Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

Downloaded from http://aidsinfo.nih.gov/guidelines on 3/18/2013

Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated February 12, 2013; last reviewed February 12, 2013) (page 1 of 5)

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, and 300 mg capsules	ARV-naive patients: 400 mg once daily, or (ATV 300 mg + RTV 100 mg) once daily With TDF or in ARV-experienced patients: (ATV 300 mg + RTV 100 mg) once daily With EFV in ARV-naive patients: (ATV 400 mg + RTV 100 mg) once daily **For recommendations on dosing with H2 antagonists and PPIs, refer to Table 16a.** Take with food	CYP3A4 inhibitor and substrate Dosage adjustment in patients with hepatic insufficiency is recommended. (see Appendix B, Table 7).	7 hours	Room temperature (up to 25ºC or 77ºF)	• Indirect hyperbilirubinemia • PR interval prolongation: First degree symptomatic 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 • Cholelithiasis • Nephrolithiasis • Skin rash (20%) • Serum transaminase elevations • Hyperlipidemia (especially with RTV boosting)
Darunavir (DRV)/ Prezista	75, 150, 300, 400, 600, and 800 mg tablets 100 mg/mL oral suspension	ARV-naive 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 hours (when combined with RTV)	Room temperature (up to 25ºC or 77ºF)	• Skin rash (10%): DRV has a sulfonamide moiety; Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, 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

Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated February 12, 2013; last reviewed February 12, 2013) (page 2 of 5)

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.)
Fosamprenavir (FPV)/ Lexiva (a prodrug of amprenavir [APV])	• 700 mg tablet • 50 mg/mL oral suspension	ARV-naive patients: FPV 1400 mg BID, or (FPV 1400 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 1400 mg + RTV 300 mg) once daily *Tablet:* Take without regard to meals (if not boosted with RTV tablet) *Suspension:* Take without food *FPV with RTV tablet:* Take with meals	APV is a CYP3A4 substrate, inhibitor, and inducer. Dosage adjustment in patients with hepatic insufficiency is recommended (see Appendix B, Table 7).	7.7 hours (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
Indinavir (IDV)/ Crixivan	100, 200, and 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 patients with hepatic insufficiency is recommended (see Appendix B, Table 7).	1.5–2 hours	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

Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated February 12, 2013; last reviewed February 12, 2013) (page 3 of 5)

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.)
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-naive 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 hours	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 for up to 2 months when stored at room temperature (up to 25ºC or 77ºF).	• 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 and 625 mg tablets • 50 mg/g oral powder	1250 mg BID or 750 mg TID Dissolve tablets in a small amount of water, mix admixture well, and consume immediately. Take with food	CYP2C19 and 3A4 substrate—metabolized to active M8 metabolite; CYP 3A4 inhibitor	3.5–5 hours	Room temperature (15º–30ºC/ 59º–86ºF)	• Diarrhea • Hyperlipidemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • Serum transaminase elevation

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 tablet • 100 mg soft gel capsule • 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:* To improve tolerability, take with food if possible.	CYP3A4 >2D6 substrate; potent 3A4, 2D6 inhibitor	3–5 hours	Tablets do not require refrigeration. Refrigerate capsules. Capsules can be left at room temperature (up to 25ºC or 77ºF) for up to 30 days. 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 (SQV)/ Invirase	• 500 mg tablet • 200 mg hard gel capsule	(SQV 1000 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 hours	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).

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.)
Tipranavir (TPV)/ Aptivus	• 250 mg capsule • 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	CYP P450 3A4 inducer and substrate Net effect when combined with RTV (CYP 3A4, 2D6 inhibitor)	6 hours 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 bottle is opened.	• Hepatotoxicity: Clinical hepatitis (including hepatic decompensation and hepatitis-associated fatalities) has been reported; monitor patients closely, especially those 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

Key to Abbreviations: APV = amprenavir, ARV = antiretroviral, ATV = atazanavir, AV = atrioventricular, BID = twice daily, CYP = cytochrome P, DRV = darunavir, EFV = efavirenz, FPV = fosamprenavir, GI = gastrointestinal, IDV = indinavir, LPV = lopinavir, LPV/r = lopinavir + ritonavir, msec = millisecond, NFV = nelfinavir, NVP = nevirapine, PI = protease inhibitor, PPI = proton pump inhibitor, RTV = ritonavir, SQV = saquinavir, TDF = tenofovir disoproxil fumarate, TID = three times a day, TPV = tipranavir