Appendix B, Table 3. Characteristics of Protease Inhibitors (PIs) (Updated January 10, 2011)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations (For dosage adjustment in hepatic insufficiency, see Appendix B, Table 7)	Elimination	Serum Half-life	Storage	Adverse Events (Also see Table 13)
Atazanavir (ATV)/ Reyataz	100-, 150-, 200-, 300-mg capsules	ARV-naïve patients: 400 mg once daily or (ATV 300 mg + RTV 100 mg) once daily With TDF or for ARV-experienced patients: (ATV 300 mg + RTV 100 mg) once daily With EFV in ARV-naïve patients: (ATV 400 mg + RTV 100 mg) once daily (For dosing recommendations with H_2 antagonists and proton pump inhibitor (PPIs), refer to Table 16a) Take with food	CYP3A4 inhibitor and substrate Dosage adjustment in hepatic insufficiency recommended (See Appendix B, Table 7.)	7 hrs	Room temperature (up to 25ºC or 77ºF)	• Indirect hyperbilirubinemia • PR interval prolongation: First degree symptomatic atrioventricular (AV) block reported. Use with caution in patients with underlying conduction defects or on concomitant medications that can cause PR prolongation. • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • Nephrolithiasis • Skin rash (20%) • Serum transaminase elevations • Hyperlipidemia (especially with RTV boosting)
Darunavir (DRV)/ Prezista	75-, 150-, 300-, 400-, 600-mg tablets	ARV-naïve patients or ARV-experienced patients with no DRV mutations: (DRV 800 mg + RTV 100 mg) once daily ARV-experienced patients with at least one DRV mutation: (DRV 600 mg + RTV 100 mg) BID Unboosted DRV is **not** recommended Take with food	CYP3A4 inhibitor and substrate	15 hrs (when combined with RTV)	Room temperature (up to 25ºC or 77ºF)	• Skin rash (10%): DRV has a sulfonamide moiety; Stevens-Johnson syndrome and erythrema multiforme have been reported. • Hepatotoxicity • Diarrhea, nausea • Headache • Hyperlipidemia • Serum transaminase elevation • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia
Fosamprenavir (FPV)/ Lexiva (a prodrug of amprenavir [APV])	• 700-mg tablet • 50-mg/mL oral suspension	ARV-naïve patients: • FPV 1,400 mg BID or • (FPV 1,400 mg + RTV 100–200 mg) once daily or • (FPV 700 mg + RTV 100 mg) BID PI-experienced patients (once-daily dosing **not** recommended): • (FPV 700 mg + RTV 100 mg) BID With EFV: • (FPV 700 mg + RTV 100 mg) BID or • (FPV 1,400 mg + RTV 300 mg) once daily *Tablet*: Take without regard to meals (if not boosted with RTV tablet) *Suspension*: Take without food *FPV w/RTV tablet*: Take with meals	APV is a CYP3A4 substrate, inhibitor, and inducer Dosage adjustment in hepatic insufficiency recommended (See Appendix B, Table 7.)	7.7 hrs (APV)	Room temperature (up to 25ºC or 77ºF)	• Skin rash (12%–19%) – FPV has a sulfonamide moiety • Diarrhea, nausea, vomiting • Headache • Hyperlipidemia • Serum transaminase elevation • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • Nephrolithiasis

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Indinavir (IDV)/ Crixivan	100-, 200-, 400-mg capsules	800 mg every 8 hrs Take 1 hour before or 2 hours after meals; may take with skim milk or low-fat meal With RTV: (IDV 800 mg + RTV 100–200 mg) BID Take without regard to meals	CYP3A4 inhibitor and substrate Dosage adjustment in hepatic insufficiency recommended (See Appendix B, Table 7.)	1.5–2 hrs	Room temperature (15º–30ºC/ 59º–86ºF) Protect from moisture	• Nephrolithiasis • GI intolerance, nausea • Hepatitis • Indirect hyperbilirubinemia • Hyperlipidemia • Headache, asthenia, blurred vision, dizziness, rash, metallic taste, thrombocytopenia, alopecia, and hemolytic anemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia
Lopinavir + Ritonavir (LPV/r)/ Kaletra	Tablets: (LPV 200 mg + RTV 50 mg) or (LPV 100 mg + RTV 25 mg) Oral solution: Each 5 mL contains (LPV 400 mg + RTV 100 mg) Oral solution contains 42% alcohol	LPV/r 400-mg/100-mg BID or LPV/r 800-mg/200-mg once daily Once-daily dosing is not recommended for patients with ≥3 LPV-associated mutations, pregnant women, or patients receiving EFV, NVP, FPV, NFV, carbamazepine, phenytoin, or phenobarbital. With EFV or NVP (PI-naïve or PI-experienced patients): LPV/r 500-mg/125-mg tablets BID (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.) or LPV/r 533-mg/133-mg oral solution BID *Tablet*: Take without regard to meals *Oral solution*: Take with food	CYP3A4 inhibitor and substrate	5–6 hrs	Oral tablet is stable at room temperature. Oral solution is stable at 2°–8°C (36°–46°F) until date on label and is stable when stored at room temperature (up to 25ºC or 77ºF) for 2 months.	• GI intolerance, nausea, vomiting, diarrhea • Pancreatitis • Asthenia • Hyperlipidemia (especially hypertriglyceridemia) • Serum transaminase elevation • Hyperglycemia • Insulin resistance/diabetes mellitus • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • PR interval prolongation • QT interval prolongation and torsades de pointes have been reported; however, causality could not be established.
Nelfinavir (NFV)/ Viracept	• 250-, 625-mg tablets • 50-mg/g oral powder	1,250 mg BID or 750 mg TID May dissolve tablets in a small amount of water; once dissolved, patients should mix the cloudy liquid well and consume it immediately. Take with food	CYP2C19 and 3A4 substrate—metabolized to active M8 metabolite; CYP 3A4 inhibitor	3.5–5 hrs	Room temperature (15º–30ºC/ 59º–86ºF)	• Diarrhea • Hyperlipidemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • Serum transaminase elevation

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Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations (For dosage adjustment in hepatic insufficiency, see Appendix B, Table 7)	Elimination	Serum Half-life	Storage	Adverse Events (Also see Table 13)
Ritonavir (RTV)/ Norvir	• 100-mg soft gel capsules • 100-mg tablets • 80-mg/mL oral solution Oral solution contains 43% alcohol	As pharmacokinetic booster for other PIs: 100–400 mg per day in 1–2 divided doses (refer to other PIs for specific dosing recommendations) *Tablet*: Take with food *Capsule and oral solution*: Take with food, if possible, to improve tolerability.	CYP3A4 >2D6 substrate; potent 3A4, 2D6 inhibitor	3–5 hrs	Refrigerate capsules. Capsules can be left at room temperature (up to 25ºC or 77ºF) for up to 30 days. Tablets do not require refrigeration. Oral solution should **not** be refrigerated; store at room temperature 20º–25ºC (68º–77ºF).	• GI intolerance, nausea, vomiting, diarrhea • Paresthesias—circumoral and extremities • Hyperlipidemia (especially hypertriglyceridemia) • Hepatitis • Asthenia • Taste perversion • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia
Saquinavir tablets and hard gel capsules (SQV)/ Invirase	• 500-mg tablets • 200-mg hard gel capsules	(SQV 1,000 mg + RTV 100 mg) BID Unboosted SQV is **not** recommended. Take with meals or within 2 hours after a meal	CYP3A4 inhibitor and substrate	1–2 hrs	Room temperature (15º–30ºC/ 59º–86ºF)	• GI intolerance, nausea, and diarrhea • Headache • Serum transaminase elevation • Hyperlipidemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • PR interval prolongation • QT interval prolongation, torsades de pointes have been reported. Patients with pre-SQV QT interval >450 msec should not receive SQV (See Table 5b.).
Tipranavir (TPV)/ Aptivus	• 250-mg capsules • 100-mg/mL oral solution	(TPV 500 mg + RTV 200 mg) BID Unboosted TPV is **not** recommended. TPV taken with RTV **tablets**: Take with meals TPV taken with RTV **capsules** or **solution**: Take without regard to meals	Cytochrome P450 3A4 inducer and substrate Net effect when combined with RTV (CYP 3A4, 2D6 inhibitor)	6 hrs after single dose of TPV/r	Refrigerate capsules. Capsules can be stored at room temperature (25ºC or 77ºF) for up to 60 days. Oral solution should **not** be refrigerated or frozen and should be used within 60 days after opening the bottle.	• Hepatotoxicity: Clinical hepatitis (including hepatic decompensation and hepatitis-associated fatalities) has been reported; monitor closely, especially in patients with underlying liver diseases. • Skin rash (3%–21%): 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. Risks include brain lesion, head trauma, recent neurosurgery, coagulopathy, hypertension, alcoholism,, use of anti-coagulant or anti-platelet agents including vitamin E. • Hyperlipidemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia