

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

Updated: June 3, 2021

Reviewed: June 3, 2021

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 patients for short-term use only (PO lead-in and to bridge intramuscular [IM] administration is delayed).

CAB IM and rilpivirine (RPV) IM also 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 oral NNRTIs or PIs.

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
NNRTIs					
DOR	PK Data	↔ DOR and BIC expected	↔ DOR DTG AUC ↑ 36% and C _{min} ↑ 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	With DTG 50 mg Once Daily • DTG AUC ↓ 57% and C _{min} ↓ 75%	↑ or ↓ EVG, COBI, and EFV possible	With RAL 400 mg Twice Daily • RAL AUC ↓ 36% and C _{min} ↓ 21% With RAL 1,200 mg Once Daily • ↔ RAL AUC and C _{min}

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

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
	Dose	Do not coadminister.	<p>In Patients Without INSTI Resistance</p> <ul style="list-style-type: none"> • DTG 50 mg twice daily <p>In Patients with Certain INSTI-Associated Resistance^a or Clinically Suspected INSTI Resistance</p> <ul style="list-style-type: none"> • Consider alternative combination. 	Do not coadminister.	No dose adjustment needed.
ETR	PK Data	↓ BIC expected	<p>ETR 200 mg Twice Daily plus DTG 50 mg Once Daily</p> <ul style="list-style-type: none"> • DTG AUC ↓ 71% and C_{min} ↓ 88% <p>ETR 200 mg Twice Daily with (DRV 600 mg plus RTV 100 mg) Twice Daily and DTG 50 mg Once Daily</p> <ul style="list-style-type: none"> • DTG AUC ↓ 25% and C_{min} ↓ 37% <p>ETR 200 mg Twice Daily with (LPV 400 mg plus RTV 100 mg) Twice Daily and DTG 50 mg Once Daily</p> <ul style="list-style-type: none"> • DTG AUC ↑ 11% and C_{min} ↑ 28% 	↑ or ↓ EVG, COBI, and ETR possible	<p>ETR 200 mg Twice Daily plus RAL 400 mg Twice Daily</p> <ul style="list-style-type: none"> • ETR C_{min} ↑ 17% • RAL C_{min} ↓ 34%

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

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
	Dose	Do not coadminister.	<p>Do not coadminister ETR and DTG without concurrently administering ATV/r, DRV/r, or LPV/r.</p> <p>In Patients Without INSTI Resistance</p> <ul style="list-style-type: none"> DTG 50 mg once daily with ETR (concurrently with ATV/r, DRV/r, or LPV/r) <p>In Patients with Certain INSTI-Associated Resistance^a or Clinically Suspected INSTI Resistance</p> <ul style="list-style-type: none"> DTG 50 mg twice daily with ETR (concurrently with ATV/r, DRV/r, or LPV/r) 	Do not coadminister.	<p>RAL 400 mg twice daily</p> <p>Coadministration with RAL 1,200 mg once daily is not recommended.</p>
NVP	PK Data	↓ BIC expected	<p>With DTG 50 mg Once Daily</p> <ul style="list-style-type: none"> DTG AUC ↓ 19% and C_{min} ↓ 34% 	↑ or ↓ EVG, COBI, and NVP possible	No data
	Dose	Do not coadminister.	No dose adjustment needed.	Do not coadminister.	No dose adjustment needed.
RPV	PK Data	No data	<p>With DTG 50 mg Once Daily</p> <ul style="list-style-type: none"> ↔ DTG AUC and C_{min} ↑ 22% ↔ RPV PO AUC and C_{min} ↑ 21% 	↑ or ↓ EVG, COBI, and RPV PO possible	<p>↔ RPV PO</p> <p>RAL C_{min} ↑ 27%</p>
	Dose	No dose adjustment needed.	No dose adjustment needed.	Do not coadminister.	No dose adjustment needed.

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

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
PIs					
ATV	PK Data	ATV 400 mg Once Daily plus BIC 75 mg Single Dose • BIC AUC ↑ 315%	(ATV 400 mg plus DTG 30 mg) Once Daily • DTG AUC ↑ 91% and C _{min} ↑ 180%	↑ or ↓ EVG, COBI, and ATV possible	With Unboosted ATV • RAL AUC ↑ 72% With Unboosted ATV and RAL 1,200 mg • RAL AUC ↑ 67%
	Dose	Do not coadminister.	No dose adjustment needed.	Do not coadminister.	No dose adjustment needed.
ATV/c	PK Data	BIC AUC ↑ 306%	No data	Not applicable	No data
	Dose	Do not coadminister.	No dose adjustment needed.	Do not coadminister two COBI-containing products.	No dose adjustment needed.
ATV/r	PK Data	↑ BIC expected	(ATV 300 mg plus RTV 100 mg) Once Daily plus DTG 30 mg Once Daily • DTG AUC ↑ 62% and C _{min} ↑ 121%	Not applicable	With (ATV 300 mg plus RTV 100 mg) Once Daily • RAL AUC ↑ 41%
	Dose	Do not coadminister.	No dose adjustment needed.	Do not coadminister RTV and COBI.	No dose adjustment needed.
DRV	PK Data	Not applicable	Not applicable	↔ DRV or EVG expected	Not applicable
	Dose	Do not administer DRV without RTV or COBI.	Do not administer DRV without RTV or COBI.	No dose adjustment needed.	Do not administer DRV without RTV or COBI.

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

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
DRV/c	PK Data	BIC AUC ↑ 74%	DRV/c plus DTG Once Daily <ul style="list-style-type: none"> ↔ DTG, DRV, and COBI DTG 50 mg Once Daily and DRV/r Once Daily Switched to DRV/c <ul style="list-style-type: none"> DTG C_{min} ↑ 100% 	Not applicable	No data
	Dose	No dose adjustment needed.	No dose adjustment needed.	Do not coadminister two COBI-containing products.	No dose adjustment needed.
DRV/r	PK Data	No data	(DRV 600 mg plus RTV 100 mg) Twice Daily with DTG 30 mg Once Daily <ul style="list-style-type: none"> DTG AUC ↓ 22% and C_{min} ↓ 38% 	Not applicable	With (DRV 600 mg plus RTV 100 mg) Twice Daily <ul style="list-style-type: none"> RAL AUC ↓ 29% and C_{min} ↑ 38%
	Dose	No dose adjustment needed.	No dose adjustment needed.	Do not coadminister RTV and COBI.	No dose adjustment needed.
LPV/r	PK Data	No data	With (LPV 400 mg plus RTV 100 mg) Twice Daily and DTG 30 mg Once Daily <ul style="list-style-type: none"> ↔ DTG 	Not applicable	↓ RAL ↔ LPV/r
	Dose	Consider alternative combination.	No dose adjustment needed.	Do not coadminister RTV and COBI.	No dose adjustment needed.

^a Refer to DTG product label for details.

Key to Symbols

- ↑ = increase
- ↓ = decrease
- ↔ = no change

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

Key: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C_{\min} = minimum plasma concentration; CAB = cabotegravir; 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; IM = intramuscular; INSTI = integrase strand transfer inhibitor; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; PO = oral; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir