Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

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Appendix B, Table 5. Characteristics of Protease Inhibitors (Last updated July 10, 2019; last reviewed July 10, 2019) (page 1 of 6)

Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Atazanavir (ATV) *Reyataz* (ATV/c) *Evotaz* **Note:** Generic capsule formulations of ATV are available.	**Reyataz:** • 150, 200, and 300 mg capsules • 50 mg single packet oral powder **Evotaz:** • ATV 300 mg/ COBI 150 mg tablet	**Reyataz** *In ARV-Naive Patients:* • (ATV 300 mg plus RTV 100 mg) once daily; *or* • ATV 400 mg once daily • Take with food. *With TDF or in ARV-Experienced Patients:* • (ATV 300 mg plus RTV 100 mg) once daily • Unboosted ATV **is not recommended**. • Take with food. *With EFV in ARV-Naive Patients:* • (ATV 400 mg plus RTV 100 mg) once daily • Take with food. **Evotaz:** • One tablet once daily • Take with food. • The use of ATV/c **is not recommended** for patients who are taking TDF and who have with baseline CrCl <70 mL/min (see Appendix B, Table 10 for the equation for calculating CrCl). For dosing recommendations with H2 antagonists and PPIs, refer to Table 21a	**ATV:** • CYP3A4 inhibitor and substrate • Weak CYP2C8 inhibitor • UGT1A1 inhibitor **COBI:** • CYP3A inhibitor and substrate • CYP2D6 inhibitor Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 10).	7 hours	Indirect hyperbilirubinemia PR interval prolongation. First degree symptomatic AV block has been reported. Use with caution in patients who have underlying conduction defects or who are on concomitant medications that can cause PR prolongation. Cholelithiasis Nephrolithiasis Renal insufficiency Serum transaminase elevations Hyperlipidemia (especially with RTV boosting) Skin rash Hyperglycemia Fat maldistribution An increase in serum creatinine may occur when ATV is administered with COBI

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Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Darunavir (DRV) *Prezista* (DRV/c) *Prezcobix*	**Prezista:** • 75, 150, 600, and 800 mg tablets • 100 mg/mL oral suspension **Prezcobix:** • DRV 800 mg/ COBI 150 mg tablet Also available as part of the STR Symtuza (DRV/c/ TAF/FTC)	**Prezista** *In ARV-Naive Patients or ARV-Experienced Patients with No DRV Mutations:* • (DRV 800 mg plus RTV 100 mg) once daily • Take with food. *In ARV-Experienced Patients with One or More DRV Resistance Mutations:* • (DRV 600 mg plus RTV 100 mg) twice daily • Take with food. Unboosted DRV **is not recommended**. **Prezcobix:** • One tablet once daily • Take with food. • **Not recommended** for patients with one or more DRV resistance-associated mutations. • Coadministering Prezcobix and TDF **is not recommended** for patients with baseline CrCl <70 mL/ min (see Appendix B, Table 10 for the equation for calculating CrCl). See Appendix B, Table 1 for dosing information for Symtuza.	**DRV:** • CYP3A4 inhibitor and substrate • CYP2C9 inducer **COBI:** • CYP3A inhibitor and substrate • CYP2D6 inhibitor	15 hours when combined with RTV 7 hours when combined with COBI	**Skin Rash:** DRV has a sulfonamide moiety; Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and erythema multiforme have been reported. Hepatotoxicity Diarrhea, nausea Headache Hyperlipidemia Serum transaminase elevation Hyperglycemia Fat maldistribution An increase in serum creatinine may occur when DRV is administered with COBI

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Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Fosamprenavir (FPV, a prodrug of APV) *Lexiva* **Note:** Generic is available.	**Lexiva:** • 700 mg tablet • 50 mg/mL oral suspension	*In ARV-Naive Patients:* • FPV 1,400 mg twice daily, *or* • (FPV 1,400 mg plus RTV 100–200 mg) once daily, *or* • (FPV 700 mg plus RTV 100 mg) twice daily *In PI-Experienced Patients:* • (FPV 700 mg plus RTV 100 mg) twice daily • Once-daily dosing **is not recommended** for these patients *In Patients Taking EFV:* • (FPV 700 mg plus RTV 100 mg) twice daily, *or* • (FPV 1,400 mg plus RTV 300 mg) once daily **Food Restrictions** *Without RTV Tablet:* • Take the FPV tablet without regard to meals. *With RTV Tablet:* • Take the RTV tablet and FPV tablet with meals. *Oral Suspension:* • Take without food.	APV is a CYP3A4 substrate, inhibitor, and inducer. Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 10).	7.7 hours (APV)	Skin rash has been reported in 12% to 19% of patients on FPV. FPV has a sulfonamide moiety. Diarrhea, nausea, vomiting Headache Hyperlipidemia Serum transaminase elevation Hyperglycemia Fat maldistribution Possible increase in the frequency of bleeding episodes in patients with hemophilia Nephrolithiasis
Indinavir (IDV) *Crixivan*	**Crixivan:** • 200 and 400 mg capsules	**Crixivan:** • IDV 800 mg every 8 hours • Take 1 hour before or 2 hours after meals; may take with skim milk or a low-fat meal. *With RTV:* • (IDV 800 mg plus RTV 100–200 mg) twice daily • Take without regard to meals. Patients should drink at least 48 ounces of water daily while taking IDV.	CYP3A4 inhibitor and substrate Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 10).	1.5–2 hours	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 increase in the frequency of bleeding episodes in patients with hemophilia

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Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Lopinavir/ Ritonavir (LPV/r) *Kaletra* **Note:** LPV is only available as a component of an FDC tablet that also contains RTV.	**Kaletra:** • LPV/r 200 mg/50 mg tablets • LPV/r 100 mg/25 mg tablets • LPV/r 400 mg/100 mg per 5 mL of oral solution. Oral solution contains 42% alcohol.	**Kaletra:** • LPV/r 400 mg/100 mg twice daily, *or* • LPV/r 800 mg/200 mg once daily. However, Once-daily dosing **is not recommended** for patients with three or more LPV-associated mutations, pregnant women, or patients receiving EFV, NVP, FPV, NFV, carbamazepine, phenytoin, or phenobarbital. *With EFV or NVP in PI-Naive or PI-Experienced Patients:* • LPV/r 500 mg/125 mg tablets twice daily (use a combination of two LPV/r 200 mg/50 mg tablets plus 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 twice daily **Food Restrictions** *Tablet:* • Take without regard to meals. *Oral Solution:* • Take with food.	CYP3A4 inhibitor and substrate	5–6 hours	GI intolerance, nausea, vomiting, diarrhea Pancreatitis Asthenia Hyperlipidemia (especially hypertriglyceridemia) Serum transaminase elevation Hyperglycemia Insulin resistance/diabetes mellitus Fat maldistribution Possible increase in the frequency of 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*	**Viracept:** • 250 and 625 mg tablets	**Viracept:** • NFV 1,250 mg twice daily, *or* • NFV 750 mg three times a day 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 CYP3A4 inhibitor	3.5–5 hours	Diarrhea Hyperlipidemia Hyperglycemia Fat maldistribution Possible increase in the frequency of bleeding episodes in patients with hemophilia Serum transaminase elevation

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Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Ritonavir (RTV) *Norvir* **Note:** Generic is available. Although RTV was initially developed as a PI for HIV treatment, RTV is currently used at a lower dose of 100 mg to 200 mg once or twice daily as a PK enhancer to increase the concentrations of other PIs.	**Norvir:** • 100 mg tablet • 100 mg soft gel capsule • 80 mg/mL oral solution. Oral solution contains 43% alcohol. • 100 mg single packet oral powder Also available as part of the FDC tablet Kaletra (LPV/r)	**As a PK Booster (or Enhancer) for Other PIs:** • RTV 100–400 mg per day in one or two divided doses (refer to other PIs for specific dosing recommendations). **Food Restrictions** *Tablet:* • Take with food. *Capsule and Oral Solution:* • To improve tolerability, take with food if possible.	CYP3A4 > 2D6 substrate Potent CYP3A4 and 2D6 inhibitor Inducer of UGT1A1 and CYPs 1A2, 2C8, 2C9, and 2C19	3–5 hours	GI intolerance, nausea, vomiting, diarrhea Paresthesia (circumoral and extremities) Hyperlipidemia (especially hypertriglyceridemia) Hepatitis Asthenia Taste perversion Hyperglycemia Fat maldistribution Possible increase in the frequency of bleeding episodes in patients with hemophilia
Saquinavir (SQV) *Invirase*	**Invirase:** • 500 mg tablet • 200 mg capsule	**Invirase:** • (SQV 1,000 mg plus RTV 100 mg) twice daily Unboosted SQV **is not recommended**. Take with meals or within 2 hours after a meal.	CYP3A4 substrate	1–2 hours	GI intolerance, nausea, and diarrhea Headache Serum transaminase elevation Hyperlipidemia Hyperglycemia Fat maldistribution Possible increase in the frequency of bleeding episodes in patients with hemophilia PR interval prolongation QT interval prolongation. Cases of Torsades de Pointes have been reported. Patients with pre-SQV QT intervals >450 msec should not receive SQV.

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Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Tipranavir (TPV) *Aptivus*	**Aptivus:** • 250 mg capsule • 100 mg/mL oral solution	**Aptivus:** • (TPV 500 mg plus RTV 200 mg) twice daily • Unboosted TPV **is not recommended**. **Food Restrictions** *With RTV Tablets:* • Take with meals. *With RTV Capsules or Solution:* • Take without regard to meals.	CYP3A4 inducer and substrate CYP2D6 inhibitor; CYP3A4, 1A2, and 2C19 inducer Net effect of combining TPV and RTV is a CYP3A4 and 2D6 inhibitor	6 hours after single dose of TPV/r	Hepatotoxicity. Clinical hepatitis (including hepatic decompensation and hepatitis-associated fatalities) has been reported; monitor patients closely, especially those 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. Risks include brain lesion, head trauma, recent neurosurgery, coagulopathy, hypertension, alcoholism, and the use of anticoagulant or antiplatelet agents (including vitamin E). Hyperlipidemia Hyperglycemia Fat maldistribution Possible increase in the frequency of bleeding episodes in patients with hemophilia

[a] For dose adjustments in patients with hepatic insufficiency, see Appendix B, Table 10.

[b] Also see Table 17.

Key: APV = amprenavir; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; AV = atrioventricular; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; EFV = efavirenz; FDC = fixed-dose combination; FPV = fosamprenavir; FTC = emtricitabine; GI = gastrointestinal; IDV = indinavir; LPV = lopinavir; LPV/r = lopinavir/ritonavir; msec = millisecond; NFV = nelfinavir; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; RTV = ritonavir; SQV = saquinavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; UGT = uridine diphosphate glucuronyl transferase