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

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Table 16b. Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors* (Last updated March 27, 2012; last reviewed February 2013) (page 1 of 3)

* Delavirdine (DLV), indinavir (IDV), and nelfinavir (NFV) are not included in this table. Refer to the DLV, IDV, and NFV Food and Drug Administration package inserts for information regarding drug interactions.

		EFV	ETR	NVP	RPV[a]
ATV +/- RTV	**PK data**	With unboosted ATV ATV: AUC ↓ 74% EFV: no significant change With (ATV 300 mg + RTV 100 mg) once daily with food ATV concentrations similar to those with unboosted ATV without EFV	With unboosted ATV ETR: AUC ↑ 50%, C_{max} ↑ 47%, and C_{min} ↑ 58% ATV: AUC ↓ 17% and C_{min} ↓ 47% With (ATV 300 mg + RTV 100 mg) once daily ETR: AUC, C_{max}, and C_{min} ↑ approximately 30% ATV: AUC ↓ 14% and C_{min} ↓ 38%	With (ATV 300 mg + RTV 100 mg) once daily ATV: AUC ↓ 42% and C_{min} ↓ 72% NVP: AUC ↑ 25%	With boosted and unboosted ATV ↑ RPV possible
	Dose	**Do not co-administer with unboosted ATV.** In ART-naive patients (ATV 400 mg + RTV 100 mg) once daily **Do not co-administer in ART-experienced patients.**	**Do not co-administer with ATV +/– RTV.**	**Do not co-administer with ATV +/– RTV.**	Standard
DRV (always use with RTV)	**PK data**	With (DRV 300 mg + RTV 100 mg) BID DRV: AUC ↓ 13%, C_{min} ↓ 31% EFV: AUC ↑ 21%	ETR 100 mg BID with (DRV 600 mg + RTV 100 mg) BID DRV: no significant change ETR: AUC ↓ 37%, C_{min} ↓ 49%	With (DRV 400 mg + RTV 100 mg) BID DRV: AUC ↑ 24%[b] NVP: AUC ↑ 27% and C_{min} ↑ 47%	RPV 150 mg once daily with (DRV 800 mg + RTV 100 mg) once daily DRV: no significant change RPV: AUC ↑ 130% and C_{min} ↑ 178%
	Dose	Clinical significance unknown. Use standard doses and monitor patient closely. Consider monitoring drug levels.	Standard (ETR 200 mg BID). Safety and efficacy of this combination, despite decreased ETR concentration, have been established in a clinical trial.	Standard	Standard
EFV	**PK data**	•	↓ ETR possible	NVP: no significant change EFV: AUC ↓ 22%	↓ RPV possible
	Dose		**Do not co-administer.**	**Do not co-administer.**	**Do not co-administer.**
ETR	**PK data**	↓ ETR possible	•	↓ ETR possible	↓ RPV possible
	Dose	**Do not co-administer.**		**Do not co-administer.**	**Do not co-administer.**

Table 16b. Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors, and Protease Inhibitors* (Last updated March 27, 2012; last reviewed February 2013) (page 2 of 3)

		EFV	ETR	NVP	RPV[a]
FPV	**PK data**	With (FPV 1400 mg + RTV 200 mg) once daily APV: C_{min} ↓ 36%	With (FPV 700 mg + RTV 100 mg) BID APV: AUC ↑ 69%, C_{min} ↑ 77%	With unboosted FPV 1400 mg BID APV: AUC ↓ 33% NVP: AUC ↑ 29% With (FPV 700 mg + RTV 100 mg) BID NVP: C_{min} ↑ 22%	With boosted and unboosted FPV ↑ RPV possible
	Dose	(FPV 1400 mg + RTV 300 mg) once daily or (FPV 700 mg + RTV 100 mg) BID EFV standard	**Do not co-administer with FPV +/– RTV.**	(FPV 700 mg + RTV 100 mg) BID NVP standard	Standard
LPV/r	**PK data**	With LPV/r tablets 500/125 mg BID[c] + EFV 600 mg LPV levels similar to LPV/r 400/100 mg BID without EFV	With LPV/r tablets ETR: AUC ↓ 35% (comparable to the decrease with DRV/r) LPV: AUC↓ 13%	With LPV/r capsules LPV: AUC ↓ 27% and C_{min} ↓51%	RPV 150 mg once daily with LPV/r capsules LPV: no significant change RPV: AUC ↑ 52% and C_{min} ↑ 74%
	Dose	LPV/r tablets 500/125 mg[c] BID; LPV/r oral solution 533/133 mg BID EFV standard	Standard	LPV/r tablets 500/125 mg[c] BID; LPV/r oral solution 533/133 mg BID NVP standard	Standard
NVP	**PK data**	NVP: no significant change EFV: AUC ↓ 22%	↓ ETR possible	•	↓ RPV possible
	Dose	**Do not co-administer.**	**Do not co-administer.**		**Do not co-administer.**
RPV	**PK data**	↓ RPV possible	↓ RPV possible	↓ RPV possible	•
	Dose	**Do not co-administer.**	**Do not co-administer.**	**Do not co-administer.**	
RTV	**PK data** **Dose**	Refer to information for boosted PI.	Refer to information for boosted PI.	Refer to information for boosted PI.	Refer to information for boosted PI.
SQV (always use with RTV)	**PK data**	With SQV 1200 mg TID SQV: AUC ↓ 62% EFV: AUC ↓ 12%	With (SQV 1000 mg + RTV 100 mg) BID SQV: AUC unchanged ETR: AUC ↓ 33%, C_{min} ↓ 29% Reduced ETR levels similar to reduction with DRV/r	With 600 mg TID SQV: AUC ↓ 24% NVP: no significant change	↑ RPV possible
	Dose	(SQV 1000 mg + RTV 100 mg) BID	(SQV 1000 mg + RTV 100 mg) BID	Dose with SQV/r not established	Standard

Table 16b. Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors, and Protease Inhibitors* (Last updated March 27, 2012; last reviewed February 2013) (page 3 of 3)

		EFV	ETR	NVP	RPV[a]
TPV (always use with RTV)	**PK data**	With (TPV 500 mg + RTV 100 mg) BID TPV: AUC ↓ 31%, C_{min} ↓ 42% EFV: no significant change With (TPV 750 mg + RTV 200 mg) BID TPV: no significant change EFV: no significant change	With (TPV 500 mg + RTV 200 mg) BID ETR: AUC ↓ 76%, C_{min} ↓ 82% TPV: AUC ↑ 18%, C_{min} ↑ 24%	With (TPV 250 mg + RTV 200 mg) BID and with (TPV 750 mg + RTV 100 mg) BID NVP: no significant change TPV: no data	↑ RPV possible
	Dose	Standard	**Do not co-administer.**	Standard	Standard

[a] Approved dose for RPV is 25 mg once daily. Most PK interaction studies were performed using 75 mg to 150 mg per dose.

[b] Based on between-study comparison.

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

Key to Abbreviations: APV = amprenavir, ART = antiretroviral therapy, ATV = atazanavir, AUC = area under the curve, BID = twice daily, C_{max} = maximum plasma concentration, C_{min} = minimum plasma concentration, CYP = cytochrome P, DLV = delavirdine, DRV = darunavir, DRV/r = darunavir/ritonavir, EFV = efavirenz, ETR = etravirine, FDA = Food and Drug Administration, FPV = fosamprenavir, IDV = indinavir, LPV = lopinavir, LPV/r = lopinavir/ritonavir, MVC = maraviroc, NFV = nelfinavir, NVP = nevirapine, PI = protease inhibitor, PK = pharmacokinetic, RAL = raltegravir, RPV = rilpivirine, RTV = ritonavir, SQV = saquinavir, SQV/r = saquinavir/ritonavir, TID = three times a day, TPV = tipranavir