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Table 17. Characteristics of Protease Inhibitors (PIs)

Generic Name/ Trade Name	Form	Dosing Recommendations	Food Effect	Oral Bio-availability	Serum half-life	Route of Metabolism	Storage	Adverse Events
Amprenavir/ Agenerase®	50 mg, 150 mg capsules 15 mg/mL oral solution (capsules and solution NOT inter-changeable on mg per mg basis) Note: Oral solution contains propylene glycol; contraindicated in pregnant women and children <4 years old, patients with hepatic or renal failure, and patients treated with disulfiram or metronidazole	Body weight >50 kg: 1200 mg two times/day (capsules) or, 1400 mg two times/day (oral solution) Body weight < 50 kg: 20mg/kg two times/day (capsules) maximum 2400 mg daily total; 1.5mL/kg two times/day (oral solution) maximum 2800 mg daily total; (See Table 22 for dosage when used with low dose ritonavir)	High-fat meal decreases blood concentration curve 21%; can be taken with or without food, but high fat meal should be avoided.	Not determined in humans	7.1–10.6 hours	Cytochrome P450 (3A4 inhibitor (less than ritonavir; similar to indinavir, nelfinavir), inducer, and substrate	Room temperature	• GI intolerance, nausea, vomiting, diarrhea • Rash • Oral paresthesias • Transaminase elevation • Hyperglycemia† • Fat redistribution and lipid abnormalities ‡ • Possible increased bleeding episodes in patients with hemophilia
Atazanavir/ Reyataz™	100, 150, 200 mg capsules	400 mg once daily If taken with efavirenz (or tenofovir): Ritonavir 100mg + atazanavir 300mg once daily	Administration with food increases bioavailability Take with food	Not determined	7 hours	Cytochrome P450 3A4 inhibitor and substrate	Room temperature	• Indirect hyperbilirubinemia • Prolong PR interval – some patients experienced asymptomatic 1st degree AV block • Use with caution in patients with underlying condition defects or on concomitant medications that can cause PR prolongation • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia
Fosamprenavir (f-APV)/ Lexiva™	700 mg tablet	ARV-naïve patients: • f-APV 1,400mg two times/day; or • (f-APV 1,400 + RTV 200mg) once daily; or • (f-APV 700mg + RTV 100mg) two times/day PI-experienced pts (once daily regimen not recommended): • (f-APV 700mg + RTV 100mg) two times/day Co-administration w/ efavirenz (Unboosted f-APV not recommended): • (f-APV 700mg + RTV 100mg) two times/day; or • (f-APV 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	Room temperature	• Skin rash (19%) • Diarrhea, nausea, vomiting • Headache • Transaminase elevation • Hyperglycemia • Fat maldistribution and lipid abnormalities • Possible increased bleeding episodes in patients with hemophilia
Indinavir/ Crixivan®	200, 333, 400 mg capsules	800 mg every 8 hours; (see Table 22 for dosing recommendation with ritonavir)	Levels decrease 77% Take 1 hour before or 2 hours after meals; may take with skim milk or low-fat meal	65%	1.5–2 hours	Cytochrome P450 3A4 inhibitor (less than ritonavir)	Room temperature	• Nephrolithiasis • GI intolerance, nausea • Lab: Increased indirect bilirubinemia (inconsequential) • Misc.: Headache, asthenia, blurred vision, dizziness, rash, metallic taste, thrombocytopenia, alopecia, and hemolytic anemia • Hyperglycemia† • Fat redistribution and lipid abnormalities‡ • Possible increased bleeding episodes in patients with hemophilia

Table 17: two of two pages

Table 17. Characteristics of Protease Inhibitors (PIs)

Generic Name/ Trade Name	Form	Dosing Recommendations	Food Effect	Oral Bio-availability	Serum half-life	Route of Metabolism	Storage	Adverse Events
Lopinavir + Ritonavir/ Kaletra®	Each capsule contains lopinavir 133.3mg+ ritonavir 33.3 mg Oral solution: Each mL contains lopinavir 80 mg+ ritonavir 20 mg	400 mg lopinavir + 100 mg ritonavir (3 capsules) two times/day	Moderate fat meal increases AUC of capsules and solution by 48% and 80%, respectively. Take with food.	Not determined in humans	5–6 hours	Cytochrome P450 (3A4 inhibitor)	Refrigerated capsules are stable until date on label expires; if stored at room temperature stable for 2 months	• GI intolerance, nausea, vomiting, diarrhea • Asthenia • Elevated serum transaminases • Hyperglycemia† • Fat redistribution and lipid abnormalities‡ • Possible increased bleeding episodes in patients with hemophilia • Oral solution contains 42% alcohol
Nelfinavir/ Viracept®	250 mg tablets 625 mg tablets - FDA approved, not yet in market 50 mg/g oral powder	750 mg three times/day or 1,250 mg two times/day	Levels increase 2-3 fold Take with meal or snack	20–80%	3.5–5 hours	Cytochrome P450 (3A4 inhibitor; less than ritonavir)	Room temperature	• Diarrhea • Hyperglycemia† • Fat redistribution and lipid abnormalities‡ • Possible increased bleeding episodes among patients with hemophilia • Serum transaminase elevation
Ritonavir/ Norvir®	100 mg capsules 600 mg/7.5 mL solution	600 mg every 12 hours* (when ritonavir is used as sole PI) See Table 22 for alternative dosing suggestions when ritonavir is used as a pharmacokinetic enhancer for other PIs	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 for ≤30 days; Oral solution should NOT be refrigerated	• GI intolerance, nausea, vomiting, diarrhea • Paresthesias – circumoral and extremities • Hepatitis • Pancreatitis • Asthenia • Taste perversion • Lab.: Triglycerides increase > 200%, transaminase elevation, elevated CPK and uric acid • Hyperglycemia† • Fat redistribution and lipid abnormalities‡ • Possible increased bleeding episodes in patients with hemophilia
Saquinavir hard gel capsule/ Invirase®	200 mg capsules	Invirase is not recommended to be used as sole PI With Ritonavir: • (ritonavir 100 mg + Invirase 1,000 mg) two times/day • ritonavir 400 mg + Invirase 400 mg two times/day	No food effect when taken with ritonavir	4% erratic	1–2 hours	Cytochrome P450 (3A4 inhibitor (less than ritonavir)	Room temperature	• GI intolerance, nausea and diarrhea • Headache • Elevated transaminase enzymes • Hyperglycemia † • Fat redistribution and lipid abnormalities ‡ • Possible increased bleeding episodes in patients with hemophilia
Saquinavir soft gel capsule/ Fortovase®	200 mg capsules	1,200 mg three times/day With Ritonavir: • (ritonavir 100 mg + Fortovase 1,000 mg) two times/day • ritonavir 400 mg + Fortovase 400 mg two times/day	Levels increase 6-fold. Take with large meal	Not determined	1–2 hours	Cytochrome P450 (3A4 inhibitor (less than ritonavir)	Refrigerate or store at room temperature (up to 3 months)	• GI intolerance, nausea, diarrhea, abdominal pain and dyspepsia • Headache • Elevated transaminase enzymes • Hyperglycemia† • Fat redistribution and lipid abnormalities‡ • Possible increased bleeding episodes in patients with hemophilia

NOTE: For information regarding drug interactions, see Tables 20-23.

† Cases of worsening glycemic control among patients with preexisting diabetes, and cases of new-onset diabetes, including diabetic ketoacidosis, have been reported with the use of all protease inhibitors.

‡ Patients with hypertriglyceridemia or hypercholesterolemia should be evaluated for risk for cardiovascular events and pancreatitis. Interventions can include dietary modification, lipid-lowering agents, or discontinuation of PIs.

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