



Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

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Table 20b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated July 14, 2016; last reviewed July 14, 2016) (page 1 of 4)

ARV Drugs by Drug Class		INSTIs			
		DTG	EVG/c	EVG (when used with PI/r)	RAL
NNRTIs					
EFV	PK Data	<u>With DTG 50 mg once daily:</u> • DTG AUC ↓ 57% and C _{min} ↓ 75%	↑ or ↓ EVG, COBI, EFV possible	↓ EVG expected	<u>RAL:</u> • AUC ↓ 36%
	Dose	<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.	Do not coadminister.	Standard doses
ETR	PK Data	<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	No significant interaction between EVG/r and ETR	• ETR C _{min} ↓ 17% • RAL C _{min} ↓ 34%
	Dose	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^a or clinically suspected INSTI resistance:</u> • DTG 50 mg BID with ETR (concurrently with ATV/r, DRV/r, or LPV/r)	Do not coadminister.	May coadminister EVG with ETR plus (ATV/r, DRV/r, or LPV/r) <u>EVG:</u> • Standard dose depending on the concomitant PI (see below)	Standard doses

Table 20b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated July 14, 2016; last reviewed July 14, 2016) (page 2 of 4)

ARV Drugs by Drug Class		INSTIs			
		DTG	EVG/c	EVG (when used with PI/r)	RAL
NNRTIs, continued					
NVP	PK Data	With DTG 50 mg once daily: DTG AUC ↓ 19% and C _{min} ↓ 34%	↑ or ↓ EVG, COBI, NVP possible	↓ EVG possible	No data
	Dose	Standard doses	Do not coadminister.	Do not coadminister.	Standard doses
RPV	PK Data	With DTG 50 mg once daily: • DTG AUC ↔ and C _{min} ↑ 22% • RPV AUC ↔ and C _{min} ↑ 21%	↑ or ↓ EVG, COBI, RPV possible	↑ RPV expected	• RPV ↔ • RAL C _{min} ↑ 27%
	Dose	Standard doses	Do not coadminister.	<u>EVG:</u> • Standard dose depending on the concomitant PI (see below) <u>RPV:</u> • Standard dose	Standard doses
PIs					
ATV/c	PK Data	No data	<u>ATV/c plus EVG/c:</u> • No data	No data	No data
	Dose	Standard doses	Do not coadminister.	Do not coadminister.	Standard doses
ATV +/- RTV	PK Data	<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>EVG 85 mg with (ATV 300 mg plus RTV 100 mg) once daily:</u> • EVG AUC ↔ and C _{min} ↑ 38% • ATV AUC and C _{min} ↔	<u>With unboosted ATV:</u> • RAL AUC ↑ 72% <u>With (ATV 300 mg plus RTV 100 mg) once daily:</u> • RAL AUC ↑ 41%
	Dose	Standard doses	Do not coadminister.	• EVG 85 mg once daily • (ATV 300 mg plus RTV 100 mg) once daily	Standard doses
DRV/c	PK Data	No data	<u>DRV/c plus EVG/c:</u> • ↓ EVG possible	No data	No data
	Dose	Standard doses	Do not coadminister.	Do not coadminister.	Standard doses

Table 20b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated July 14, 2016; last reviewed July 14, 2016) (page 3 of 4)

ARV Drugs by Drug Class		INSTIs			
		DTG	EVG/c	EVG (when used with PI/r)	RAL
PIs, continued					
DRV/r	PK 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>EVG 125 mg once daily with (DRV 600 mg plus RTV 100 mg) BID:</u> • EVG AUC and C _{min} ↔ • DRV AUC and C _{min} ↔	<u>With (DRV 600 mg plus RTV 100 mg) BID:</u> • RAL AUC ↓ 29% and C _{min} ↑ 38%
	Dose	<u>Standard doses:</u> • Once or twice daily dosing of DRV/r	Do not coadminister.	• EVG 150 mg once daily • (DRV 600 mg plus RTV 100 mg) BID	Standard doses
FPV +/- RTV	PK Data	<u>With (FPV 700 mg plus RTV 100 mg) BID and DTG 50 mg once daily:</u> • DTG AUC ↓ 35% and C _{min} ↓ 49%	↑ or ↓ EVG, COBI, FPV possible	No significant interaction with FPV and EVG	FPV: No significant effect
	Dose	<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.	• EVG 150 mg once daily • (FPV 700 mg plus RTV 100 mg) BID	Standard doses
LPV/r	PK Data	<u>With (LPV 400 mg plus RTV 100 mg) BID and DTG 30 mg once daily:</u> • DTG: no significant effect	↑ or ↓ EVG, COBI, LPV possible RTV and COBI have similar effects on CYP3A.	<u>EVG 125 mg once daily with (LPV 400 mg plus RTV 100 mg) BID:</u> • EVG AUC ↑ 75% and C _{min} ↑ 138% • LPV AUC and C _{min} ↔	• ↓ RAL • ↔ LPV/r
	Dose	<u>Standard doses:</u> • Once or twice daily dosing of LPV/r	Do not coadminister.	• EVG 85 mg once daily • (LPV 400 mg plus RTV 100 mg) BID	Standard doses
SQV/r	PK Data	No data	↑ or ↓ EVG, COBI, SQV possible RTV and COBI have similar effects on CYP3A.	No data	No data
	Dose	Standard doses	Do not coadminister.	No dosage recommendation	Standard doses

Table 20b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated July 14, 2016; last reviewed July 14, 2016) (page 4 of 4)

ARV Drugs by Drug Class		INSTIs			
		DTG	EVG/c	EVG (when used with PI/r)	RAL
PIs, continued					
TPV/r	PK Data	<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>EVG 200 mg once daily with (TPV 500 mg plus RTV 200 mg) BID:</u> • EVG AUC and C _{min} ↔ • TPV AUC and C _{min} ↔	<u>With (TPV 500 mg plus RTV 200 mg) BID:</u> • RAL AUC ↓ 24%
	Dose	<u>In patients without INSTI resistance:</u> • DTG 50 mg BID <u>In patients with certain INSTI-associated resistance or clinically suspected INSTI resistance:</u> • Consider alternative combination.	Do not coadminister.	• EVG 150 mg once daily • (TPV 500 mg plus RTV 200 mg) BID	Standard doses

^a Refer to dolutegravir product labeling for details.

Key to Symbols: ↑ = increase; ↓ = decrease; ↔ = no change

Key to Abbreviations: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BID = twice daily; C_{min} = minimum plasma concentration; COBI, c = cobicistat; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; EVG/c/TDF/FTC = elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine; EVG/r = elvitegravir/ritonavir; FPV = fosamprenavir; INSTI = integrase strand transfer inhibitor; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; PK = pharmacokinetic; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; SQV/r = saquinavir/ritonavir; TPV = tipranavir; TPV/r = tipranavir/ritonavir