Table 25a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors

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Note: Interactions associated with DLV, FPV, IDV, NFV, TPV, and SQV are **not** included in this table. Please refer to the Food and Drug Administration product labels for information regarding interactions between these drugs and other concomitant drugs.

Rilpivirine (RPV) intramuscular (IM) is not included in this table, because the combination of cabotegravir IM plus RPV IM is a two-drug co-packaged product. Therefore, RPV IM is not expected to be used as a protease inhibitor.

PIs		NNRTIs				
		DOR	EFV	ETR	NVP	RPV
ATV Unboosted	PK Data	↑ DOR expected ↔ ATV expected	↔ EFV ATV AUC ↓ 74%	ETR AUC ↑ 50% and C_{min} ↑ 58% ↔ ATV AUC and C_{min} ↓ 47%	↑ NVP possible ↓ ATV possible	↑ RPV PO possible ↔ ATV expected
	Dose	No dose adjustment needed.	Do not coadminister.	Do not coadminister.	Do not coadminister.	No dose adjustment needed.
ATV/c	PK Data	↑ DOR expected ↔ ATV expected	↔ EFV expected ↓ ATV possible ↓ COBI possible	↑ ETR possible ↓ ATV possible ↓ COBI possible	↑ NVP possible ↓ ATV possible ↓ COBI possible	↑ RPV PO possible ↔ ATV expected
	Dose	No dose adjustment needed.	ATV/c in ART-Naive Patients • ATV 400 mg plus COBI 150 mg once daily • Do not use coformulated ATV 300 mg/ COBI 150 mg.	Do not coadminister.	Do not coadminister.	No dose adjustment needed.

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		DOR	EFV	ETR	NVP	RPV
			ATV/c in ART-Experienced Patients • Do not coadminister. No dose adjustment needed for EFV.			
ATV/r	PK Data	↑ DOR expected ↔ ATV expected	↔ EFV expected (ATV 400 mg plus RTV 100 mg) Once Daily • ATV concentrations similar to (ATV 300 mg plus RTV 100 mg) without EFV	(ATV 300 mg plus RTV 100 mg) Once Daily • ETR AUC and C_{min} both ↑ ~30% • ↔ ATV AUC and C_{min}	(ATV 300 mg plus RTV 100 mg) Once Daily • ATV AUC ↓ 42% and C_{min} ↓ 72% • NVP AUC ↑ 25%	↑ RPV PO possible ↔ ATV expected
	Dose	No dose adjustment needed.	ATV/r in ART-Naive Patients • (ATV 400 mg plus RTV 100 mg) once daily ATV/r in ART-Experienced Patients: • Do not coadminister. No dose adjustment needed for EFV.	No dose adjustment needed.	Do not coadminister.	No dose adjustment needed.
DRV/c	PK Data	↑ DOR expected ↔ DRV expected	↔ EFV expected ↓ DRV possible ↓ COBI possible	ETR 400 mg Once Daily with (DRV 800 mg plus COBI 150 mg) Once Daily • ↔ ETR AUC and C_{min}	↑ NVP possible ↓ DRV possible ↓ COBI possible	↔ DRV expected ↑ RPV PO possible

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		DOR	EFV	ETR	NVP	RPV
				• ↔ DRV AUC and C_{min} ↓ 56% • COBI AUC ↓ 30% and C_{min} ↓ 66%		
	Dose	No dose adjustment needed.	Do not coadminister.	Do not coadminister.	Do not coadminister.	No dose adjustment needed.
DRV/r	PK Data	↑ DOR expected ↔ DRV expected	With (DRV 300 mg plus RTV 100 mg) Twice Daily • EFV AUC ↑ 21% • ↔ DRV AUC and C_{min} ↓ 31%	ETR 100 mg Twice Daily with (DRV 600 mg plus RTV 100 mg) Twice Daily • ETR AUC ↓ 37% and C_{min} ↓ 49% • ↔ DRV	With (DRV 400 mg plus RTV 100 mg) Twice Daily • NVP AUC ↑ 27% and C_{min} ↑ 47% • DRV AUC ↑ 24%[a]	RPV 150 mg PO Once Daily with (DRV 800 mg plus RTV 100 mg) Once Daily • RPV PO AUC ↑ 130% and C_{min} ↑ 178% • ↔ DRV
	Dose	No dose adjustment needed.	Clinical significance unknown. Use standard doses and monitor patient closely. Consider monitoring drug levels.	No dose adjustment needed. Despite reduced ETR concentration, safety and efficacy of this combination have been established in a clinical trial.	No dose adjustment needed.	No dose adjustment needed.
LPV/r	PK Data	↑ DOR expected ↔ LPV expected	↔ EFV expected With LPV/r 500 mg/125 mg[b] Twice Daily • LPV concentration similar to that of LPV/r 400 mg/100 mg twice daily without EFV	ETR AUC ↓ 35% (comparable to the decrease seen with DRV/r) ↔ LPV AUC	↑ NVP possible LPV AUC ↓ 27% and C_{min} ↓ 51%	RPV 150 mg PO Once Daily with LPV/r • RPV PO AUC ↑ 52% and C_{min} ↑ 74% • ↔ LPV

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PIs		NNRTIs				
		DOR	EFV	ETR	NVP	RPV
	Dose	No dose adjustment needed.	LPV/r 500 mg/ 125 mg[a] twice daily LPV/r 533 mg/ 133 mg twice daily when using oral solution No dose adjustment needed for EFV.	No dose adjustment needed.	LPV/r 500 mg/ 125 mg[a] twice daily LPV/r 533 mg/133 mg twice daily when using oral solution No dose adjustment needed for NVP.	No dose adjustment needed.

[a] Use a combination of two LPV/r 200 mg/50 mg tablets plus one LPV/r 100 mg/25 mg tablet to make a total dose of LPV/r 500 mg/125 mg.

Key to Symbols

↑ = increase
↓ = decrease
↔ = no change

Key: ART = antiretroviral therapy; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{min} = minimum plasma concentration; COBI = cobicistat; DLV = delavirdine; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETR = etravirine; FPV = fosamprenavir; IDV = indinavir; IM = intramuscular; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PO = oral; PK = pharmacokinetic; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; TPV = tipranavir