

Please refer to the **What to Start** section of the Adult Guidelines for more detailed discussions.

**Appendix Table 4. Characteristics of Protease Inhibitors (PIs) (Updated November 3, 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
<b>Atazanavir (ATV)/ REYATAZ</b>	100mg, 150mg, 200mg, 300mg capsules	400mg once daily (unboosted ARV only recommended for PI-naïve pts) <u>With efavirenz or tenofovir TDF, or for ARV-experienced pts:</u> (ATV 300mg + RTV 100mg) once daily <u>With EFV in treatment-naïve pts:</u> (ATV 400mg + RTV 100mg) once daily (for dosing recommendations with H2 antagonists and PPIs, please refer to <a href="#">Table 15a</a> )	Administration with food increases bioavailability. Take with food; avoid taking simultaneously with antacids	Not determined	7 hours	Cytochrome P450 3A4 inhibitor and substrate  Dosage adjustment in hepatic insufficiency recommended (See <a href="#">Appendix Table 8</a> )	Room temperature (up to 25°C or 77°F)	<ul style="list-style-type: none"> <li>• Indirect hyperbilirubinemia</li> <li>• Prolonged PR interval— 1<sup>st</sup> degree symptomatic AV block in some pts</li> <li>• Use with caution in pts with underlying conduction defects or on concomitant medications that can cause PR prolongation</li> <li>• Hyperglycemia</li> <li>• Fat maldistribution</li> <li>• Possible increased bleeding episodes in pts with hemophilia</li> <li>• Nephrolithiasis</li> </ul>
<b>Darunavir (DRV)/ PREZISTA</b>	300mg, 400mg, 600mg tablets	<u>ARV-naïve pts:</u> (DRV 800mg + RTV 100mg) once daily  <u>ARV-experienced pts:</u> (DRV 600mg + RTV 100mg) BID  Unboosted DRV is <b>not</b> recommended	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"> <li>• Skin rash (7%) – DRV has a sulfonamide moiety; Stevens-Johnson syndrome &amp; erythema multiforme have been reported.</li> <li>• Hepatotoxicity</li> <li>• Diarrhea, nausea</li> <li>• Headache</li> <li>• Hyperlipidemia</li> <li>• Transaminase elevation</li> <li>• Hyperglycemia</li> <li>• Fat maldistribution</li> <li>• Possible increased bleeding episodes in pts with hemophilia</li> </ul>
<b>Fosamprenavir (FPV)/ LEXIVA</b>	700mg tablet or 50mg/mL oral suspension	<u>ARV-naïve pts:</u> • FPV 1,400mg BID or • (FPV 1,400mg + RTV 100-200mg) once daily or • (FPV 700mg + RTV 100mg) BID <u>PI-experienced pts (once daily dosing not recommended):</u> • (FPV 700mg + RTV 100mg) BID <u>With EFV (FPV boosted only):</u> • (FPV 700mg + RTV 100mg) BID or • (FPV 1,400mg + RTV 300mg) once daily	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 <a href="#">Appendix Table 8</a> )	Room temperature (up to 25°C or 77°F)	<ul style="list-style-type: none"> <li>• Skin rash (19%)</li> <li>• Diarrhea, nausea, vomiting</li> <li>• Headache</li> <li>• Hyperlipidemia</li> <li>• Transaminase elevation</li> <li>• Hyperglycemia</li> <li>• Fat maldistribution</li> <li>• Possible increased bleeding episodes in patients with hemophilia</li> </ul>
<b>Indinavir/ CRIVAN</b>	200mg, 333mg, 400mg capsules	800mg every 8 hours;  <u>With RTV:</u> (IDV 800mg + RTV 100-200mg) BID	<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 <a href="#">Appendix Table 8</a> )	Room temperature 15°–30°C (59°–86°F), protect from moisture	<ul style="list-style-type: none"> <li>• Nephrolithiasis</li> <li>• GI intolerance, nausea</li> <li>• Indirect hyperbilirubinemia</li> <li>• Hyperlipidemia</li> <li>• Headache, asthenia, blurred vision, dizziness, rash, metallic taste, thrombocytopenia, alopecia, and hemolytic anemia</li> <li>• Hyperglycemia</li> <li>• Fat maldistribution</li> <li>• Possible increased bleeding episodes in pts with hemophilia</li> </ul>

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<b>Lopinavir + Ritonavir (LPV/r)/ KALETRA</b>	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) BID or LPV 800mg + RTV 200mg (4 tablets or 10mL) once daily ( <b>Note:</b> once-daily dosing only recommended for treatment-naïve pts; not for pregnant women or patients receiving EFV, NVP, FPV, or NFV)  <u>With EFV or NVP:</u> For ARV-experienced pts: LPV 600mg + RTV 150mg (3 tablets) BID or LPV 533 mg + RTV 133 mg (6.7 mL oral solution) BID with food	Oral tablet -No food effect; take with or without food  Oral solution - Moderately fatty meal ↑ LPV AUC & Cmin 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"> <li>• GI intolerance, nausea, vomiting, diarrhea (higher incidence with once-daily than twice-daily dosing)</li> <li>• Asthenia</li> <li>• Hyperlipidemia (esp. hypertriglyceridemia)</li> <li>• Elevated serum transaminases</li> <li>• Hyperglycemia</li> <li>• Fat maldistribution</li> <li>• Possible increased bleeding episodes in patients with hemophilia</li> </ul>
<b>Nelfinavir (NFV)/ VIRACEPT</b>	250mg, 625mg tablets  50mg/g oral powder	1,250mg BID or 750mg TID	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"> <li>• Diarrhea</li> <li>• Hyperlipidemia</li> <li>• Hyperglycemia</li> <li>• Fat maldistribution</li> <li>• Possible increased bleeding episodes among patients with hemophilia</li> <li>• Serum transaminase elevation</li> <li>•</li> </ul>
<b>Ritonavir (RTV)/ NORVIR</b>	100mg capsules or 80 mg/mL oral solution	As pharmacokinetic booster for other PIs: 100mg – 400mg per day in 1–2 divided doses (please refer to other PIs for specific dosing recommendations)  600mg every 12 hours (when ritonavir is used as sole PI)	Levels increase 15%  Take with food if possible; this may improve tolerability	Not determined	3–5 hours	Cytochrome P450 (3A4 > 2D6) substrate; Potent 3A4, 2D6 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"> <li>• GI intolerance, nausea, vomiting, diarrhea</li> <li>• Paresthesias – circumoral and extremities</li> <li>• Hyperlipidemia, esp. hypertriglyceridemia</li> <li>• Hepatitis</li> <li>• Asthenia</li> <li>• Taste perversion</li> <li>• Hyperglycemia</li> <li>• Fat maldistribution</li> <li>• Possible increased bleeding episodes in patients with hemophilia</li> </ul>
<b>Saquinavir tablets and hard gel capsules (SQV)/ INVIRASE</b>	200mg hard gel capsules, 500mg tablets	(SQV 1,000mg + RTV 100mg) PO BID  Unboosted SQV is <b>not</b> recommended	Take within 2 hours of a meal	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"> <li>• GI intolerance, nausea and diarrhea</li> <li>• Headache</li> <li>• Elevated transaminase enzymes</li> <li>• Hyperlipidemia</li> <li>• Hyperglycemia</li> <li>• Fat maldistribution</li> <li>• Possible increased bleeding episodes in patients with hemophilia</li> </ul>

\* 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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<b>Tipranavir (TPV)/ APTIVUS</b>	250mg capsules	(TPV 500mg + RTV 200mg) PO BID  Unboosted TPV is <u>not</u> recommended	No clinically significant change in TPV pharmacokinetics in fed or fasting state	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"> <li>• Hepatotoxicity – clinical hepatitis including hepatic decompensation has been reported, monitor closely, esp. in patients with underlying liver diseases</li> <li>• Skin rash – TPV has a sulfonamide moiety, use with caution in patients with known sulfonamide allergy</li> <li>• 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</li> <li>• Hyperlipidemia (esp. hypertriglyceridemia)</li> <li>• Hyperglycemia</li> <li>• Fat maldistribution</li> <li>• Possible increased bleeding episodes in patients with hemophilia</li> </ul>