

Table 12. Characteristics of Protease Inhibitors (PIs)
(Updated **January 29, 2008**)

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Generic Name/ Trade Name	Formulation	Dosing Recommendations	Food Effect	Oral Bio- availability	Serum half-life	Route of Metabolism	Storage	Adverse Events
Atazanavir (ATV)/ REYATAZ	100, 150, 200mg capsules	400mg once daily <u>If taken with efavirenz or tenofovir:</u> RTV 100mg + ATV 300mg once daily	Administration with food increases bioavailability Take with food; avoid taking with antacids	Not determined	7 hours	Cytochrome P450 3A4 inhibitor and substrate Dosage adjustment in hepatic insufficiency recommended (See Table 16)	Room temperature (up to 25°C or 77°F)	<ul style="list-style-type: none"> ● Indirect hyperbilirubinemia ● Prolonged PR interval— 1st degree symptomatic AV block in some pts ● Use with caution in pts with underlying conduction defects or on concomitant medications that can cause PR prolongation ● Hyperglycemia ● Fat maldistribution ● Possible increased bleeding episodes in pts with hemophilia ● Nephrolithiasis
Darunavir (DRV)/ PREZISTA	300mg tablet	(DRV 600mg + RTV 100mg) twice daily	Food ↑ Cmax & AUC by 30% - should be administered with food	<u>Absolute bioavailability:</u> DRV alone – 37%; w/ RTV – 82%;	15 hours (when combined with RTV)	Cytochrome P450 3A4 inhibitor and substrate	Room temperature (up to 25°C or 77°F)	<ul style="list-style-type: none"> ● Skin rash (7%) – DRV has a sulfonamide moiety; Stevens-Johnson syndrome & erythema multiforme have been reported. ● Diarrhea, nausea ● Headache ● Hyperlipidemia ● Transaminase elevation ● Hyperglycemia ● Fat maldistribution ● Possible increased bleeding episodes in pts with hemophilia
Fosamprenavir (FPV)/ LEXIVA	700mg tablet Oral suspension: 50mg/mL	<u>ARV-naïve patients:</u> <ul style="list-style-type: none"> ● FPV 1,400mg BID or ● (FPV 1,400mg + RTV 200mg) QD or ● (FPV 700mg + RTV 100mg) BID ● (FPV 1,400mg + RTV 100mg) QD <u>PI-experienced pts (QD not recommended):</u> <ul style="list-style-type: none"> ● (FPV 700mg + RTV 100mg) BID <u>Coadministration w/ EFV (FPV boosted only):</u> <ul style="list-style-type: none"> ● (FPV 700mg + RTV 100mg) BID or ● (FPV 1,400mg + RTV 300mg) QD 	No significant change in amprenavir pharmacokinetics in fed or fasting state	Not established	7.7 hours (amprenavir)	Amprenavir is a cytochrome P450 3A4 inhibitor, inducer, and substrate Dosage adjustment in hepatic insufficiency recommended (See Table 16)	Room temperature (up to 25°C or 77°F)	<ul style="list-style-type: none"> ● Skin rash (1%) ● Diarrhea, nausea, vomiting ● Headache ● Hyperlipidemia ● Transaminase elevation ● Hyperglycemia ● Fat maldistribution ● Possible increased bleeding episodes in patients with hemophilia
Indinavir/ CRIXIVAN	200, 333, 400mg capsules	800mg every 8 hours; <u>With RTV:</u> (IDV 800mg + RTV 100 or 200mg) every 12 hours	<u>Unboosted IDV:</u> Levels decrease by 77% Take 1 hour before or 2 hours after meals; may take with skim milk or low-fat meal <u>RTV-boosted IDV:</u> Take with or without food	65%	1.5–2 hours	Cytochrome P450 3A4 inhibitor (less than ritonavir) Dosage adjustment in hepatic insufficiency recommended (See Table 16)	Room temperature 15°–30°C (59°–86°F), protect from moisture	<ul style="list-style-type: none"> ● Nephrolithiasis ● GI intolerance, nausea ● Indirect hyperbilirubinemia ● Hyperlipidemia ● Headache, asthenia, blurred vision, dizziness, rash, metallic taste, thrombocytopenia, alopecia, and hemolytic anemia ● Hyperglycemia ● Fat maldistribution ● Possible increased bleeding episodes in pts with hemophilia

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Lopinavir + Ritonavir (LPV/r)/ KALETRA	Each tablet contains LPV 200mg + RTV 50mg Oral solution: Each 5 mL contains LPV 400mg + RTV 100mg Note: Oral solution contains 42% alcohol	LPV 400mg + RTV 100mg (2 tablets or 5 mL) twice daily or LPV 800mg + RTV 200mg (4 tablets or 10mL) once daily (Note: once-daily dosing only recommended for treatment-naïve pts; not for patients receiving EFV, NVP, FPV, or NFV) <u>With EFV or NVP:</u> For treatment-experienced pts: LPV 600mg + RTV 150mg (3 oral tablets) twice daily or LPV 533 mg + RTV 133 mg (6.7 mL oral solution) twice daily with food	Oral tablet -No food effect; take with or without food Oral solution - Moderately fatty meal ↑ LPV AUC & C _{min} by 80% & 54%, respectively; take with food	Not determined in humans	5–6 hours	Cytochrome P450 (3A4 inhibitor and substrate)	Oral tablet is stable at room temperature Oral solution is stable at 2°–8°C until date on label; is stable when stored at room temperature (up to 25°C or 77°F) for 2 months	<ul style="list-style-type: none"> • GI intolerance, nausea, vomiting, diarrhea (higher incidence with once-daily than twice-daily dosing) • Asthenia • Hyperlipidemia (esp. hypertriglyceridemia) • Elevated serum transaminases • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia
Nelfinavir (NFV)/ VIRACEPT	250mg tablets or 625 mg tablets 50mg/g oral powder	1,250mg two times/day or 750mg three times/day	Levels increase 2–3 fold Take with meal or snack	20%–80%	3.5–5 hours	Cytochrome P450 3A4 inhibitor and substrate	Room temperature 15°–30°C (59°–86°F)	<ul style="list-style-type: none"> • Diarrhea • Hyperlipidemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes among patients with hemophilia • Serum transaminase elevation
Ritonavir (RTV)/ NORVIR	100mg capsules or 600mg/7.5 mL solution	600mg every 12 hours (when ritonavir is used as sole PI) As pharmacokinetic booster for other PIs – 100mg – 400mg per day in 1–2 divided doses	Levels increase 15% Take with food if possible; this may improve tolerability	Not determined	3–5 hours	Cytochrome P450 (3A4 > 2D6; Potent 3A4 inhibitor)	Refrigerate capsules Capsules can be left at room temperature (up to 25°C or 77°F) for ≤30 days; Oral solution should NOT be refrigerated	<ul style="list-style-type: none"> • GI intolerance, nausea, vomiting, diarrhea • Paresthesias – circumoral and extremities • Hyperlipidemia, esp. hypertriglyceridemia • Hepatitis • Asthenia • Taste perversion • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia
Saquinavir tablets and hard gel capsules (SQV)/ INVIRASE	200mg hard gel capsules, 500mg tablets	(SQV 1,000mg + RTV 100mg) PO BID	Take within 2 hours of a meal when taken with RTV	4% erratic (when taken as sole PI)	1–2 hours	Cytochrome P450 (3A4 inhibitor and substrate)	Room temperature 15°–30°C (59°–86°F)	<ul style="list-style-type: none"> • GI intolerance, nausea and diarrhea • Headache • Elevated transaminase enzymes • Hyperlipidemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia

* Dose escalation for Ritonavir when used as sole PI: Days 1 and 2: 300mg two times; Days 3–5: 400mg two times; Days 6–13: 500mg two times; Day 14: 600mg two times/day.

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Tipranavir (TPV)/ APTIVUS	250mg capsules	500mg twice daily with ritonavir 200mg twice daily Unboosted tipranavir is <u>not</u> recommended	Take both TPV & RTV with food. Bio-availability increased with high- fat meal	Not determined	6 hours after single dose of TPV/ RTV	TPV – Cytochrome P450 (3A4 inducer and substrate) Net effect when combined with RTV – CYP 3A4 inhibitor and CYP 2D6 inhibitor	Refrigerated capsules are stable until date on label; if stored at room temperature (up to 25°C or 77°F) – must be used within 60 days	<ul style="list-style-type: none"> • Hepatotoxicity – clinical hepatitis including hepatic decompensation has been reported, monitor closely, esp. in patients with underlying liver diseases • Skin rash – TPV has a sulfonamide moiety, use with caution in patients with known sulfonamide allergy • Rare cases of fatal and nonfatal intracranial hemorrhages have been reported. Most patients had underlying comorbidity such as brain lesion, head trauma, recent neurosurgery, coagulopathy, hypertension, alcoholism, or on medication with increase risk for bleeding • Hyperlipidemia (esp. hypertriglyceridemia) • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia