

## Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

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Recommendations for managing a particular drug interaction may differ depending on whether a new antiretroviral (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.

Information on drug interactions with oral (PO) cabotegravir (CAB) is not included in this table. The CAB PO tablet is not available in retail pharmacies and will be provided directly to people with HIV for short-term use only (PO lead-in and to bridge if intramuscular [IM] administration is delayed).

CAB IM and rilpivirine (RPV) IM are not included in this table because the combination is a two-drug, co-packaged product. Therefore, it is not anticipated that they will be used with PO non-nucleoside reverse transcriptase inhibitors (NNRTIs) or protease inhibitors (PIs).

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
<b>NNRTIs</b>					
DOR	PK Data	↔ DOR and BIC expected	↔ DOR DTG AUC ↑ 36% and C <sub>min</sub> ↑ 27%	↑ DOR expected ↔ EVG	↔ DOR and RAL expected
	Dose	No dose adjustment needed.	No dose adjustment needed.	No dose adjustment needed.	No dose adjustment needed.
EFV	PK Data	↓ BIC expected	<b>With DTG 50 mg Once Daily</b> • DTG AUC ↓ 57% and C <sub>min</sub> ↓ 75%	↑ or ↓ EVG, COBI, and EFV possible	<b>With RAL 400 mg Twice Daily</b> • RAL AUC ↓ 36% and C <sub>min</sub> ↓ 21% <b>With RAL 1,200 mg Once Daily</b> • ↔ RAL AUC and C <sub>min</sub>

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ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
	Dose	Do not coadminister.	<p><b>In Patients Without INSTI Resistance</b></p> <ul style="list-style-type: none"> <li>DTG 50 mg twice daily</li> </ul> <p><b>In Patients With Certain INSTI-Associated Resistance<sup>a</sup> or Clinically Suspected INSTI Resistance</b></p> <ul style="list-style-type: none"> <li>Consider alternative combination</li> </ul>	Do not coadminister.	No dose adjustment needed.
ETR	PK Data	↓ BIC expected	<p><b>ETR 200 mg Twice Daily Plus DTG 50 mg Once Daily</b></p> <ul style="list-style-type: none"> <li>DTG AUC ↓ 71% and C<sub>min</sub> ↓ 88%</li> </ul> <p><b>ETR 200 mg Twice Daily With (DRV 600 mg Plus RTV 100 mg) Twice Daily and DTG 50 mg Once Daily</b></p> <ul style="list-style-type: none"> <li>DTG AUC ↓ 25% and C<sub>min</sub> ↓ 37%</li> </ul>	↑ or ↓ EVG, COBI, and ETR possible	<p><b>ETR 200 mg Twice Daily Plus RAL 400 mg Twice Daily</b></p> <ul style="list-style-type: none"> <li>ETR C<sub>min</sub> ↑ 17%</li> <li>RAL C<sub>min</sub> ↓ 34%</li> </ul>
	Dose	Do not coadminister.	<p><b>Do not coadminister ETR and DTG without concurrently administering ATV/r or DRV/r.</b></p> <p><b>In Patients Without INSTI Resistance</b></p> <ul style="list-style-type: none"> <li>DTG 50 mg once daily with ETR (concurrently with ATV/r or DRV/r)</li> </ul>	Do not coadminister.	<p>RAL 400 mg twice daily</p> <p>Coadministration with RAL 1,200 mg once daily <b>is not recommended.</b></p>

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ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
			<p><b>In Patients With Certain INSTI-Associated Resistance<sup>a</sup> or Clinically Suspected INSTI Resistance</b></p> <ul style="list-style-type: none"> <li>DTG 50 mg twice daily with ETR (concurrently with ATV/r or DRV/r)</li> </ul>		
RPV	PK Data	No data	<p><b>With DTG 50 mg Once Daily</b></p> <ul style="list-style-type: none"> <li>↔ DTG AUC and C<sub>min</sub> ↑ 22%</li> <li>↔ RPV PO AUC and C<sub>min</sub> ↑ 21%</li> </ul>	↑ RPV PO possible	↔ RPV PO RAL C <sub>min</sub> ↑ 27%
	Dose	No dose adjustment needed.	No dose adjustment needed.	<b>Do not coadminister.</b>	No dose adjustment needed.
<b>PIs</b>					
ATV/c	PK Data	BIC AUC ↑ 306%	No data	Not applicable	No data
	Dose	<b>Do not coadminister.</b>	No dose adjustment needed.	<b>Do not coadminister</b> two COBI-containing products.	No dose adjustment needed.
ATV/r	PK Data	↑ BIC expected	<p><b>(ATV 300 mg Plus RTV 100 mg) Once Daily Plus DTG 30 mg Once Daily</b></p> <ul style="list-style-type: none"> <li>DTG AUC ↑ 62% and C<sub>min</sub> ↑ 121%</li> </ul>	Not applicable	<p><b>With (ATV 300 mg Plus RTV 100 mg) Once Daily</b></p> <ul style="list-style-type: none"> <li>RAL AUC ↑ 41%</li> </ul>
	Dose	<b>Do not coadminister.</b>	No dose adjustment needed.	Do not coadminister RTV and COBI.	No dose adjustment needed.

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ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
DRV	PK Data	Not applicable	Not applicable	↔ DRV or EVG expected	Not applicable
	Dose	<b>Do not administer</b> DRV without RTV or COBI.	<b>Do not administer</b> DRV without RTV or COBI.	No dose adjustment needed.	<b>Do not administer</b> DRV without RTV or COBI.
DRV/c	PK Data	BIC AUC ↑ 74%	<b>DRV/c Plus DTG Once Daily</b> <ul style="list-style-type: none"> <li>↔ DTG, DRV, and COBI</li> </ul> <b>DTG 50 mg Once Daily and DRV/r Once Daily Switched to DRV/c</b> <ul style="list-style-type: none"> <li>DTG C<sub>min</sub> ↑ 100%</li> </ul>	Not applicable	No data
	Dose	No dose adjustment needed.	No dose adjustment needed.	<b>Do not coadminister</b> two COBI-containing products.	No dose adjustment needed.
DRV/r	PK Data	No data	<b>(DRV 600 mg Plus RTV 100 mg) Twice Daily With DTG 30 mg Once Daily</b> <ul style="list-style-type: none"> <li>DTG AUC ↓ 22% and C<sub>min</sub> ↓ 38%</li> </ul>	Not applicable	<b>With (DRV 600 mg Plus RTV 100 mg) Twice Daily</b> <ul style="list-style-type: none"> <li>RAL AUC ↓ 29% and C<sub>min</sub> ↑ 38%</li> </ul>
	Dose	No dose adjustment needed.	No dose adjustment needed.	<b>Do not coadminister</b> RTV and COBI.	No dose adjustment needed.

<sup>a</sup> Refer to DTG product label for details.

**Key to Symbols**

↑ = increase

↓ = decrease

↔ = less than 20% change in AUC

**Key:** ARV = antiretroviral; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C<sub>min</sub> = minimum plasma concentration; COBI = cobicistat; 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; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; **PO = oral**; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir