.	Tadalafil AUC ↑ 124%. Start with a 5mg dose, and do not exceed a single dose of 10mg every 72 hours.
Vardenafil	No data, but vardenafil AUC may be substantially increased. Start with a 2.5mg dose and do not exceed a single 2.5mg dose in 24 hours. Do not exceed 2.5mg in 72 hours if administered with RTV.	Vardenafil AUC ↑ 49-fold. RTV AUC ↓ 20%. Dose: Vardenafil: Start with a 2.5mg dose and do not exceed a single 2.5mg dose in 72 hours. RTV: Maintain current dose.
Miscellaneous		Many possible interactions. <u>Desipramine</u> ↑ 145%; reduce dose. <u>Trazodone</u> AUC ↑ 2.4-fold when given with RTV 200mg BID. Use lowest dose of trazodone and monitor for CNS and CV adverse effects. <u>Theophylline</u> ↓ 47%; monitor theophylline levels. RTV 100mg BID significantly increases systemic exposure of inhaled (oral or nasal) fluticasone and may predispose patients to systemic corticosteroid effects. Coadministration not recommended unless benefit of fluticasone outweighs the risk.

* Drugs for which plasma concentrations may be decreased by coadministration with ritonavir: anticoagulants (warfarin), anticonvulsants (phenytoin, divaproex, lamotrigine), antiparasitics (atovaquone).

^g Rifabutin: At least 3x/week is recommended if CD4 cell count is <100/mm³.

Table 22a. Drug Interactions Among Antiretrovirals and Other Drugs: PIs and Maraviroc

Page 5 of 6

(Updated **January 29, 2008**)

Drug Interactions Requiring Dose Modifications or Cautious Use			
Drugs Affected	Saquinavir[†] (SQV)	Tipranavir + Ritonavir (TPV/RTV)	Maraviroc (MVC)
ANTIFUNGALS			
Itraconazole	Bi-directional interaction between itraconazole & SQV has been observed. Dose: Not established, but decreased itraconazole dosage may be warranted. Consider therapeutic drug monitoring for itraconazole.	No data. Use with caution; do not exceed 200mg itraconazole daily.	Possible increase in maraviroc concentration. Dose: 150mg BID.
Ketoconazole	Levels: SQV ↑ 3X. Dose: No dosage adjustment necessary.	No data. Use with caution; do not exceed 200mg ketoconazole daily.	Levels: MVC AUC ↑ 5x. Dose: 150mg BID.
Voriconazole	No data, but potential for bi-directional inhibition between voriconazole and PIs, monitor for toxicities	Potential for bi-directional inhibition between voriconazole and PIs exists. Voriconazole AUC ↓ 39% with RTV 100mg BID; interaction between TPV and voriconazole unknown. Coadministration is not recommended unless the benefit outweighs the risk.	No data, monitor for toxicities.
ANTI-MYCOBACTERIALS			
Clarithromycin	Levels: Clarithromycin ↑ 45%. SQV ↑ 177%. Dose: No dose adjustment.	Levels: TPV ↑ 66%, Clarithromycin ↑ 19%, 14-hydroxy-clarithromycin metabolite ↓ 97%. Dose: No adjustment for patients with normal renal function; reduce clarithromycin dose by 50% for CrCl 30–60 mL/min; reduce clarithromycin dose by 75% for CrCl <30 mL/min.	Possible increase in maraviroc concentration. Dose: 150mg BID.
Rifampin	Levels: SQV ↓ 84%. Marked elevation of transaminases was seen in a pharmacokinetic study, where healthy volunteers received a combination of rifampin 600mg QD + RTV/SQV 100/1,000mg BID. This combination should not be used.	No data; should not be coadministered.	Levels: MVC AUC ↓ 64%. Dose: 600mg BID or use rifabutin instead of rifampin.
Rifabutin	Levels: SQV ↓ 40%. Dose: Rifabutin 150mg QOD or 3x/week. [‡]	Levels: Rifabutin AUC ↑ 2.9-fold. 25-O-desacetyl metabolite ↑ 20.7-fold. Dose: Decrease rifabutin dose to 150mg QOD or 3x/week. [‡] Single-dose study, thus the effect of multiple doses of rifabutin on TPV/r PK was not assessed.	No data, potential for induction of MVC metabolism. If used without a strong CYP3A inducer or inhibitor: 300mg BID. Monitor for virologic response. If used with a strong CYP3A inhibitor: 150mg BID.
HORMONAL CONTRACEPTIVES			
	No data.	Levels: Ethinyl estradiol C _{max} and AUC ↓ ~ 50%. [‡] Use alternative or additional method. Women on estrogen may have increased risk of nonserious rash. Used as hormone replacement therapy, monitor clinically for signs of estrogen deficiency.	No significant interaction, safe to use in combination.
LIPID-LOWERING AGENTS			
Atorvastatin	Levels: 450% ↑ when administered with SQV/RTV combination. Use lowest possible starting dose of atorvastatin with careful monitoring.	Levels: Atorvastatin AUC ↑ 9-fold. Dose: Use lowest possible starting dose of atorvastatin with careful monitoring.	No data, potentially safe to use in combination.
Pravastatin	Levels: 50% ↓ when administered with SQV/RTV combination. No dose adjustment needed. Dose: Pravastatin dosage adjustment based on lipid response.	No data.	No data, potentially safe to use in combination.
Simvastatin Lovastatin	Levels: Potential for large increase in statin levels. Avoid concomitant use.	Potential for large increase in statin levels. Avoid concomitant use.	No data, potentially safe to use in combination.
ANTICONVULSANTS			
Carbamazepine Phenobarbital Phenytoin	Unknown, but may markedly ↓ SQV levels. Consider alternative anticonvulsant. Monitor anticonvulsant levels and consider monitoring SQV level.	No data. Consider alternative anticonvulsant. Monitor anticonvulsant levels and consider obtaining TPV level.	Possible decrease in maraviroc concentration Dose: 600mg BID or use alternative antiepileptic agent.
Methadone	Methadone AUC ↓ 19% when coadministered with SQV/RTV 1,000/100mg BID. Dose: No adjustment for this PI regimen, but monitor and titrate to methadone response as necessary.	No data. Dosage of methadone may need to be increased when coadministered with TPV/r.	No data, potentially safe to use in combination.

[‡] Study conducted with TPV/r dose(s) other than FDA-approved dose of 500/200mg BID.[†] Some drug interaction studies were conducted with Invirase[®] soft gel capsule.

Table 22a. Drug Interactions Among Antiretrovirals and Other Drugs: PIs and MaravirocPage 6 of 6 (Updated **January 29, 2008**)

Drug Interactions Requiring Dose Modifications or Cautious Use			
Drugs Affected	Saquinavir [†] (SQV)	Tipranavir + Ritonavir (TPV/RTV)	Maraviroc (MVC)
ERECTILE DYSFUNCTION AGENTS			
Sildenafil	Sildenafil AUC ↑ 2-fold. Use a 25mg starting dose of sildenafil.	No data. Starting dose should not exceed 25 mg sildenafil within 48 hours.	No data, potentially safe to use in combination.
Tadalafil	Concomitant administration will result in substantial increase in tadalafil AUC and half-life (normal = 17.5 h). Start with a 5mg dose, and do not exceed a single dose of 10mg every 72 hours.	No data. Starting dose should not exceed 10mg tadalafil every 72 hours.	No data, potentially safe to use in combination.
Vardenafil	No data, but vardenafil AUC may be substantially increased. Start with a 2.5mg dose and do not exceed a single 2.5mg dose in 24 hours. Do not exceed a single 2.5mg dose in 72 hours if administered with RTV.	No data. Starting dose should not exceed 2.5mg vardenafil every 72 hours.	No data, potentially safe to use in combination.
Miscellaneous	Grapefruit juice ↑ SQV levels. Dexamethasone ↓ SQV levels.	<u>Abacavir</u> ↓ 35%–44%. ^a Appropriate doses for the combination of ABC and TPV/r have not been established. <u>Zidovudine</u> ↓ 31%–43%. Appropriate doses for the combination of ZDV and TPV/r have not been established. <u>Loperamide</u> ↓ 51%. ^a TPV C _{min} ↓ 26% with loperamide. <u>Antacids</u> ↓ TPV ~30%, TPV should be administered 2 hrs before or 1 hr after these medications. <u>Fluconazole</u> : Doses >200mg/day are not recommended to be given with TPV. TPV capsules contain alcohol. Avoid use of disulfiram and metronidazole.	No data.

^a Study conducted with TPV/r dose(s) other than FDA-approved dose of 500/200mg BID.[†] Some drug interaction studies were conducted with Invirase[®] soft gel capsule.