

**Table 14b. Drug Interactions Between NNRTIs\* and Other Drugs (Updated December 1, 2009)**

Page 1 of 3

\*Delavirdine is not included in this table. Please refer to the FDA package insert for information regarding delavirdine drug interactions.

This table provides information relating to pharmacokinetic interactions between NNRTIs and non-antiretroviral drugs. For interactions among antiretroviral agents and for dosing recommendations, refer to [Table 15b](#).

Concomitant Drug Class/Name	NNRTI	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comment
<b>Antifungals</b>			
Fluconazole	EFV	No significant effect	
	ETR	↑ ETR possible	No dosage adjustment necessary
	NVP	NVP AUC ↑ 110%	Increased risk of hepatotoxicity possible with this combination. Monitor NVP toxicity or use alternative antiretroviral agent.
Itraconazole	EFV	itraconazole and OH-itraconazole AUC, C <sub>max</sub> , and C <sub>min</sub> ↓ 35%–44%	Dose adjustments for itraconazole may be necessary. Monitor itraconazole level.
	ETR	↓ itraconazole possible ↑ ETR possible	Dose adjustments for itraconazole may be necessary. Monitor itraconazole level.
	NVP	↓ itraconazole possible ↑ NVP possible	Consider monitoring NNRTI and itraconazole levels.
Ketoconazole	EFV	↓ ketoconazole possible	
	ETR	↓ ketoconazole possible ↑ ETR possible	Dose adjustment for ketoconazole may be necessary depending on other coadministered drugs.
	NVP	ketoconazole AUC ↓ 72% ↑ NVP 15%–30%	<b>Coadministration not recommended.</b>
Posaconazole	EFV	posaconazole AUC ↓ 50%	Consider alternative antifungal if possible or consider monitoring posaconazole level if available.
	ETR	↑ ETR possible	No dosage adjustment necessary
Voriconazole	EFV	voriconazole AUC ↓ 77% EFV AUC ↑ 44%	<b>Contraindicated at standard doses.</b> Dose: voriconazole 400mg BID, EFV 300mg daily
	ETR	↑ voriconazole possible ↑ ETR possible	Dose adjustments for voriconazole may be necessary depending on other coadministered drugs. Monitor voriconazole level.
	NVP	↓ voriconazole possible ↑ NVP possible	Monitor for toxicity and antifungal outcome and/or voriconazole level.
<b>Anticonvulsants</b>			
Carbamazepine Phenobarbital Phenytoin	EFV	carbamazepine + EFV: carbamazepine AUC ↓ 27% and EFV AUC ↓ 36% phenytoin + EFV: ↓ EFV and ↓ phenytoin possible	Monitor anticonvulsant and EFV levels, or if possible, use alternative anticonvulsant.
	ETR	↓ anticonvulsant and ETR possible	<b>Do not coadminister.</b> Consider alternative anticonvulsants.
	NVP	↓ anticonvulsant and NVP possible	Monitor anticonvulsant and NVP levels and virologic responses.
<b>Anti-mycobacterials</b>			
Clarithromycin	EFV	clarithromycin AUC ↓ 39%	Monitor for efficacy or consider alternative agent, such as azithromycin, for MAC prophylaxis and treatment.
	ETR	clarithromycin AUC ↓ 39% OH-clarithromycin AUC ↑ 21% ETR AUC ↑ 42%	Consider alternative agent, such as azithromycin, for MAC prophylaxis and treatment.
	NVP	Clarithromycin AUC ↓ 31% OH-clarithromycin AUC ↑ 42%	Monitor for efficacy or use alternative agent, such as azithromycin, for MAC prophylaxis and treatment.
Rifabutin	EFV	Rifabutin ↓ 38%	Dose: rifabutin 450–600mg once daily or 600mg 3x/week if EFV is not coadministered with a PI.
	ETR	rifabutin and metabolite AUC ↓ 17% ETR AUC ↓ 37%	Dose: rifabutin 300mg once daily <b>if ETR is not coadministered with a RTV-boosted PI.</b> <b>If ETR is coadministered with a RTV-boosted PI, rifabutin should not be coadministered.</b>
	NVP	rifabutin AUC ↑ 17% and metabolite AUC ↑ 24% NVP C <sub>min</sub> ↓ 16%	No dosage adjustment necessary. Use with caution.
Rifampin	EFV	EFV AUC ↓ 26%	Maintain EFV dose at 600mg once daily and monitor for virologic response. Some clinicians suggest EFV 800mg dose in patients >60kg.
	ETR	Significant ↓ ETR possible	<b>Do not coadminister.</b>
	NVP	NVP ↓ 20%–58%	<b>Do not coadminister.</b>

Concomitant Drug Class/Name	NNRTI	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comment
<b>Benzodiazepines</b>			
<b>Alprazolam</b>	EFV, ETR, NVP	No data	Monitor for therapeutic efficacy of alprazolam.
<b>Diazepam</b>	ETR	↑ diazepam possible	Decreased dose of diazepam may be necessary.
<b>Lorazepam</b>	EFV	lorazepam Cmax ↑ 16%, AUC no significant effect	No dosage adjustment necessary
<b>Midazolam</b>	EFV	Significant ↑ midazolam expected	<b>Do not coadminister with oral midazolam.</b> Parenteral midazolam can be used with caution as a single dose and can be given in a monitored situation for procedural sedation.
<b>Triazolam</b>	EFV	Significant ↑ triazolam expected	<b>Do not coadminister.</b>
<b>Cardiac Medications</b>			
<b>Dihydropyridine Calcium channel blockers (CCBs)</b>	EFV, NVP	↓ CCBs possible	Titrate CCB dose based on clinical response.
<b>Diltiazem</b>	EFV	diltiazem AUC ↓ 69%	Titrate diltiazem dose based on clinical response.
	NVP	↓ diltiazem possible	
<b>Herbal Products</b>			
<b>St. John's wort</b>	EFV, ETR, NVP	↓ NNRTI	<b>Do not coadminister.</b>
<b>Hormonal Contraceptives</b>			
<b>Hormonal contraceptives</b>	EFV	ethinyl estradiol AUC ↑ 37%	Clinical significance unknown
	ETR	ethinyl estradiol AUC ↑ 22% norethindrone: no significant effect	No dosage adjustment necessary
	NVP	ethinyl estradiol AUC ↓ 20% norethindrone AUC ↓ 19%	Use alternative or additional methods.
		depomedroxyprogesterone acetate: no significant change	No dosage adjustment necessary
<b>HMG-CoA Reductase Inhibitors</b>			
<b>Atorvastatin</b>	EFV, ETR, NVP	atorvastatin AUC ↓ 32%–43% with EFV, ETR	Adjust atorvastatin according to lipid responses, not to exceed the maximum recommended dose.
<b>Fluvastatin</b>	ETR	↑ fluvastatin possible	Dose adjustments for fluvastatin may be necessary.
<b>Lovastatin Simvastatin</b>	EFV	simvastatin AUC ↓ 68%	Adjust 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.
	ETR	↓ lovastatin possible ↓ simvastatin possible	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.
	NVP	↓ lovastatin possible ↓ simvastatin possible	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.
<b>Pravastatin Rosuvastatin</b>	EFV	pravastatin AUC ↓ 44% rosuvastatin: no data	Adjust statin dose according to lipid responses, not to exceed the maximum recommended dose.
	ETR	No significant effect expected	No dosage adjustment necessary
<b>Methadone</b>			
<b>Methadone</b>	EFV	methadone AUC ↓ 52%	Potential for opiate withdrawal; increased methadone dose often necessary.
	ETR	No significant effect	No dosage adjustment necessary
	NVP	↓ methadone NVP: no significant effect	Opiate withdrawal common; increased methadone dose often necessary.
<b>Oral Anticoagulant</b>			
<b>Warfarin</b>	EFV, NVP	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin accordingly.
	ETR	↑ warfarin possible	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
EFV	<b>Sertraline</b>	sertraline AUC ↓ 39%	Titrate sertraline dose based on clinical response.
	<b>Bupropion</b>	bupropion AUC ↓ 55%	Titrate bupropion dose based on clinical response.
ETR	<b>Dexamethasone</b>	↓ ETR	Use systemic dexamethasone with caution or consider alternative corticosteroid for long-term use.
	<b>Sildenafil</b>	sildenafil AUC ↓ 57%	May need to increase sildenafil dose based on clinical effect.

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