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

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<th>Generic Name (Abbreviations)</th>
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<th>Dosing Recommendations&lt;sup&gt;a&lt;/sup&gt;</th>
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<th>Serum Half-Life</th>
<th>Adverse Events&lt;sup&gt;b&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>Atazanavir (ATV) Reyataz</td>
<td>Reyataz</td>
<td></td>
<td>ATV:</td>
<td>7 hours</td>
<td>Indirect hyperbilirubinemia</td>
</tr>
<tr>
<td>(ATV/c) Evotaz</td>
<td></td>
<td>In ARV-Naive Patients:</td>
<td>• CYP3A4 inhibitor and substrate</td>
<td>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</td>
<td></td>
</tr>
<tr>
<td>Note: Generic capsule formulations of ATV are available.</td>
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</tr>
</tbody>
</table>

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**Reyataz**
- **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
**Appendix B, Table 5. Characteristics of Protease Inhibitors** *(Last updated July 10, 2019; last reviewed July 10, 2019)* *(page 2 of 6)*

<table>
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<tr>
<th>Generic Name (Abbreviations)</th>
<th>Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendations(^a)</th>
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<th>Adverse Events(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darunavir (DRV)</td>
<td>Prezista</td>
<td>Prezista:</td>
<td>Prezista</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(DRV/c)</td>
<td>Prezcobix</td>
<td>• 75, 150, 600, and 800 mg tablets&lt;br&gt;• 100 mg/mL oral suspension</td>
<td>• DRV 800 mg plus RTV 100 mg) once daily&lt;br&gt;• Take with food.</td>
<td>DRV: &lt;br&gt;• CYP3A4 inhibitor and substrate&lt;br&gt;• CYP2C9 inducer</td>
<td>7 hours when combined with RTV&lt;br&gt;15 hours when combined with COBI</td>
<td>Skin Rash: DRV has a sulfonamide moiety; Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and erythema multiforme have been reported.&lt;br&gt;Hepatotoxicity&lt;br&gt;Diarrhea, nausea&lt;br&gt;Headache&lt;br&gt;Hyperlipidemia&lt;br&gt;Serum transaminase elevation&lt;br&gt;Hyperglycemia&lt;br&gt;Fat maldistribution&lt;br&gt;An increase in serum creatinine may occur when DRV is administered with COBI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prezcobix:</td>
<td>• DRV 800 mg/ COBI 150 mg tablet</td>
<td>• DRV 600 mg plus RTV 100 mg) twice daily&lt;br&gt;• Take with food.</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Also available as part of the STR Symtuza (DRV/c/ TAF/FTC)</td>
<td>Unboosted DRV is not recommended.</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Prezcobix:</td>
<td>• One tablet once daily&lt;br&gt;• Take with food.&lt;br&gt;• Not recommended for patients with one or more DRV resistance-associated mutations. &lt;br&gt;• Coadministering Prezcobix and TDF is not recommended for patients with baseline CrCl &lt;70 mL/ min (see Appendix B, Table 10 for the equation for calculating CrCl).</td>
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</tbody>
</table>

\(^a\) Dosing recommendations include dosing with and without ritonavir (RTV) and the coadministration of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC).

\(^b\) Adverse events listed are those associated with darunavir and/or cobicistat (COBI) and are included as examples. Adverse events not specifically listed for darunavir and/or cobicistat may also occur.
### Fosamprenavir

**Generic Name:** Fosamprenavir (FPV, a prodrug of APV)  
**Trade Name:** Lexiva

**Note:** Generic is available.

**Formulations:**
- 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.

**Elimination/Metabolic Pathway:**
- APV is a CYP3A4 substrate, inhibitor, and inducer.
- Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 10).

**Serum Half-Life:**
- 7.7 hours (APV)

**Adverse Events:**
- 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

**Generic Name:** Indinavir (IDV)  
**Trade Name:** Crixivan

**Formulations:**
- 200 and 400 mg capsules

**In ARV-Naive Patients:**
- 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.**

**Elimination/Metabolic Pathway:**
- CYP3A4 inhibitor and substrate
- Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 10).

**Serum Half-Life:**
- 1.5–2 hours

**Adverse Events:**
- 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
### Appendix B, Table 5. Characteristics of Protease Inhibitors *(Last updated July 10, 2019; last reviewed July 10, 2019)* (page 4 of 6)

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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Lopinavir/Ritonavir</strong> <em>(LPV/r)</em></td>
<td>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. <strong>Note:</strong> LPV is only available as a component of an FDC tablet that also contains RTV.</td>
<td>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</td>
<td>CYP3A4 inhibitor and substrate</td>
<td>5–6 hours</td>
<td>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.</td>
</tr>
<tr>
<td><strong>Nelfinavir</strong> <em>(NFV)</em></td>
<td>Viracept:  - 250 and 625 mg tablets</td>
<td>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.</td>
<td>CYP2C19 and 3A4 substrate; metabolized to active M8 metabolite CYP3A4 inhibitor</td>
<td>3.5–5 hours</td>
<td>Diarrhea  Hyperlipidemia  Hyperglycemia  Fat maldistribution  Possible increase in the frequency of bleeding episodes in patients with hemophilia  Serum transaminase elevation</td>
</tr>
</tbody>
</table>
## Appendix B, Table 5. Characteristics of Protease Inhibitors (Last updated July 10, 2019; last reviewed July 10, 2019) (page 5 of 6)

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</tr>
</thead>
<tbody>
<tr>
<td>Ritonavir (RTV) Norvir</td>
<td></td>
<td>Norvir:</td>
<td>As a PK Booster (or Enhancer) for Other PIs:</td>
<td>CYP3A4 &gt; 2D6 substrate</td>
<td>3–5 hours</td>
<td>GI intolerance, nausea, vomiting, diarrhea</td>
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<tr>
<td></td>
<td></td>
<td>• 100 mg tablet</td>
<td>• RTV 100–400 mg per day in one or two divided doses (refer to other PIs for specific dosing recommendations).</td>
<td>Potent CYP3A4 and 2D6 inhibitor</td>
<td></td>
<td>Paresthesia (circumoral and extremities)</td>
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<td></td>
<td></td>
<td>• 100 mg soft gel capsule</td>
<td></td>
<td>Inducer of UGT1A1 and CYPs 1A2, 2C8, 2C9, and 2C19</td>
<td></td>
<td>Hyperlipidemia (especially hypertriglyceridemia)</td>
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<tr>
<td></td>
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<td>• 80 mg/mL oral solution. Oral solution contains 43% alcohol.</td>
<td></td>
<td></td>
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<td>Hepatitis</td>
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<td>• 100 mg single packet oral powder</td>
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<td>Asthenia</td>
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<td></td>
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<td>Also available as part of the FDC tablet Kaletra (LPV/r)</td>
<td></td>
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<td>Taste perversion</td>
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<td>Hyperglycemia</td>
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<td>Fat maldistribution</td>
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<td></td>
<td>Possible increase in the frequency of bleeding episodes in patients with hemophilia</td>
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<tr>
<td>Saquinavir (SQV) Invirase</td>
<td></td>
<td>Invirase:</td>
<td></td>
<td>CYP3A4 substrate</td>
<td>1–2 hours</td>
<td>GI intolerance, nausea, and diarrhea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 500 mg tablet</td>
<td>Unboosted SQV is not recommended.</td>
<td></td>
<td></td>
<td>Headache</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 200 mg capsule</td>
<td>Take with meals or within 2 hours after a meal.</td>
<td></td>
<td></td>
<td>Serum transaminase elevation</td>
</tr>
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<td></td>
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<td></td>
<td></td>
<td>Hyperlipidemia</td>
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<td></td>
<td></td>
<td></td>
<td>Hyperglycemia</td>
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<td></td>
<td></td>
<td>Fat maldistribution</td>
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<td></td>
<td>Possible increase in the frequency of bleeding episodes in patients with hemophilia</td>
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<td></td>
<td>PR interval prolongation</td>
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<td></td>
<td>QT interval prolongation. Cases of Torsades de Pointes have been reported. Patients with pre-SQV QT intervals &gt;450 msec should not receive SQV.</td>
</tr>
</tbody>
</table>
### Tipranavir (TPV) Aptivus

<table>
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</tr>
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</table>
| • 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 |

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<td><strong>Tipranavir (TPV) Aptivus</strong></td>
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</tr>
</tbody>
</table>

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 = atiroventricular; 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