

Please refer to the **Drug Interactions** section of the Adult Guidelines for more detailed discussions.

Table 15b. Drug Interactions Between NNRTIs and Other Drugs

This table provides information relating to pharmacokinetic interactions between NNRTIs and non-antiretroviral drugs. For interactions among antiretroviral agents and dosing recommendations, please refer to [Table 16b](#).

Concomitant Drug Class/Name	NNRTI	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comment
Antifungals			
Fluconazole	DLV, EFV	No significant effect	
	ETR	↑ ETR	No dosage adjustment necessary.
	NVP	NVP Cmax, AUC, and Cmin ↑ 100%	Increased risk of hepatotoxicity possible with this combination. Monitor NVP toxicity.
Itraconazole	DLV, NVP	No data, potential for bi-directional interactions	Consider monitoring NNRTI and itraconazole levels.
	EFV	itraconazole and OH-itraconazole AUC, Cmax, and Cmin ↓ 35%–44%	Dose adjustments for itraconazole may be necessary. Monitor itraconazole level.
	ETR	↑ ETR ↓ itraconazole	Dose adjustments for itraconazole may be necessary. Monitor itraconazole level.
Ketoconazole	DLV	↑ DLV	No dosage adjustment necessary.
	EFV	No data	
	ETR	↑ ETR ↓ ketoconazole	Dose adjustment for ketoconazole may be necessary depending on other coadministered drugs.
	NVP	ketoconazole ↓ 63%, NVP ↑ 15%–30%	Coadministration not recommended.
Posaconazole	DLV, NVP	No data	
	EFV	Posaconazole AUC ↓ 50%, Cmax ↓ 45% EFV Cmax ↑ 13%	Consider alternative antifungal if possible or consider monitoring posaconazole level if available
	ETR	↑ ETR	No dosage adjustment necessary.
Voriconazole	DLV	No data	Potential for bi-directional inhibition of metabolism. Monitor for toxicity.
	EFV	EFV ↑ 44% voriconazole ↓ 77%	Contraindicated at standard doses. Dose: voriconazole 400mg BID, EFV 300mg daily
	ETR	↑ ETR ↑ voriconazole	Dose adjustments for voriconazole may be necessary depending on other coadministered drugs. Monitor voriconazole level.
	NVP	No data	Potential for induction of voriconazole metabolism and inhibition of NVP metabolism. Monitor for toxicity and antifungal outcome.
Anticonvulsants			
Carbamazepine Phenobarbital Phenytoin	DLV	DLV Cmin ↓ 90% by phenytoin, phenobarbital, and carbamazepine	Contraindicated – do not coadminister.
	EFV	carbamazepine + EFV: AUCs ↓ 27% and 36%, respectively, when combined. EFV + phenytoin: ↓EFV concentrations (case report)	Monitor anticonvulsant levels, or if possible, use alternative anticonvulsant.
	ETR	No data. Potential for ↓ ETR and anticonvulsant concentrations.	Do not coadminister. Consider alternative anticonvulsants.
	NVP	No data	

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Concomitant Drug Class/Name	NNRTI	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comment
Anti-mycobacterials			
Clarithromycin	DLV	clarithromycin ↑ 100% DLV ↑ 44%	Reduce clarithromycin dose by 50% in patients with CrCl 30–60mL/min and by 75% in patients with CrCl <30mL/min.
	EFV	clarithromycin ↓ 39%	Monitor for efficacy or consider alternative agent, such as azithromycin, for MAC prophylaxis and treatment.
	ETR	ETR AUC ↑ 42%, clarithromycin AUC ↓ 39% and Cmin ↓ 53%, OH-clarithromycin AUC ↑ 21%	Consider alternative agent, such as azithromycin, for MAC prophylaxis and treatment.
	NVP	NVP ↑ 26%, clarithromycin ↓ 30%	Monitor for efficacy or use alternative agent.
Rifabutin	DLV	DLV ↓ 80% rifabutin ↑ 100%	Coadministration not recommended.
	EFV	rifabutin ↓ 35%	Dose: rifabutin 450–600mg once daily or 600mg 3x/week if EFV is not coadministered with a PI.
	ETR	ETR AUC ↓ 37% & Cmin ↓ 35% rifabutin AUC ↓ 17% & Cmin ↓ 24%, 25-O-desacetyl-rifabutin AUC ↓ 17% & Cmin ↓ 22%	Dose: rifabutin 300mg once daily if ETR is not coadministered with a RTV-boosted PI. If ETR is coadministered with DRV/r or SQV/r and rifabutin is needed, consider alternative ARV agent to ETR. If ETR is coadministered with LPV/r, use rifabutin 150mg QOD or 3x/week. Acquired rifamycin resistance has been reported in patients with inadequate rifabutin levels while on 150mg twice weekly and RTV-boosted PIs. Consider therapeutic drug monitoring and adjust dose accordingly.
	NVP	↓ NVP ↑ Rifabutin	No dosage adjustment necessary.
Rifampin	DLV	DLV ↓ 96%	Contraindicated—do not coadminister.
	EFV	↓ EFV 25%	Maintain efavirenz dose at 600mg once daily and monitor for viral response. Some clinicians suggest EFV 800mg dose in patients >60kg.
	ETR	Potential for significant ↓ ETR levels	Do not coadminister.
	NVP	↓ NVP 20%–58%	Do not coadminister.
Benzodiazepines			
Alprazolam	DLV	No data May ↑ alprazolam	Do not coadminister. Consider alternative benzodiazepines, such as lorazepam, oxazepam, or temazepam.
	EFV, NVP, ETR	No data	Monitor for therapeutic efficacy of alprazolam.
Diazepam	DLV	No data May ↑ diazepam	Consider alternative benzodiazepines, such as lorazepam, oxazepam, or temazepam.
	EFV, NVP	No data	
	ETR	↑ diazepam	Decreased dose of diazepam may be necessary.
Lorazepam	DLV, ETR, NVP	No data	
	EFV	Lorazepam Cmax ↑ 16%, no significant effect on lorazepam AUC	No dosage adjustment necessary.
Midazolam	DLV, EFV	No data May ↑ midazolam	Do not coadminister with oral midazolam. Parenteral midazolam can be used with caution as a single dose and can be given in a monitored situation for procedural sedation.
	ETR, NVP	No data	

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Triazolam	DLV, EFV	No data May ↑ triazolam	Do not coadminister.
	ETR, NVP	No data	
Herbal Products			
St. John's wort	All NNRTIs	↓ NNRTI	Administration of St. John's wort with NNRTIs is not recommended.
Hormonal Contraceptives			
Hormonal Contraceptives	DLV	No data Potential for ↑ ethinyl estradiol levels.	Clinical significance unknown.
	EFV	↑ ethinyl estradiol	Use alternative or additional methods. No data on other components.
	ETR	↑ ethinyl estradiol No effect on norethindrone levels.	No dosage adjustment necessary.
	NVP	ethinyl estradiol ↓ 20%.	Use alternative or additional methods.
HMG-CoA Reductase Inhibitors			
Atorvastatin	DLV	No data Potential for inhibition of atorvastatin metabolism.	Use lowest possible dose and monitor for toxicity, or consider other HMG-CoA reductase inhibitors with less potential for interaction.
	EFV	atorvastatin AUC ↓ 37%–43%.	Adjust atorvastatin according to lipid responses, not to exceed the maximum recommended dose.
	ETR	↓ atorvastatin AUC 37%	Dose: standard, adjust dose according to response.
	NVP	No data Potential for induction of atorvastatin metabolism	Dose: standard, adjust dose according to response.
Fluvastatin	DLV, EFV, NVP	No data	
	ETR	↑ fluvastatin	Dose adjustments for fluvastatin may be necessary.
Lovastatin Simvastatin	DLV	No data Potential for large increase in statin levels.	Avoid concomitant use.
	EFV	simvastatin AUC ↓ 68%	Adjust simvastatin dose according to lipid responses, not to exceed the maximum recommended dose.
	ETR	↓ lovastatin ↓ simvastatin	Adjust lovastatin or simvastatin dose according to lipid responses, not to exceed the maximum recommended dose. If used with RTV-boosted PI, simvastatin and lovastatin should be avoided.
Pravastatin Rosuvastatin	DLV, NVP	No data	
	EFV	pravastatin AUC ↓ 44%.	Adjust pravastatin dose according to lipid responses, not to exceed the maximum recommended dose.
	ETR	No effect	Dose: standard
Methadone			
Methadone	DLV	No effect on DLV Potential for ↑ methadone	Monitor for methadone toxicity and need for dose reduction
	EFV	Methadone ↓ 60%	Potential for opiate withdrawal; increased methadone dose often necessary.
	ETR	No effect	Dose: standard
	NVP	↓ methadone No effect on NVP	Opiate withdrawal common; increased methadone dose often necessary.

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Concomitant Drug Class/Name	NNRTI	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comment
Oral Anticoagulant			
Warfarin	DLV	No data	May increase warfarin levels. Monitor INR.
	EFV, NVP	No data	May increase or decrease warfarin levels. Monitor INR.
	ETR	↑ warfarin	Monitor INR and adjust warfarin dose accordingly.

Abbreviations: DLV = delavirdine, EFV = efavirenz, ETR = etravirine, NNRTI = non-nucleoside reverse transcriptase inhibitor, NVP = nevirapine, CBZ = carbamazepine.

Drug-Specific Interactions

NNRTI	Concomitant Drug Class/Name	Effect on NNRTI or Concomitant Drug Concentrations	Dosage Recommendations and Clinical Comment
DLV	Fluoxetine	↑ DLV	No dosage adjustment necessary.
	Quinidine	No data May increase quinidine levels.	Monitor quinidine level and toxicities.
	Sildenafil Vardenafil Tadalafil	No data Potential for increased phosphodiesterase inhibitor levels.	Use cautiously. Start with reduced dose of sildenafil 25mg Q48H, vardenafil 2.5mg Q24H, and tadalafil 5mg Q72H.
ETR	Antiarrhythmics	↓ antiarrhythmics	Use with caution with antiarrhythmic level monitoring if available.
	Dexamethasone	↓ ETR	Use systemic dexamethasone with caution or consider alternative corticosteroid for long-term use.
	Sildenafil	↓ sildenafil	May need to increase sildenafil dose based on clinical effect. Levels: sildenafil AUC ↓ 57%.