



## Resource: ART Drug-Drug Interactions

April 2023

Table 25: Acid-Reducing Agents (also see drug package inserts)		
→ Proton pump inhibitors (PPIs), histamine-2 receptor agonists (H2RAs)		
Class or Drug	Mechanism of Action	Clinical Comments
<ul style="list-style-type: none"> <li>• NRTIs</li> <li>• Dolutegravir (DTG)</li> <li>• Bictegravir (BIC)</li> <li>• Raltegravir (RAL)</li> <li>• Elvitegravir (EVG), boosted</li> <li>• Efavirenz (EFV)</li> <li>• Etravirine (ETR)</li> <li>• Doravirine (DOR)</li> <li>• Fostemsavir (FTR)</li> </ul>	No clinically significant interactions reported.	No dose adjustments are necessary.
Atazanavir (ATV), unboosted	<ul style="list-style-type: none"> <li>• ATV requires acidic gastric pH for absorption, and acid-reducing agents interfere with ATV absorption.</li> <li>• <b>PPIs</b> markedly reduce ATV concentration and AUC.</li> <li>• <b>H2RAs</b> reduce ATV absorption.</li> </ul>	<p><b>PPIs:</b> Do not coadminister with <i>unboosted</i> ATV if it is possible to use an alternative acid-reducing agent, alternative PI, or boosted ATV.</p> <ul style="list-style-type: none"> <li>• <b>Timing:</b> Administer ≥12 hours before RTV- or COBI-boosted ATV.</li> <li>• <b>ART-naive:</b> If use cannot be avoided, do not exceed omeprazole 20 mg per day or equivalent (e.g., pantoprazole 40 mg; lansoprazole 30 mg; esomeprazole 20 mg).</li> <li>• <b>ART-experienced:</b> Consult with experienced HIV care provider or GI specialist.</li> </ul> <p><b>H2RAs:</b></p> <ul style="list-style-type: none"> <li>• <b>ART-naive:</b> Administer ATV 400 mg (unboosted) with food at least 2 hours before or 10 hours after.</li> <li>• <b>ART-experienced:</b> Do not use unboosted ATV + famotidine in combination.</li> <li>• Do not exceed dose equivalent to famotidine 20 mg of any H2RA. Total daily dose should not exceed 40 mg famotidine or equivalent, e.g., ranitidine or nizatidine 150 mg (300 mg daily).</li> </ul>
Atazanavir (ATV), boosted	<ul style="list-style-type: none"> <li>• ATV requires acidic gastric pH for absorption, and acid-reducing agents interfere with ATV absorption.</li> <li>• <b>PPIs</b> markedly reduce ATV concentration and AUC.</li> <li>• <b>H2RAs</b> reduce ATV absorption.</li> </ul>	<p><b>PPIs:</b></p> <ul style="list-style-type: none"> <li>• <b>Timing:</b> Administer ≥12 hours before RTV- or COBI-boosted ATV.</li> <li>• <b>ART-naive:</b> Do not exceed omeprazole 20 mg per day or equivalent (pantoprazole 40 mg; lansoprazole 30 mg; esomeprazole 20 mg).</li> </ul>

**Table 25: Acid-Reducing Agents** (also see drug package inserts)

→ Proton pump inhibitors (PPIs), histamine-2 receptor agonists (H2RAs)

Class or Drug	Mechanism of Action	Clinical Comments
		<ul style="list-style-type: none"> <li>• <b>ART-experienced:</b> Not recommended; consultation with experienced HIV care provider or GI specialist is recommended before prescribing PPI.</li> </ul> <p><b>H2RAs:</b></p> <ul style="list-style-type: none"> <li>• <b>ART-naive:</b> Administer ATV 300 mg + RTV 100 mg simultaneously with or ≥10 hours after H2RA.               <ul style="list-style-type: none"> <li>– If patient is <i>not</i> taking TFV: Do not exceed famotidine 20 mg twice per day (40 mg daily) or equivalent, e.g., ranitidine or nizatidine 150 mg twice per day (300 mg daily).</li> <li>– If patient <i>is</i> taking TFV: Do not exceed famotidine 40 mg twice per day (80 mg daily) or equivalent, e.g., ranitidine or nizatidine 300 mg twice per day (600 mg daily).</li> </ul> </li> <li>• <b>ART-experienced:</b> Administer ATV 300 mg + COBI 150 mg or RTV 100 mg simultaneously with or ≥10 hours after H2RA.</li> <li>• <b>Pregnancy:</b> In trimesters 2 and 3, increase dose of ATV to 400 mg per day with RTV 100 mg per day. (Volume of distribution increases as duration of pregnancy increases, which can reduce ATV levels, especially during second and third trimesters of pregnancy.)               <ul style="list-style-type: none"> <li>– H2RA use is contraindicated if pregnant patient takes TFV + boosted ATV during pregnancy.</li> <li>– If patient is pregnant and is taking TFV, ATV is dosed at 400 mg per day with RTV 100 mg per day; unboosted ATV is not recommended.</li> </ul> </li> </ul>
Darunavir (DRV)/ritonavir (RTV)	No clinically significant interactions reported.	<b>Omeprazole:</b> Do not exceed omeprazole 40 mg per day.
Rilpivirine (RPV)	<ul style="list-style-type: none"> <li>• PPIs and H2RAs inhibit gastric acid secretion by proton pumps, thereby increasing gastric pH.</li> <li>• Oral RPV requires acidic environment for optimal absorption.</li> <li>• <b>H2RAs:</b> Concomitant use may decrease RPV absorption.</li> </ul>	<p><b>PPIs:</b></p> <ul style="list-style-type: none"> <li>• Concurrent use of PPIs with <i>oral</i> RPV is contraindicated.</li> <li>• Use of PPIs with <i>injectable</i> RPV is acceptable.</li> </ul> <p><b>H2RAs:</b></p> <ul style="list-style-type: none"> <li>• Administer H2RA at least 12 hours before or 4 hours after.</li> <li>• Use lowest effective dose.</li> <li>• Administer with food.</li> <li>• Use of H2RAs with <i>injectable</i> RPV is acceptable.</li> </ul>
<p><b>Abbreviations:</b> ART, antiretroviral therapy; ARV, antiretroviral; AUC, area under the curve; COBI, cobicistat; GI, gastrointestinal; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PK, pharmacokinetic; TFV, tenofovir.</p>		