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

<table>
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<tr>
<th>Generic Name (Abbreviations)</th>
<th>Formulations</th>
<th>Dosing Recommendations&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Elimination/Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Adverse Events&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atazanavir (ATV) Reyataz</td>
<td>Reyataz</td>
<td>In ARV-Naive Patients:</td>
<td>AT:</td>
<td>7 hours</td>
<td>Indirect hyperbilirubinemia</td>
</tr>
<tr>
<td>(ATV/c) Evotaz</td>
<td></td>
<td>• (ATV 300 mg plus RTV 100 mg) once daily; or</td>
<td>• CYP3A4 inhibitor and substrate</td>
<td></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.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ATV 400 mg once daily</td>
<td>• Weak CYP2C8 inhibitor</td>
<td></td>
<td>Cholelithiasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Take with food.</td>
<td>• UGT1A1 inhibitor</td>
<td></td>
<td>Nephrolithiasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>With TDF or in ARV-Experienced Patients:</td>
<td></td>
<td></td>
<td>Serum transaminase elevations</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• (ATV 300 mg plus RTV 100 mg) once daily</td>
<td></td>
<td></td>
<td>Hyperlipidemia (especially with RTV boosting)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Unboosted ATV is not recommended.</td>
<td></td>
<td></td>
<td>Skin rash</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Take with food.</td>
<td></td>
<td></td>
<td>Hyperglycemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>With EFV in ARV-Naive Patients:</td>
<td></td>
<td></td>
<td>Fat maldistribution</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• (ATV 400 mg plus RTV 100 mg) once daily</td>
<td></td>
<td></td>
<td>An increase in serum creatinine may occur when ATV is administered with COBI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Take with food.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Evotaz:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ATV 300 mg/COBI 150 mg tablet</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The use of ATV/c is not recommended for patients who are taking TDF and who have with baseline CrCl &lt;70 mL/min (see Appendix B, Table 10 for the equation for calculating CrCl).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>For dosing recommendations with H2 antagonists and PPIs, refer to Table 21a</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**Note:** Generic capsule formulations of ATV are available.
### Appendix B, Table 5. Characteristics of Protease Inhibitors

**Last updated July 10, 2019; last reviewed July 10, 2019**

<table>
<thead>
<tr>
<th>Generic Name (Abbreviations)</th>
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<th>Dosing Recommendations(^a)</th>
<th>Elimination/Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Adverse Events(^b)</th>
</tr>
</thead>
</table>
| 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. |
### Fosamprenavir (FPV, a prodrug of APV) *Lexiva*

**Note:** Generic is available.

#### Formulations
- 700 mg tablet
- 50 mg/mL oral suspension

#### Dosing Recommendations
**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 (IDV) *Crixivan*

#### Formulations
- 200 and 400 mg capsules

#### Dosing Recommendations
**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).

#### 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

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**Appendix B, Table 5. Characteristics of Protease Inhibitors** *(Last updated July 10, 2019; last reviewed July 10, 2019)* (page 3 of 6)
### Appendix B, Table 5. Characteristics of Protease Inhibitors *(Last updated July 10, 2019; last reviewed July 10, 2019)* (page 4 of 6)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviations) Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendations&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Elimination/Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Adverse Events&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lopinavir/Ritonavir (LPV/r) Kaletra</strong></td>
<td>Kaletra:</td>
<td>Kaletra:</td>
<td>CYP3A4 inhibitor and substrate</td>
<td>5–6 hours</td>
<td>GI intolerance, nausea,</td>
</tr>
<tr>
<td><strong>Note:</strong> LPV is only available as a component of an FDC tablet that also contains RTV.</td>
<td>• LPV/r 200 mg/50 mg tablets</td>
<td>• LPV/r 400 mg/100 mg twice daily, or</td>
<td></td>
<td></td>
<td>vomiting, diarrhea</td>
</tr>
<tr>
<td></td>
<td>• LPV/r 100 mg/25 mg tablets</td>
<td>• LPV/r 800 mg/200 mg once daily. However, Once-daily dosing <strong>is not recommended</strong> for patients with three or more LPV-associated mutations, pregnant women, or patients receiving EFV, NVP, FPV, NFV, carbamazepine, phenytoin, or phenobarbital.</td>
<td></td>
<td></td>
<td>Pancreatitis</td>
</tr>
<tr>
<td></td>
<td>• LPV/r 400 mg/100 mg per 5 mL of oral solution. Oral solution contains 42% alcohol.</td>
<td></td>
<td></td>
<td></td>
<td>Asthenia</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>Hyperlipidemia (especially hypertriglyceridemia)</td>
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<td></td>
<td></td>
<td></td>
<td>Serum transaminase elevation</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hyperglycemia</td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td>Insulin resistance/diabetes mellitus</td>
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<td></td>
<td></td>
<td></td>
<td>Fat maldistribution</td>
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<td></td>
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<td></td>
<td></td>
<td>Possible increase in the frequency of bleeding episodes in patients with hemophilia</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>PR interval prolongation</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td>QT interval prolongation and Torsades de Pointes have been reported; however, causality could not be established.</td>
</tr>
<tr>
<td><strong>Nelfinavir (NFV) Viracept</strong></td>
<td>Viracept:</td>
<td>Viracept:</td>
<td>CYP2C19 and 3A4 substrate; metabolized to active M8 metabolite CYP3A4 inhibitor</td>
<td>3.5–5 hours</td>
<td>Diarrhea</td>
</tr>
<tr>
<td></td>
<td>• 250 and 625 mg tablets</td>
<td>• NFV 1,250 mg twice daily, or</td>
<td></td>
<td></td>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• NFV 750 mg three times a day</td>
<td></td>
<td></td>
<td>Hyperglycemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dissolve tablets in a small amount of water, mix admixture well, and consume immediately.</td>
<td></td>
<td></td>
<td>Fat maldistribution</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Take with food.</td>
<td></td>
<td></td>
<td>Possible increase in the frequency of bleeding episodes in patients with hemophilia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Serum transaminase elevation</td>
</tr>
<tr>
<td>Generic Name (Abbreviations)</td>
<td>Trade Name</td>
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<td>Dosing Recommendations&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>-----------------------------</td>
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</tr>
<tr>
<td><strong>Ritonavir</strong>&lt;br&gt;(RTV)&lt;br&gt;Norvir</td>
<td>Note: Generic is available.</td>
<td>Norvir:&lt;br&gt;• 100 mg tablet&lt;br&gt;• 100 mg soft gel capsule&lt;br&gt;• 80 mg/mL oral solution. Oral solution contains 43% alcohol.&lt;br&gt;• 100 mg single packet oral powder</td>
<td>As a PK Booster (or Enhancer) for Other PIs:&lt;br&gt;• RTV 100–400 mg per day in one or two divided doses (refer to other PIs for specific dosing recommendations).&lt;br&gt;<strong>Food Restrictions</strong>&lt;br&gt;Tablet:&lt;br&gt;• Take with food.&lt;br&gt;Capsule and Oral Solution:&lt;br&gt;• To improve tolerability, take with food if possible.</td>
<td>CYP3A4 &gt; 2D6 substrate&lt;br&gt;Potent CYP3A4 and 2D6 inhibitor&lt;br&gt;Inducer of UGT1A1 and CYPs 1A2, 2C8, 2C9, and 2C19</td>
<td>3–5 hours</td>
</tr>
<tr>
<td><strong>Saquinavir</strong>&lt;br&gt;(SQV)&lt;br&gt;Invirase</td>
<td>Invirase:&lt;br&gt;• 500 mg tablet&lt;br&gt;• 200 mg capsule</td>
<td>Invirase:&lt;br&gt;• (SQV 1,000 mg plus RTV 100 mg) twice daily&lt;br&gt;Unboosted SQV is not recommended.&lt;br&gt;Take with meals or within 2 hours after a meal.</td>
<td>CYP3A4 substrate</td>
<td>1–2 hours</td>
<td>GI intolerance, nausea, and diarrhea&lt;br&gt;Headache&lt;br&gt;Serum transaminase elevation&lt;br&gt;Hyperlipidemia&lt;br&gt;Hyperglycemia&lt;br&gt;Fat maldistribution&lt;br&gt;Possible increase in the frequency of bleeding episodes in patients with hemophilia&lt;br&gt;PR interval prolongation&lt;br&gt;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>

<sup>a</sup>As a PK Booster (or Enhancer) for Other PIs:

<sup>b</sup>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

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

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<th>Serum Half-Life</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tipranavir (TPV)</strong> Aptivus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aptivus:</td>
<td></td>
<td>• 250 mg capsule&lt;br&gt;• 100 mg/mL oral solution</td>
<td><strong>Aptivus</strong>:&lt;br&gt;• (TPV 500 mg plus RTV 200 mg) twice daily&lt;br&gt;• Unboosted TPV <strong>is not recommended</strong>.&lt;br&gt;&lt;br&gt;<strong>Food Restrictions</strong>&lt;br&gt;<strong>With RTV Tablets</strong>:&lt;br&gt;• Take with meals.&lt;br&gt;<strong>With RTV Capsules or Solution</strong>:&lt;br&gt;• Take without regard to meals.</td>
<td>CYP3A4 inducer and substrate&lt;br&gt;CYP2D6 inhibitor; CYP3A4, 1A2, and 2C19 inducer&lt;br&gt;Net effect of combining TPV and RTV is a CYP3A4 and 2D6 inhibitor</td>
<td>6 hours after single dose of TPV/r</td>
<td>Hepatotoxicity. Clinical hepatitis (including hepatic decompensation and hepatitis-associated fatalities) has been reported; monitor patients closely, especially those with underlying liver diseases.&lt;br&gt;Skin rash. TPV has a sulfonamide moiety; use with caution in patients with known sulfonamide allergy.&lt;br&gt;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).&lt;br&gt;Hyperlipidemia&lt;br&gt;Hyperglycemia&lt;br&gt;Fat maldistribution&lt;br&gt;Possible increase in the frequency of bleeding episodes in patients with hemophilia</td>
</tr>
</tbody>
</table>

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* For dose adjustments in patients with hepatic insufficiency, see Appendix B, Table 10.

* 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