



Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

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Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018) (page 1 of 3)

Recommendations for managing a particular drug interaction may differ depending on whether a new ARV is being initiated in a patient on a stable concomitant medication or if 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.

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
NNRTIs					
DOR	PK Data	↔ DOR, BIC expected	↔ DOR DTG AUC ↑ 36% and C _{min} ↑ 27%	↑ DOR expected ↔ EVG	↔ DOR, RAL expected
	Dose	Standard doses	Standard doses	Standard doses	Standard doses
EFV	PK Data	↓ BIC expected	<u>With DTG 50 mg Once Daily:</u> • DTG AUC ↓ 57% and C _{min} ↓ 75%	↑ or ↓ EVG, COBI, EFV possible	<u>With RAL 400 mg BID:</u> • RAL AUC ↓ 36% and C _{min} ↓ 21% <u>With RAL 1200 mg Once Daily:</u> • RAL AUC ↓ 14% and ↔ C _{min}
	Dose	Do not coadminister.	<u>In Patients Without INSTI Resistance:</u> • DTG 50 mg BID <u>In Patients With Certain INSTI-Associated Resistance^a or Clinically Suspected INSTI Resistance:</u> • Consider alternative combination.	Do not coadminister.	Standard doses
ETR	PK Data	↓ BIC expected	<u>ETR 200 mg BID plus DTG 50 mg Once Daily:</u> • DTG AUC ↓ 71% and C _{min} ↓ 88% <u>ETR 200 mg BID with (DRV 600 mg plus RTV 100 mg) BID and DTG 50 mg Once Daily:</u> • DTG AUC ↓ 25% and C _{min} ↓ 37% <u>ETR 200 mg BID with (LPV 400 mg plus RTV 100 mg) BID and DTG 50 mg Once Daily:</u> • DTG AUC ↑ 11% and C _{min} ↑ 28%	↑ or ↓ EVG, COBI, ETR possible	<u>ETR 200 mg BID plus RAL 400 mg BID:</u> • ETR C _{min} ↑ 17% • RAL C _{min} ↓ 34%

Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018) (page 2 of 3)

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
NNRTIs, continued					
ETR, continued	Dose	Do not coadminister.	Do not coadminister ETR and DTG without concurrently administering ATV/r, DRV/r, or LPV/r. <u>In Patients Without INSTI Resistance:</u> • DTG 50 mg once daily with ETR (concurrently with ATV/r, DRV/r, or LPV/r) <u>In Patients With Certain INSTI-Associated Resistance or Clinically Suspected INSTI Resistance:</u> • DTG 50 mg BID with ETR (concurrently with ATV/r, DRV/r, or LPV/r)	Do not coadminister.	RAL 400 mg BID Coadministration with RAL 1200 mg once daily is not recommended.
NVP	PK Data	↓ BIC expected	<u>With DTG 50 mg Once Daily:</u> • DTG AUC ↓ 19% and C _{min} ↓ 34%	↑ or ↓ EVG, COBI, NVP possible	No data
	Dose	Do not coadminister.	Standard doses	Do not coadminister.	Standard doses
RPV	PK Data	No data	<u>With DTG 50 mg Once Daily:</u> • DTG AUC ↔ and C _{min} ↑ 22% • RPV AUC ↔ and C _{min} ↑ 21%	↑ or ↓ EVG, COBI, RPV possible	↔ RPV RAL C _{min} ↑ 27%
	Dose	Standard doses	Standard doses	Do not coadminister.	Standard doses
PIs					
ATV/c	PK Data	BIC AUC ↑ 305%	No data	No data	No data
	Dose	Do not coadminister.	Standard doses	Do not coadminister.	Standard doses
ATV +/- RTV	PK Data	BIC AUC ↑ 310%	<u>Unboosted ATV plus DTG 30 mg Once Daily:</u> • DTG AUC ↑ 91% and C _{min} ↑ 180% <u>(ATV 300 mg plus RTV 100 mg) Once Daily plus DTG 30 mg Once Daily:</u> • DTG AUC ↑ 62% and C _{min} ↑ 121%	↑ or ↓ EVG, COBI, ATV possible	<u>With Unboosted ATV:</u> • RAL AUC ↑ 72% <u>With Unboosted ATV and RAL 1200 mg:</u> • RAL AUC ↑ 67% <u>With (ATV 300 mg plus RTV 100 mg) Once Daily:</u> • RAL AUC ↑ 41%
	Dose	Do not coadminister.	Standard doses	Do not coadminister.	Standard doses
DRV/c	PK Data	BIC AUC ↑ 74%	<u>DRV/c plus DTG Once Daily:</u> • ↔ DTG, DRV, COBI <u>DTG 50 mg Once Daily and DRV/r Once Daily Switched to DRV/c:</u> • DTG C _{min} ↑ 100%	<u>DRV/c plus EVG/c:</u> • ↓ EVG possible	No data
	Dose	Standard doses	Standard doses	Do not coadminister.	Standard doses

Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018) (page 3 of 3)

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
PIs, continued					
DRV/r	PK Data	No data	<u>(DRV 600 mg plus RTV 100 mg) BID with DTG 30 mg Once Daily:</u> • DTG AUC ↓ 22% and C _{min} ↓ 38%	↑ or ↓ EVG, COBI, DRV possible	<u>With (DRV 600 mg plus RTV 100 mg) BID:</u> • RAL AUC ↓ 29% and C _{min} ↑ 38%
	Dose	Standard doses	Standard doses	Do not coadminister.	Standard doses
LPV/r	PK Data	No data	<u>With (LPV 400 mg plus RTV 100 mg) BID and DTG 30 mg Once Daily:</u> • ↔ DTG	↑ or ↓ EVG, COBI, LPV possible RTV and COBI have similar effects on CYP3A.	↓ RAL ↔ LPV/r
	Dose	Consider alternative combination.	Standard doses	Do not coadminister.	Standard doses
TPV/r	PK Data	↓ BIC possible	<u>With (TPV 500 mg plus RTV 200 mg) BID and DTG 50 mg Once Daily:</u> • DTG AUC ↓ 59% and C _{min} ↓ 76%	↑ or ↓ EVG, COBI, TPV possible RTV and COBI have similar effects on CYP3A.	<u>With (TPV 500 mg plus RTV 200 mg) BID and RAL 400 mg BID:</u> • RAL AUC ↓ 24% and C _{min} ↓ 55%
	Dose	Do not coadminister.	<u>In Patients Without INSTI Resistance:</u> • DTG 50 mg BID <u>In Patients With Certain INSTI-Associated Resistance^a or Clinically Suspected INSTI Resistance:</u> • Consider alternative combination.	Do not coadminister.	RAL 400 mg BID Coadministration with RAL 1200 mg once daily is not recommended.

^a Refer to DTG product labeling for details.

Key to Symbols:

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

Key to Acronyms: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; BID = twice daily; C_{min} = 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