



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

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Table 20a. Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors^a (Last updated September 9, 2016; last reviewed April 8, 2015) (Page 1 of 3)

Note: DLV, IDV, and 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.

| PIs | | NNRTIs | | | |
|------------------|----------------|--|---|--|----------------------------------|
| | | EFV | ETR | NVP | RPV ^a |
| ATV Unboosted | PK Data | EFV: no significant change ATV AUC ↓ 74% | ETR AUC ↑ 50% and C _{min} ↑ 58% ATV AUC ↓ 17% and C _{min} ↓ 47% | ↓ ATV possible | ↑ RPV possible |
| | Dose | Do not coadminister. | Do not coadminister. | Do not coadminister. | Standard doses |
| ATV/c | PK Data | ↓ ATV ↓ COBI | ↓ ATV ↓ COBI | ↓ COBI | ↑ RPV possible ↔ ATV expected |
| | Dose | EFV standard dose <u>In ART-Naive Patients:</u> • ATV 400 mg plus COBI 150 mg Once Daily Do not coadminister in ART-experienced patients. | Do not coadminister. | Do not coadminister. | Standard doses |
| ATV/r | PK Data | <u>(ATV 300 mg plus RTV 100 mg) Once Daily:</u> • ATV concentrations are similar to those with unboosted ATV without EFV. | <u>(ATV 300 mg plus RTV 100 mg) Once Daily:</u> • ETR AUC and C _{min} both ↑ ~30% • ATV AUC ↔ and C _{min} ↓ 18% | <u>(ATV 300 mg plus RTV 100 mg) Once Daily:</u> • ATV AUC ↓ 42% and C _{min} ↓ 72% • NVP AUC ↑ 25% | ↑ RPV possible |
| | Dose | EFV standard dose <u>In ART-Naive Patients:</u> • (ATV 400 mg plus RTV 100 mg) Once Daily Do not coadminister in ART-experienced patients. | ETR standard dose (ATV 300 mg plus RTV 100 mg) Once Daily | Do not coadminister. | Standard doses |
| DRV/c | PK Data | ↓ DRV possible ↓ COBI possible | Effect on DRV unknown ↓ COBI possible | Effect on DRV unknown ↓ COBI possible | ↔ DRV expected ↑ RPV possible |
| | Dose | Do not coadminister. | Do not coadminister. | Do not coadminister. | Standard doses |

Table 20a. Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors, and Protease Inhibitors^a (Last updated September 9, 2016; last reviewed April 8, 2015) (Page 2 of 3)

| PIs | | NNRTIs | | | |
|-------------|----------------|--|---|---|---|
| | | EFV | ETR | NVP | RPV ^a |
| DRV/r | PK Data | <p><u>With (DRV 300 mg plus RTV 100 mg) BID:</u></p> <ul style="list-style-type: none"> • EFV AUC ↑ 21% • DRV AUC ↓ 13% and C_{min} ↓ 31% | <p><u>ETR 100 mg BID with (DRV 600 mg plus RTV 100 mg) BID:</u></p> <ul style="list-style-type: none"> • ETR AUC ↓ 37% and C_{min} ↓ 49% • DRV: no significant change | <p><u>With (DRV 400 mg plus RTV 100 mg) BID:</u></p> <ul style="list-style-type: none"> • NVP AUC ↑ 27% and C_{min} ↑ 47% • DRV AUC ↑ 24%^b | <p><u>RPV 150 mg Once Daily with (DRV 800 mg plus RTV 100 mg) Once Daily:</u></p> <ul style="list-style-type: none"> • RPV AUC ↑ 130% and C_{min} ↑ 178% • DRV: no significant change |
| | Dose | Clinical significance unknown. Use standard doses and monitor patient closely. Consider monitoring drug levels. | Standard doses Safety and efficacy of this combination, despite reduced ETR concentration, have been established in a clinical trial. | Standard doses | Standard doses |
| FPV +/- RTV | PK Data | <p><u>With (FPV 1400 mg plus RTV 200 mg) Once Daily:</u></p> <ul style="list-style-type: none"> • APV C_{min} ↓ 36% | <p><u>With (FPV 700 mg plus RTV 100 mg) BID:</u></p> <ul style="list-style-type: none"> • APV AUC ↑ 69% and C_{min} ↑ 77% | <p><u>With Unboosted FPV 1400 mg BID:</u></p> <ul style="list-style-type: none"> • NVP AUC ↑ 29% • APV AUC ↓ 33% <p><u>With (FPV 700 mg plus RTV 100 mg) BID:</u></p> <ul style="list-style-type: none"> • NVP C_{min} ↑ 22% | <p><u>With Boosted and Unboosted FPV:</u></p> <ul style="list-style-type: none"> • ↑ RPV possible |
| | Dose | (FPV 1400 mg plus RTV 300 mg) Once Daily or (FPV 700 mg plus RTV 100 mg) BID EFV standard dose | Do not coadminister with FPV +/- RTV. | (FPV 700 mg plus RTV 100 mg) BID NVP standard dose | Standard doses |
| LPV/r | PK Data | <p><u>With LPV/r Tablets 500/125 mg^c BID:</u></p> <ul style="list-style-type: none"> • LPV concentration similar to that with LPV/r 400/100 mg BID without EFV | <p><u>With LPV/r Tablets:</u></p> <ul style="list-style-type: none"> • ETR AUC ↓ 35% (comparable to the decrease with DRV/r) • LPV AUC ↓ 13% | <p><u>With LPV/r Capsules:</u></p> <ul style="list-style-type: none"> • LPV AUC ↓ 27% and C_{min} ↓ 51% | <p><u>RPV 150 mg Once Daily with LPV/r Capsules:</u></p> <ul style="list-style-type: none"> • RPV AUC ↑ 52% and C_{min} ↑ 74% • LPV no significant change |
| | Dose | LPV/r tablets 500/125 mg ^c BID; LPV/r oral solution 520/130 mg BID EFV standard dose | Standard doses | LPV/r tablets 500/125 mg ^c BID; LPV/r oral solution 533/133 mg BID NVP standard dose | Standard doses |

Table 20a. Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors, and Protease Inhibitors^a (Last updated September 9, 2016; last reviewed April 8, 2015) (Page 3 of 3)

| PIs | | NNRTIs | | | |
|----------------------------|---------|---|---|--|------------------|
| | | EFV | ETR | NVP | RPV ^a |
| SQV Always use with RTV | PK Data | <u>With SQV 1200 mg TID:</u> • EFV AUC ↓ 12% • SQV AUC ↓ 62% | <u>With (SQV 1000 mg plus RTV 100 mg) BID:</u> • ETR AUC ↓ 33% and C _{min} ↓ 29% • SQV AUC ↔ ↓ ETR levels similar to reduction with DRV/r | <u>With SQV 600 mg TID:</u> • NVP: no significant change • SQV AUC ↓ 24% | ↑ RPV possible |
| | Dose | (SQV 1000 mg plus RTV 100 mg) BID | (SQV 1000 mg plus RTV 100 mg) BID | Dose with SQV/r not established | Standard doses |
| TPV Always use with RTV | PK Data | <u>With (TPV 500 mg plus RTV 100 mg) BID:</u> • EFV no significant change • TPV AUC ↓ 31% and C _{min} ↓ 42% <u>With (TPV 750 mg plus RTV 200 mg) BID:</u> • EFV: no significant change • TPV: no significant change | <u>With (TPV 500 mg plus RTV 200 mg) BID:</u> • ETR AUC ↓ 76% and C _{min} ↓ 82% • TPV AUC ↑ 18% and C _{min} ↑ 24% | <u>With (TPV 250 mg plus RTV 200 mg) BID or with (TPV 750 mg plus RTV 100 mg) BID:</u> • NVP: no significant change • TPV: no data | ↑ RPV possible |
| | Dose | Standard doses | Do not coadminister. | Standard doses | Standard doses |

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

^b Based on between-study comparison.

^c 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 to Acronyms: APV = amprenavir; ART = antiretroviral therapy; ATV = atazanavir; ATV/c = atazanavir/cobicistat; 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/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETR = etravirine; FDA = Food and Drug Administration; FPV = fosamprenavir; IDV = indinavir; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NFV = nelfinavir; NVP = nevirapine; PK = pharmacokinetic; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; SQV/r = saquinavir/ritonavir; TID = three times a day; TPV = tipranavir