Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors  *(Last updated December 18, 2019; last reviewed December 18, 2019)*  (page 1 of 4)

Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

<table>
<thead>
<tr>
<th>ARV Drugs by Drug Class</th>
<th>INSTIs</th>
<th>BIC</th>
<th>DTG</th>
<th>EVG/c</th>
<th>RAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NNRTIs</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>DOR</strong></td>
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<td></td>
</tr>
<tr>
<td>PK Data</td>
<td>↔ DOR and BIC expected</td>
<td>↔ DOR</td>
<td>DTG AUC ↑ 36% and C\text{min} ↑ 27%</td>
<td>↑ DOR expected</td>
<td>↔ DOR and RAL expected</td>
</tr>
<tr>
<td>Dose</td>
<td>No dose adjustment needed.</td>
<td>No dose adjustment needed.</td>
<td>No dose adjustment needed.</td>
<td>No dose adjustment needed.</td>
<td></td>
</tr>
<tr>
<td><strong>EFV</strong></td>
<td></td>
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</tr>
<tr>
<td>PK Data</td>
<td>↓ BIC expected</td>
<td>With DTG 50 mg Once Daily: • DTG AUC ↓ 57% and C\text{min} ↓ 75%</td>
<td>↑ or ↓ EVG, COBI, and EFV possible</td>
<td>With RAL 400 mg Twice Daily: • RAL AUC ↓ 36% and C\text{min} ↓ 21%</td>
<td>With RAL 1,200 mg Once Daily: • ↔ RAL AUC and C\text{min}</td>
</tr>
<tr>
<td>Dose</td>
<td>Do not coadminister.</td>
<td>In Patients Without INSTI Resistance: • DTG 50 mg twice daily</td>
<td>Do not coadminister.</td>
<td>In Patients With Certain INSTI-Associated Resistance* or Clinically Suspected INSTI Resistance: • Consider alternative combination.</td>
<td></td>
</tr>
<tr>
<td><strong>ETR</strong></td>
<td></td>
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</tr>
<tr>
<td>PK Data</td>
<td>↓ BIC expected</td>
<td>ETR 200 mg Twice Daily plus DTG 50 mg Once Daily: • DTG AUC ↓ 71% and C\text{min} ↓ 88%</td>
<td>↑ or ↓ EVG, COBI, and ETR possible</td>
<td>ETR 200 mg Twice Daily plus RAL 400 mg Twice Daily: • ETR C\text{min} ↑ 17%</td>
<td>RAL C\text{min} ↓ 34%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ETR 200 mg Twice Daily with (DRV 600 mg plus RTV 100 mg) Twice Daily and DTG 50 mg Once Daily: • DTG AUC ↓ 25% and C\text{min} ↓ 37%</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>ETR 200 mg Twice Daily with (LPV 400 mg plus RTV 100 mg) Twice Daily and DTG 50 mg Once Daily: • DTG AUC ↑ 11% and C\text{min} ↑ 28%</td>
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</tr>
</tbody>
</table>
Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors *(Last updated December 18, 2019; last reviewed December 18, 2019)* (page 2 of 4)

<table>
<thead>
<tr>
<th>ARV Drugs by Drug Class</th>
<th>INSTIs</th>
<th>BIC</th>
<th>DTG</th>
<th>EVG/c</th>
<th>RAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NNRTIs, continued</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>ETR</td>
<td>Dose</td>
<td>Do not coadminister.</td>
<td>Do not coadminister ETR and DTG without concurrently administering ATV/r, DRV/r, or LPV/r.</td>
<td>Do not coadminister.</td>
<td>RAL 400 mg twice daily Coadministration with RAL 1,200 mg once daily is not recommended.</td>
</tr>
<tr>
<td></td>
<td>PK Data</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>↓ BIC expected</td>
<td>With DTG 50 mg Once Daily: • DTG AUC ↓ 19% and C_{min} ↓ 34%</td>
<td>↑ or ↓ EVG, COBI, and NVP possible</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>Do not coadminister.</td>
<td>No dose adjustment needed.</td>
<td>Do not coadminister.</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>No data</td>
<td>With DTG 50 mg Once Daily: • ↔ DTG AUC and C_{min} ↑ 22% • ↔ RPV AUC and C_{min} ↑ 21%</td>
<td>↑ or ↓ EVG, COBI, and RPV possible</td>
<td>↔ RPV RAL C_{min} ↑ 27%</td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>No dose adjustment needed.</td>
<td>No dose adjustment needed.</td>
<td>Do not coadminister.</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td><strong>PIs</strong></td>
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<tr>
<td>ATV</td>
<td>PK Data</td>
<td>ATV 400 mg Once Daily plus BIC 75 mg Single Dose: • BIC AUC ↑ 315%</td>
<td>(ATV 400 mg plus DTG 30 mg) Once Daily: • DTG AUC ↑ 91% and C_{min} ↑ 180%</td>
<td>↑ or ↓ EVG, COBI, and ATV possible</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>Do not coadminister.</td>
<td>No dose adjustment needed.</td>
<td>Do not coadminister.</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>ATP/c</td>
<td>PK Data</td>
<td>BIC AUC ↑ 306%</td>
<td>No data</td>
<td>Not applicable</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>Do not coadminister.</td>
<td>No dose adjustment needed.</td>
<td>Do not coadminister two COBI-containing products.</td>
<td>No dose adjustment needed.</td>
</tr>
</tbody>
</table>
Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 3 of 4)

<table>
<thead>
<tr>
<th>ARV Drugs by Drug Class</th>
<th>INSTIs</th>
<th>BIC</th>
<th>DTG</th>
<th>EVG/c</th>
<th>RAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pi's, continued</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ATV/r</strong></td>
<td>PK</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PK Data</strong></td>
<td>↑ BIC expected</td>
<td>(ATV 300 mg plus RTV 100 mg) Once Daily plus DTG 30 mg Once Daily:</td>
<td></td>
<td>Not applicable</td>
<td>With Unboosted ATV:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• DTG AUC ↑ 62% and C&lt;sub&gt;min&lt;/sub&gt; ↑ 121%</td>
<td></td>
<td></td>
<td>• RAL AUC ↑ 72%</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>With Unboosted ATV and RAL 1,200 mg:</td>
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<td></td>
<td></td>
<td>• RAL AUC ↑ 67%</td>
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<td></td>
<td></td>
<td>With (ATV 300 mg plus RTV 100 mg) Once Daily:</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• RAL AUC ↑ 41%</td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td>Do not coadminister.</td>
<td>No dose adjustment needed.</td>
<td>Do not coadminister RAL, ATP, and COBI.</td>
<td>No dose adjustment needed.</td>
<td></td>
</tr>
<tr>
<td><strong>DRV</strong></td>
<td>PK</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>↔ DRV or EVG expected</td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>PK Data</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td>Do not administer DRV without RTV or COBI</td>
<td>No dose adjustment needed.</td>
<td>No dose adjustment needed.</td>
<td>Do not administer DRV without RTV or COBI.</td>
<td></td>
</tr>
<tr>
<td><strong>DRV/c</strong></td>
<td>PK</td>
<td>BIC AUC ↑ 74%</td>
<td>DRV/c plus DTG Once Daily:</td>
<td>Not applicable</td>
<td>No data</td>
</tr>
<tr>
<td><strong>Data</strong></td>
<td></td>
<td></td>
<td>• ↔ DTG, DRV, and COBI</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DTG 50 mg Once Daily and DRV/r Once Daily Switched to DRV/c:</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• DTG C&lt;sub&gt;min&lt;/sub&gt; ↑ 100%</td>
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<td></td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td>No dose adjustment needed.</td>
<td>No dose adjustment needed.</td>
<td>Do not coadminister two COBI-containing products.</td>
<td>No dose adjustment needed.</td>
<td></td>
</tr>
<tr>
<td><strong>DRV/r</strong></td>
<td>PK</td>
<td>No data</td>
<td>(DRV 600 mg plus RTV 100 mg) Twice Daily with DTG 30 mg Once Daily:</td>
<td>Not applicable</td>
<td>With (DRV 600 mg plus RTV 100 mg) Twice Daily:</td>
</tr>
<tr>
<td><strong>Data</strong></td>
<td></td>
<td></td>
<td>• DTG AUC ↓ 22% and C&lt;sub&gt;min&lt;/sub&gt; ↓ 38%</td>
<td></td>
<td>• RAL AUC ↓ 29% and C&lt;sub&gt;min&lt;/sub&gt; ↑ 38%</td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td>No dose adjustment needed.</td>
<td>No dose adjustment needed.</td>
<td>Do not coadminister RAL, ATP, and COBI.</td>
<td>No dose adjustment needed.</td>
<td></td>
</tr>
<tr>
<td><strong>LPV/r</strong></td>
<td>PK</td>
<td>No data</td>
<td>With (LPV 400 mg plus RTV 100 mg) Twice Daily and DTG 30 mg Once Daily:</td>
<td>Not applicable</td>
<td>↓ RAL</td>
</tr>
<tr>
<td><strong>Data</strong></td>
<td></td>
<td></td>
<td>• ↔ DTG</td>
<td>↔ LPV/r</td>
<td></td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td>Consider alternative combination.</td>
<td>No dose adjustment needed.</td>
<td>Do not coadminister RAL, ATP, and COBI.</td>
<td>No dose adjustment needed.</td>
<td></td>
</tr>
<tr>
<td><strong>TPV/r</strong></td>
<td>PK</td>
<td>↓ BIC possible</td>
<td>With (TPV 500 mg plus RTV 200 mg) Twice Daily and DTG 50 mg Once Daily:</td>
<td>Not applicable</td>
<td>With (TPV 500 mg plus RTV 200 mg) Twice Daily and RAL 400 mg Twice Daily:</td>
</tr>
<tr>
<td><strong>Data</strong></td>
<td></td>
<td></td>
<td>• DTG AUC ↓ 59% and C&lt;sub&gt;min&lt;/sub&gt; ↓ 76%</td>
<td></td>
<td>• RAL AUC ↓ 24% and C&lt;sub&gt;min&lt;/sub&gt; ↓ 55%</td>
</tr>
</tbody>
</table>
Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors  *(Last updated December 18, 2019; last reviewed December 18, 2019)*  (page 4 of 4)

<table>
<thead>
<tr>
<th>ARV Drugs by Drug Class</th>
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<th>EVG/c</th>
<th>RAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TPV/r</td>
<td>Dose</td>
<td>Do not coadminister.</td>
<td>In Patients Without INSTI Resistance:</td>
<td>Do not coadminister RTV and COBI.</td>
<td>RAL 400 mg twice daily</td>
</tr>
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</tr>
</tbody>
</table>

* Refer to DTG product label for details.

**Key to Symbols:**

↑ = increase
↓ = decrease
↔ = no change

**Key:** ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; Cmin = minimum plasma concentration; COBI = cobicistat; CYP = cytochrome P; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; INSTI = integrase strand transfer inhibitor; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TPV = tipranavir; TPV/r = tipranavir/ritonavir