### Appendix B, Table 3. Characteristics of Protease Inhibitors  (Last updated October 17, 2017; last reviewed October 17, 2017)  (page 1 of 6)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation) Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendations*</th>
<th>Elimination/ Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Storage</th>
<th>Adverse Events b</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Atazanavir (ATV) Reyataz</strong></td>
<td>Reyataz:</td>
<td>In ARV-Naive Patients:</td>
<td>CYP3A4 inhibitor and substrate; weak CYP2C8 inhibitor; UGT1A1 inhibitor</td>
<td>7 hours</td>
<td>Room temperature (up to 25°C or 77°F)</td>
<td>• Indirect hyperbilirubinemia</td>
</tr>
<tr>
<td></td>
<td>100, 150, 200, and 300 mg capsules</td>
<td>• (ATV 300 mg + RTV 100 mg) once daily; or • ATV 400 mg once daily</td>
<td>Dosage adjustment in patients with hepatic insufficiency is recommended (see Appendix B, Table 7).</td>
<td></td>
<td></td>
<td>• PR interval prolongation: First degree symptomatic AV block reported. Use with caution in patients with underlying conduction defects or in patients on concomitant medications that can cause PR prolongation.</td>
</tr>
<tr>
<td></td>
<td>50 mg single packet oral powder</td>
<td>With TDF or in ARV- Experienced Patients: • (ATV 300 mg + RTV 100 mg) once daily</td>
<td></td>
<td></td>
<td></td>
<td>• Hyperglycemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>With EFV in ARV-Naive Patients: • (ATV 400 mg + RTV 100 mg) once daily</td>
<td></td>
<td></td>
<td></td>
<td>• Fat maldistribution</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Take with food.</td>
<td>For recommendations on dosing with H2 antagonists and PPIs, refer to Table 18a.</td>
<td></td>
<td></td>
<td>• Cholelithiasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For recommendations on dosing with H2 antagonists and PPIs, refer to Table 18a.</td>
<td></td>
<td></td>
<td></td>
<td>• Nephrolithiasis</td>
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<td></td>
<td></td>
<td></td>
<td>• Renal insufficiency</td>
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<td></td>
<td>• Serum transaminase elevations</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>• Hyperlipidemia (especially with RTV boosting)</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Skin rash</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>• Increase in serum creatinine (with COBI)</td>
</tr>
<tr>
<td><strong>Evotaz (ATV/c)</strong></td>
<td>Evotaz:</td>
<td>(ATV 300 mg + COBI 150 mg) tablet</td>
<td>ATV: As above COBI: substrate of CYP3A, CYP2D6 (minor); CYP3A inhibitor</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>1 tablet once daily</td>
<td>Take with food.</td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>With TDF:</td>
<td>• Not recommended for patients with baseline CrCl &lt;70 mL/min (see Appendix B, Table 7 for the equation for calculating CrCl).</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Dosage recommendations vary depending on patient's health status and other medications being taken.

bAdverse events may vary depending on the specific protease inhibitor and interaction with other medications.
### Appendix B, Table 3. Characteristics of Protease Inhibitors  *(Last updated October 17, 2017; last reviewed October 17, 2017)*  (page 2 of 6)

<table>
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<tr>
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<th>Elimination/ Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Storage</th>
<th>Adverse Events&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
</table>
| Darunavir (DRV) Prezista    |            | • 75, 150, 600, and 800 mg tablets  
• 100 mg/ mL oral suspension | In ARV-Naive Patients or ARV-Experienced Patients with No DRV Mutations:  
• (DRV 800 mg + RTV 100 mg) once daily  
In ARV-Experienced Patients with 1 or More DRV Resistance Mutations:  
• (DRV 600 mg + RTV 100 mg) BID  
Unboosted DRV is not recommended.  
Take with food. | CYP3A4 inhibitor and substrate CYP2C9 inducer | 15 hours (when combined with RTV) | Room temperature (up to 25º C or 77º F) | • 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  
• Serum transaminase elevation  
• Hyperglycemia  
• Fat maldistribution  
• Increase in serum creatinine (with COBI) |
| Prezobix (DRV/c)            |            | Prezobix:  
• (DRV 800 mg + COBI 150 mg) tablet  
Prezobix:  
• 1 tablet once daily  
• Take with food.  
*Not recommended* for patients with 1 or more DRV resistance-associated mutations.  
With TDF:  
• Not recommended for patients with baseline CrCl <70 mL/min (see Appendix B, Table 7 for the equation for calculating CrCl). | DRV: As above  
COBI: substrate of CYP3A, CYP2D6 (minor); CYP3A inhibitor |
### Appendix B, Table 3. Characteristics of Protease Inhibitors  *(Last updated October 17, 2017; last reviewed October 17, 2017)*  (page 3 of 6)

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<th>Adverse Events&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fosamprenavir (FPV)</strong> <em>Lexiva</em> (a prodrug of APV)</td>
<td>• 700 mg tablet  • 50 mg/mL oral suspension</td>
<td>In 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</td>
<td>APV is a CYP3A4 substrate, inhibitor, and inducer. Dosage adjustment in patients with hepatic insufficiency is recommended (see Appendix B, Table 7).</td>
<td>7.7 hours (APV)</td>
<td>Room temperature (up to 25º C or 77º F)</td>
<td>• Skin rash (12% to 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</td>
</tr>
<tr>
<td><strong>Indinavir (IDV)</strong> <em>Crixivan</em></td>
<td>• 100, 200, and 400 mg capsules</td>
<td>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 + RTV 100–200 mg) BID</td>
<td>CYP3A4 inhibitor and substrate  Dosage adjustment in patients with hepatic insufficiency is recommended (see Appendix B, Table 7).</td>
<td>1.5–2 hours</td>
<td>Room temperature (15º to 30º C or 59º to 86º F) Protect from moisture.</td>
<td>• 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</td>
</tr>
</tbody>
</table>
### Appendix B, Table 3. Characteristics of Protease Inhibitors

#### (Last updated October 17, 2017; last reviewed October 17, 2017) (page 4 of 6)

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<th>Storage</th>
<th>Adverse Eventsb</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lopinavir/ Ritonavir (LPV/r)</strong></td>
<td><strong>Kaletra</strong></td>
<td>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.</td>
<td>• (LPV 400 mg + RTV 100 mg) BID, or • (LPV 800 mg + RTV 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 500/125 mg tablets BID (use a combination of 2 LPV/r 200/50 mg tablets + 1 LPV/r 100/25 mg tablet to make a total dose of LPV/r 500/125 mg), or • LPV/r 533/133 mg oral solution BID</td>
<td>CYP3A4 inhibitor and substrate</td>
<td>5–6 hours</td>
<td>Oral tablet is stable at room temperature. Oral solution is stable at 2° to 8° C (36° to 46° F) until date on label and is stable for up to 2 months when stored at room temperature (up to 25° C or 77° F).</td>
<td>• 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.</td>
</tr>
<tr>
<td><strong>Nelfinavir (NFV)</strong></td>
<td><strong>Viracept</strong></td>
<td>• 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.</td>
<td>CYP2C19 and 3A4 substrate—metabolized to active M8 metabolite; CYP3A4 inhibitor</td>
<td>3.5–5 hours</td>
<td>Room temperature (15° to 30° C or 59° to 86° F)</td>
<td>• Diarrhea • Hyperlipidemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • Serum transaminase elevation</td>
<td></td>
</tr>
</tbody>
</table>

*Formulations Dosing Recommendations:*
- **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.

*Elimination/ Metabolic Pathway:
- **CYP2C19** and **3A4 substrate**—metabolized to active M8 metabolite; **CYP3A4 inhibitor**

*Serum Half-Life:
- Oral tablet is stable at room temperature.
- Oral solution is stable at 2° to 8° C (36° to 46° F) until date on label.

*Storage:
- Oral tablet is stable at room temperature.
- Oral solution is stable at 2° to 8° C (36° to 46° F) until date on label.

*Adverse Events:
- GI intolerance, nausea, vomiting, diarrhea
- Pancreatitis
- Fat maldistribution
- Possible increased bleeding episodes in patients with hemophilia
- PR interval prolongation
- QT interval prolongation and torsades de pointes.
### Appendix B, Table 3. Characteristics of Protease Inhibitors

(Last updated October 17, 2017; last reviewed October 17, 2017)

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</thead>
<tbody>
<tr>
<td><strong>Ritonavir (RTV) Norvir</strong>&lt;br&gt;Also available as a component of a fixed-dose combination (see lopinavir/ritonavir).</td>
<td>• 100 mg tablet&lt;br&gt;• 100 mg soft gel capsule&lt;br&gt;• 80 mg/mL oral solution&lt;br&gt;• 100 mg single-packet oral powder</td>
<td>As PK Booster (or Enhancer) for Other PIs:&lt;br&gt;• 100–400 mg per day in 1 or 2 divided doses (refer to other PIs for specific dosing recommendations).&lt;br&gt;&lt;br&gt;<strong>Tablet:</strong>&lt;br&gt;• Take with food.&lt;br&gt;<strong>Capsule and Oral Solution:</strong>&lt;br&gt;• To improve tolerability, take with food if possible.</td>
<td>CYP3A4 &gt; 2D6 substrate; potent 3A4, 2D6 inhibitor; inducer of CYPs 1A2, 2C8, 2C9, and 2C19 and UGT1A1</td>
<td>3–5 hours</td>
<td>Tablets and oral powder do not require refrigeration.&lt;br&gt;Refrigerate capsules.&lt;br&gt;Capsules can be left at room temperature (up to 25º C or 77º F) for up to 30 days.&lt;br&gt;<strong>Oral solution should not be refrigerated.</strong></td>
<td>• GI intolerance, nausea, vomiting, diarrhea&lt;br&gt;• Paresthesia (circumoral and extremities)&lt;br&gt;• Hyperlipidemia (especially hypertriglyceridemia)&lt;br&gt;• Hepatitis&lt;br&gt;• Asthenia&lt;br&gt;• Taste perversion&lt;br&gt;• Hyperglycemia&lt;br&gt;• Fat maldistribution&lt;br&gt;• Possible increased bleeding episodes in patients with hemophilia</td>
</tr>
<tr>
<td><strong>Saquinavir (SQV) Invirase</strong></td>
<td>• 500 mg tablet&lt;br&gt;• 200 mg capsule</td>
<td>• (SQV 1000 mg + RTV 100 mg) BID&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>Room temperature (15º to 30º C or 59º to 86º F)</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 increased bleeding episodes in patients with hemophilia&lt;br&gt;• PR interval prolongation&lt;br&gt;• QT interval prolongation. Torsades de pointes have been reported. Patients with pre-SQV QT interval &gt;450 msec should not receive SQV.</td>
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</tbody>
</table>
### Tipranavir (TPV)  
#### Aptivus

<table>
<thead>
<tr>
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<th>Serum Half-Life</th>
<th>Storage</th>
<th>Adverse Events</th>
</tr>
</thead>
</table>
| Tipranavir (TPV)            | Aptivus    | • 250 mg capsule  
• 100 mg/mL oral solution | • (TPV 500 mg + RTV 200 mg) BID  
Unboosted TPV is not recommended.  
With RTV Tablets:  
• Take with meals.  
With RTV Capsules or Solution:  
• Take without regard to meals. | CYP P450 3A4 inducer and substrate  
CYP2D6 inhibitor; CYP3A4, 1A2, and 2C19 inducer  
Net effect when combined with RTV (CYP3A4, 2D6 inhibitor) | 6 hours after single dose of TPV/r | Refrigerate capsules.  
Capsules can be stored at room temperature (25°C or 77°F) 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% to 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, and the use of anticoagulant or antiplatelet agents (including vitamin E).  
• Hyperlipidemia  
• Hyperglycemia  
• Fat maldistribution  
• Possible increased bleeding episodes in patients with hemophilia |

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*a For dosage adjustment in hepatic insufficiency, see Appendix B, Table 7.

*b Also see Table 14.

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