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

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Appendix B, Table 3. Characteristics of Protease Inhibitors  *(Last updated October 25, 2018; last reviewed October 25, 2018)*  (page 1 of 6)

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<th>Dosing Recommendations*</th>
<th>Elimination/Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Adverse Events*</th>
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<tbody>
<tr>
<td>Atazanavir (ATV) Reyataz</td>
<td>Reyataz:  • 150, 200, and 300 mg capsules  • 50 mg single packet oral powder</td>
<td>In ARV-Naive Patients:  • (ATV 300 mg plus RTV 100 mg) once daily; or  • ATV 400 mg once daily  With TDF or in ARV-Experienced Patients:  • (ATV 300 mg plus RTV 100 mg) once daily  With EFV in ARV-Naive Patients:  • (ATV 400 mg plus RTV 100 mg) once daily  Take with food.  For dosing recommendations with H2 antagonists and PPIs, refer to Table 19a.</td>
<td>CYP3A4 inhibitor and substrate; weak CYP2C8 inhibitor; UGT1A1 inhibitor  Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 8).</td>
<td>7 hours</td>
<td>• Indirect hyperbilirubinemia  • PR interval prolongation: First degree symptomatic AV block reported. Use with caution in patients who have underlying conduction defects or who are on concomitant medications that can cause PR prolongation.  • Hyperglycemia  • Fat maldistribution  • Cholelithiasis  • Nephrolithiasis  • Renal insufficiency  • Serum transaminase elevations  • Hyperlipidemia (especially with RTV boosting)  • Skin rash  • Increase in serum creatinine (with COBI)</td>
</tr>
<tr>
<td>(ATV/c) Evotaz</td>
<td>Evotaz:  • (ATV 300 mg plus COBI 150 mg) tablet</td>
<td>Evotaz:  • 1 tablet once daily  • Take with food.  With TDF:  • Not recommended for patients with baseline CrCl &lt;70 mL/min (see Appendix B, Table 8 for the equation for calculating CrCl).</td>
<td>ATV: as above  COBI: CYP3A inhibitor and substrate; CYP2D6 inhibitor</td>
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### Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018) (page 2 of 6)

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| **Darunavir (DRV) Prezista**           | Prezista:    | In ARV-Naive Patients or ARV-Experienced Patients with No DRV Mutations:  
• 75, 150, 600, and 800 mg tablets  
• 100 mg/mL oral suspension  
Unboosted DRV is not recommended.  
Take with food.  
In ARV-Experienced Patients with One or More DRV Resistance Mutations:  
• (DRV 600 mg plus RTV 100 mg) 
BID  
| CYP3A4 inhibitor and substrate; CYP2C9 inducer | 15 hours (when combined with RTV) | • Skin rash (10%): 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  
|  |  |  |  |  |  |
| **(DRV/c) Prezcobix**                  | Prezcobix:   | In ARV-Naive Patients or ARV-Experienced Patients with No DRV Mutations:  
• (DRV 800 mg plus RTV 100 mg) once daily  
Unboosted DRV is not recommended.  
Take with food.  
In ARV-Experienced Patients with One or More DRV Resistance Mutations:  
• (DRV 600 mg plus RTV 100 mg) BID  
| CYP3A4 inhibitor and substrate; CYP2C9 inducer; CYP2D6 inhibitor | 7 hours (when combined with COBI) | • Hyperglycemia  
• Fat maldistribution  
|  |  |  |  |  |  |
| **(DRV/c/TAF/FTC) Symtuza**           | Symtuza:     | In ARV-Naive Patients or ARV-Experienced Patients with No DRV Mutations:  
• (DRV 800 mg plus RTV 100 mg plus TAF 10 mg plus FTC 200 mg) once daily  
Unboosted DRV is not recommended.  
Take with food.  
In ARV-Experienced Patients with One or More DRV Resistance Mutations:  
• (DRV 600 mg plus RTV 100 mg) BID  
| CYP3A4 inhibitor and substrate; CYP2C9 inducer; CYP2D6 inhibitor | 7 hours (when combined with COBI) | • Hyperglycemia  
• Fat maldistribution  
|  |  |  |  |  |  |

* Dosing Recommendations for adult patients with normal renal and hepatic function unless otherwise specified.

b Adverse Events that may occur when used in combination with ritonavir-boosted protease inhibitors.
**Appendix B, Table 3. Characteristics of Protease Inhibitors** *(Last updated October 25, 2018; last reviewed October 25, 2018)*

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<tr>
<td>Fosamprenavir (FPV, a prodrug of APV)</td>
<td>Lexiva</td>
<td>Lexiva:  • 700 mg tablet  • 50 mg/mL oral suspension</td>
<td>In ARV-Naive Patients:  • FPV 1400 mg BID, or  • (FPV 1400 mg plus RTV 100–200 mg) once daily, or  • (FPV 700 mg plus RTV 100 mg) BID</td>
<td>APV is a CYP3A4 substrate, inhibitor, and inducer. Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 8).</td>
<td>7.7 hours (APV)</td>
<td>• Skin rash (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</td>
</tr>
<tr>
<td>Note: Generic is available.</td>
<td></td>
<td></td>
<td>In PI-Experienced Patients (Once-Daily Dosing Not Recommended):  • (FPV 700 mg plus RTV 100 mg) BID</td>
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<td></td>
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<td>With EFV:  • (FPV 700 mg plus RTV 100 mg) BID, or  • (FPV 1400 mg plus RTV 300 mg) once daily</td>
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<td>Tablet:  • Without RTV tablet: Take without regard to meals.  • With RTV tablet: Take with meals. Oral Suspension:  • Take without food.</td>
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<td>Indinavir (IDV)</td>
<td>Crixivan</td>
<td>Crixivan:  • 200 and 400 mg capsules</td>
<td>CYP3A4 inhibitor and substrate</td>
<td>1.5–2 hours</td>
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### Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018) (page 4 of 6)

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| **Lopinavir/ Ritonavir (LPV/r) Kaletra** | Kaletra:     | (LPV 200 mg plus RTV 50 mg), or (LPV 100 mg plus RTV 25 mg) Kaletra: (LPV 400 mg plus RTV 100 mg) BID, or (LPV 800 mg plus RTV 200 mg) once daily. | 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 1250 mg BID, or NFV 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; 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 |
### Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018) (page 5 of 6)

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| **Ritonavir** (RTV)        | Norvir     | Norvir:      | As PK Booster (or Enhancer) for Other PIs: | CYP3A4 > 2D6 substrate; potent 3A4, 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 |
| Note: Generic is available! |            | • 100 mg tablet  
• 100 mg soft gel capsule  
• 80 mg/mL oral solution  
• 100 mg single packet oral powder  
• Oral solution contains 43% alcohol. | • RTV 100–400 mg per day in 1 or 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. | | |
| **Saquinavir** (SQV)       | Invirase   | Invirase:    | Invirase: (SQV 1000 mg plus RTV 100 mg) BID  
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, torsades de pointes have been reported. Patients with pre-SQV QT interval >450 msec should not receive SQV. |
### Tipranavir (TPV) Aptivus

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<td>Tipranavir (TPV) Aptivus</td>
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<td></td>
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<td></td>
<td>CYP3A4 inducer and substrate</td>
<td>6 hours after single dose of TPV/r</td>
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<td></td>
<td></td>
<td></td>
<td>Unboosted TPV is not recommended.</td>
<td>CYP2D6 inhibitor; CYP3A4, 1A2, and 2C19 inducer</td>
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<td>With RTV Tablets:</td>
<td>Net effect of combining TPV and RTV is a CYP3A4 and 2D6 inhibitor</td>
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<td></td>
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<td></td>
<td>• Take with meals.</td>
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<td>With RTV Capsules or Solution:</td>
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<td>• Take without regard to meals.</td>
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</tbody>
</table>

**For dose adjustments in patients with hepatic insufficiency, see Appendix B, Table 8.**

**Also see Table 15.**

**Key to Acronyms:** APV = amprenavir; ARV = antiretroviral; ATV = atazanavir; AV = atrioventricular; BID = twice daily; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; EFV = efavirenz; FPV = fosamprenavir; FTC = emtricitabine; GI = gastrointestinal; IDV = indinavir; LPV = lopinavir; LPV/r = lopinavir/ritonavir; msec = millisecond; NFP = nelfinavir; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; RTV = ritonavir; SQV = saquinavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TID = three times a day; TPV = tipranavir; UGT = uridine diphosphate glucuronosyltransferase