Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Updated: September 01, 2022
Reviewed: September 01, 2022

This table provides information on the known or predicted interactions between non-nucleoside reverse transcriptase inhibitors (NNRTIs) and non-antiretroviral (ARV) drugs. Cabotegravir (CAB) intramuscular (IM) plus rilpivirine (RPV) IM are co-packaged into a single product and are coadministered as a complete regimen; therefore, the dosing recommendations and clinical comments reflect the combination of CAB IM and RPV IM treatments. Drug interaction studies were not conducted with either CAB IM or RPV IM. Drug interaction studies with oral CAB and RPV were leveraged to make the dosing recommendations for CAB IM and RPV IM. For information regarding interactions between NNRTIs and other ARV drugs, including dosing recommendations, refer to Tables 24c, 24e, 24f, 25a, and 25b.

Recommendations for managing a particular drug interaction may differ, depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. When an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication to use.

RPV 75 mg and 300 mg oral once daily (3 and 12 times the recommended dose, respectively) were shown to prolong the QTc interval. Known and expected/theoretical pharmacokinetic interactions, resulting in increased RPV exposures, are included in this table due to the safety concern of QTc prolongation. There is limited information about the potential for pharmacodynamic interactions between RPV (in the absence of increased RPV exposures) and drugs that prolong the QTc interval; therefore, these are not included in this table.

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	DOR, EFV, NVP	↔ NNRTI AUC	No dose adjustment needed.
	ETR	↔ ETR expected	No dose adjustment needed.
	RPV IM	↔ RPV expected	No dose adjustment needed.
	RPV PO	↓ RPV expected when given simultaneously	Give antacids at least 2 hours before or at least 4 hours after RPV.
H2 Receptor Antagonists	DOR, NVP	↔ NNRTI expected	No dose adjustment needed.
	EFV	↔ EFV AUC	No dose adjustment needed.
	ETR	↔ ETR AUC	No dose adjustment needed.
	RPV IM	↔ RPV expected	No dose adjustment needed.
	RPV PO	RPV AUC ↓ 76% when famotidine 40 mg is taken 2 hours prior	Give H2 receptor antagonists at least 12 hours before or at least 4 hours after RPV.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Proton Pump Inhibitors	DOR	DOR AUC ↓ 17% and C_{min} ↓ 16%	No dose adjustment needed.
	EFV, NVP	↔ EFV and NVP expected	
	ETR	With Omeprazole 40 mg Daily ETR AUC ↑ 41%	
	RPV IM	↔ RPV expected	No dose adjustment needed.
	RPV PO	With Omeprazole 20 mg Daily RPV AUC ↓ 40% and C_{min} ↓ 33%	Contraindicated.
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin,Doxazosin, Silodosin, Terazosin	DOR, RPV IM, RPV PO	↔ alpha-adrenergic antagonists expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ alpha-adrenergic antagonists expected	Consider alternative ARV or alpha-antagonist therapy. If coadministration is necessary, monitor for therapeutic effectiveness of alpha antagonist.
Tamsulosin	DOR, RPV IM, RPV PO	↔ tamsulosin expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ tamsulosin expected	Monitor for therapeutic effectiveness of tamsulosin after 2–4 weeks. May need to increase dose to tamsulosin 0.8 mg once daily for patients who fail to respond to the 0.4-mg dose.
Antimycobacterials			
Bedaquiline	DOR, RPV IM, RPV PO	↔ bedaquiline expected	No dose adjustment needed.
	EFV, ETR	↓ bedaquiline possible	Do not coadminister.
	NVP	↔ bedaquiline AUC	No dose adjustment needed.
Rifabutin	DOR	DOR AUC ↓ 50%	Increase DOR dose to 100 mg twice daily. No dose adjustment is needed for rifabutin.
	EFV	Rifabutin ↓ 38%	The recommended dosing range is rifabutin 450–600 mg per day.
	ETR	↔ rifabutin and metabolite AUC ETR AUC ↓ 37%	Do not coadminister ETR plus PI/r with rifabutin. Use rifabutin 300 mg once daily if ETR is administered without PI/r.
	NVP	Rifabutin AUC ↑ 17% and metabolite AUC ↑ 24% NVP C_{min} ↓ 16%	No dose adjustment needed.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	RPV IM	↓ RPV expected	Contraindicated.
	RPV PO	Rifabutin plus RPV 50 mg PO Once Daily Compared to RPV 25 mg Once Daily Alone ↔ RPV AUC and C_{min}	Increase RPV dose to 50 mg PO once daily. No dose adjustment for rifabutin is needed.
Rifampin	DOR	DOR AUC ↓ 88%	Contraindicated. After stopping rifampin, wait 4 weeks before initiating DOR.
	EFV	EFV AUC ↓ 26%	Do not use EFV 400 mg with rifampin. Maintain EFV dose at 600 mg once daily and monitor for virologic response.
	ETR	Significant ↓ ETR possible	Do not coadminister.
	NVP	NVP ↓ 20% to 58%	Do not coadminister.
	RPV IM	↓ RPV expected	Contraindicated.
	RPV PO	RPV AUC ↓ 80%	Contraindicated.
Rifapentine	DOR	DOR 100 mg Twice Daily plus Once-Weekly Rifapentine and Isoniazid Compared to DOR 100 mg Twice Daily Alone DOR AUC ↓ 29%, C_{min} ↓ 31%	Contraindicated. After stopping rifapentine, wait 4 weeks before initiating DOR.
	EFV	↔ EFV concentrations	No dose adjustment needed.
	ETR	↓ ETR possible	Do not coadminister.
	NVP	NVP C_{min} ↓ 27%	Do not coadminister.
	RPV IM, RPV PO	↓ RPV expected	Contraindicated.
Antibacterials—Macrolides			
Azithromycin	All NNRTIs	↔ azithromycin expected	No dose adjustment needed.
Clarithromycin	DOR	↔ clarithromycin expected ↑ DOR possible	Monitor for ARV tolerability if used in combination.
	EFV	Clarithromycin AUC ↓ 39%	Monitor for effectiveness, or consider alternative agent (e.g., azithromycin) for MAC prophylaxis and treatment.
	ETR	Clarithromycin AUC ↓ 39% ETR AUC ↑ 42%	Consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment.
	NVP	Clarithromycin AUC ↓ 31% NVP AUC ↑ 26%	Monitor for effectiveness, or consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	RPV IM, RPV PO	↔ clarithromycin expected ↑ RPV possible	Consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment. If coadministered, monitor for QTc prolongation.
Erythromycin	DOR	↑ DOR possible	Monitor for ARV tolerability if used in combination.
	EFV, ETR, NVP	↑ EFV, ETR, and NVP possible ↓ erythromycin possible	Monitor for ARV tolerability and antibiotic efficacy if used in combination.
	RPV IM, RPV PO	↑ RPV possible	Consider alternative macrolide (e.g., azithromycin). If coadministered, monitor for QTc prolongation.
Anticoagulants			
Apixaban	DOR, RPV IM, RPV PO	↔ apixaban expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ apixaban possible	Consider alternative ARV or anticoagulant therapy.
Dabigatran	All NNRTIs	↔ dabigatran expected	No dose adjustment needed.
Edoxaban	All NNRTIs	↔ edoxaban expected	No dose adjustment needed.
Rivaroxaban	DOR, RPV IM, RPV PO	↔ rivaroxaban expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ rivaroxaban possible	Consider alternative ARV or anticoagulant therapy.
Warfarin	DOR, RPV IM, RPV PO	↔ warfarin expected	No dose adjustment needed.
	EFV, ETR, NVP	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
Anticonvulsants			
Carbamazepine, Phenobarbital, Phenytoin	DOR	↓ DOR possible	Contraindicated. After stopping anticonvulsant, wait 4 weeks before initiating DOR.
	EFV	Carbamazepine plus EFV Carbamazepine AUC ↓ 27% EFV AUC ↓ 36% Phenytoin plus EFV ↓ EFV ↑ or ↓ phenytoin possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor anticonvulsant and EFV concentrations.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	ETR	↓ anticonvulsant and ETR possible	Do not coadminister.
	NVP	↓ anticonvulsant and NVP possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor anticonvulsant and NVP concentrations and virologic response.
	RPV IM, RPV PO	↓ RPV possible	Contraindicated.
Eslicarbazepine	All NNRTIs	↓ NNRTI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor virologic response and consider monitoring plasma concentrations of ARVs.
Oxcarbazepine	DOR, RPV IM, RPV PO	↓ NNRTI possible	Contraindicated.
	EFV, ETR, NVP	↓ NNRTI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor virologic response and consider monitoring plasma concentrations of ARVs.
Ethosuximide, Lacosamide, Tiagabine, Zonisamide	DOR, RPV IM, RPV PO	↔ anticonvulsant expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ anticonvulsant possible	Monitor seizure control. Consider anticonvulsant therapeutic drug monitoring.
Lamotrigine	DOR, ETR, NVP, RPV IM, RPV PO	↔ lamotrigine expected	No dose adjustment needed.
	EFV	↓ lamotrigine possible	Monitor seizure control and plasma concentrations of lamotrigine.
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below.			
Bupropion	DOR, ETR, RPV IM, RPV PO	↔ bupropion expected	No dose adjustment needed.
	EFV	Bupropion AUC ↓ 55%	Titrate bupropion dose based on clinical response.
	NVP	↓ bupropion possible	
Citalopram, Escitalopram	DOR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antidepressant possible	Titrate antidepressant dose based on clinical response.
Fluoxetine, Fluvoxamine	All NNRTIs	↔ antidepressant expected	No dose adjustment needed.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Paroxetine	DOR, NVP, RPV IM, RPV PO	↔ paroxetine expected	No dose adjustment needed.
	EFV, ETR	↔ paroxetine expected	No dose adjustment needed.
Nefazodone	DOR, RPV IM, RPV PO	↑ NNRTI possible	No dose adjustment needed.
	EFV, ETR, NVP	↓ nefazodone expected ↑ NNRTI possible	Monitor antidepressant effect. Titrate dose as necessary based on clinical response.
Sertraline	DOR, RPV IM, RPV PO	↔ sertraline expected	No dose adjustment needed.
	EFV	Sertraline AUC ↓ 39%	Monitor the antidepressant effect. Titrate dose as necessary based on clinical response.
	ETR, NVP	↓ sertraline possible	
Trazodone	DOR, RPV IM, RPV PO	↔ trazodone expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ trazodone possible	Monitor for therapeutic effectiveness of trazodone and titrate dose as necessary.
Antipsychotics			
Aripiprazole	DOR, RPV IM, RPV PO	↔ aripiprazole expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ aripiprazole expected	Monitor for therapeutic effectiveness of antipsychotic. Consider doubling usual dose of aripiprazole over 1–2 weeks. Refer to aripiprazole prescribing information for dose recommendations.
Brexpiprazole	DOR, RPV IM, RPV PO	↔ brexpiprazole expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ brexpiprazole expected	Monitor for therapeutic effectiveness of antipsychotic. Consider doubling the usual dose of brexpiprazole and making further adjustments based on clinical response. Refer to brexpiprazole prescribing information.
Cariprazine	DOR, RPV IM, RPV PO	↔ cariprazine expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ cariprazine and ↑ or ↓ active metabolite possible	Do not coadminister.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Iloperidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Lumateperone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antipsychotic possible	Do not coadminister.
Lurasidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Olanzapine	DOR, ETR, NVP, RPV IM, RPV PO	↔ olanzapine expected	No dose adjustment needed.
	EFV	↓ olanzapine possible	Monitor for therapeutic effectiveness of olanzapine.
Other Antipsychotics CYP3A4 substrates (e.g., clozapine, perphenazine, risperidone)	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Pimavanserin	DOR, RPV IM, RPV PO	↔ pimavanserin expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ pimavanserin expected	Do not coadminister.
Pimozide	DOR, RPV IM, RPV PO	↔ pimozide expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ pimozide possible	Monitor for therapeutic effectiveness of pimozide.
Quetiapine	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Ziprasidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Antifungals			
Fluconazole	DOR	↑ DOR possible	No dose adjustment needed.
	EFV	↔ fluconazole expected ↔ EFV AUC	No dose adjustment needed.
	ETR	ETR AUC ↑ 86%	No dose adjustment needed.
	NVP	NVP AUC ↑ 110%	Consider alternative ARV or antifungal agent. Increased risk of hepatotoxicity is possible with this combination.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Isavuconazole	DOR	↑ DOR possible	No dose adjustment needed.
	EFV, ETR, NVP	↓ isavuconazole possible	Monitor isavuconazole concentration and antifungal response. Dose adjustments for isavuconazole may be necessary.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Itraconazole	DOR	↑ DOR possible	No dose adjustment needed.
	EFV	Itraconazole and OH-itraconazole AUC, C_{max}, and C_{min} ↓ 37% to 44%	Do not coadminister unless potential benefits outweigh the risks. Failure to achieve therapeutic itraconazole concentrations has been reported. If coadministration is necessary, closely monitor itraconazole concentration and adjust dose accordingly.
	ETR	↓ itraconazole possible ↑ ETR possible	Dose adjustments for itraconazole may be necessary. Monitor itraconazole concentration and antifungal response.
	NVP	Itraconazole AUC ↓ 61% ↑ NVP possible	Do not coadminister unless potential benefits outweigh the risks. If coadministration is necessary, monitor itraconazole concentration and adjust dose accordingly.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Posaconazole	DOR, ETR, NVP	↑ NNRTI possible	No dose adjustment needed.
	EFV	Posaconazole AUC ↓ 50% ↔ EFV AUC	Do not coadminister unless potential benefits outweigh the risks. If coadministration is necessary, monitor posaconazole concentration and adjust dose accordingly.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Voriconazole	DOR	↑ DOR possible	No dose adjustment needed.
	EFV	Voriconazole AUC ↓ 77% EFV AUC ↑ 44%	Contraindicated at standard doses. Adjust dose to voriconazole 400 mg twice daily plus EFV 300 mg daily.
	ETR	↔ voriconazole AUC ETR AUC ↑ 36%	No dose adjustment needed.
	NVP	↓ voriconazole possible ↑ NVP possible	Consider alternative ARV or antifungal agent. If coadministration is necessary, monitor ARV tolerability and antifungal response and/or voriconazole concentration.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Antimalarials			
Artemether/Lumefantrine	DOR, RPV IM, RPV PO	↔ antimalarial expected	No dose adjustment needed.
	EFV	Artemether AUC ↓ 79% DHA AUC ↓ 75% Lumefantrine AUC ↓ 30% to 56%	Consider alternative ARV or antimalarial drug. If used in combination, monitor closely for antimalarial efficacy.
	ETR	Artemether AUC ↓ 38% ↔ DHA AUC ↔ lumefantrine AUC ↔ ETR AUC	Clinical significance of the reduced antimalarial drug concentrations is unknown. If used in combination with ETR, monitor for antimalarial efficacy.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	NVP	Artemether AUC ↓ 67% to 72% DHA Study results are conflicting. DHA AUC ↓ 37% in one study, no difference in another. Lumefantrine Study results are conflicting. Lumefantrine AUC ↓ 25% to 58% in two studies, but ↑ 50% to 56% in another.	Clinical significance is unknown. If used in combination, monitor closely for antimalarial efficacy and lumefantrine toxicity.
Atovaquone/Proguanil	DOR, ETR, NVP, RPV IM, RPV PO	No data	Monitor for antimalarial efficacy.
	EFV	Atovaquone AUC ↓ 75% Proguanil AUC ↓ 43%	No dose recommendation. Consider alternative drug for malaria prophylaxis, if possible.
Antiplatelets			
Clopidogrel	DOR, NVP, RPV IM, RPV PO	↔ clopidogrel expected	No dose adjustment needed.
	EFV, ETR	↓ activation of clopidogrel possible	Consider alternative ARV or antiplatelet. ETR may prevent metabolism of clopidogrel to its active metabolite.
Prasugrel	All NNRTIs	↔ prasugrel expected	No dose adjustment needed.
Ticagrelor	DOR, RPV IM, RPV PO	↔ ticagrelor expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ ticagrelor expected	Consider alternative ARV or anticoagulant therapy.
Vorapaxar	DOR, NVP, RPV IM, RPV PO	↔ vorapaxar expected	No dose adjustment needed.
	EFV, ETR	↓ vorapaxar expected	Insufficient data to make a dose recommendation.
Antipneumocystis and Anti-Toxoplasmosis Drugs			
Atovaquone (oral solution)	DOR, ETR, NVP, RPV IM, RPV PO	No data	Monitor for therapeutic effectiveness of atovaquone.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EFV	Atovaquone AUC ↓ 44% to 47%	Consider alternative ARV or agent for PCP or toxoplasmosis treatment or prophylaxis. If coadministration is necessary, monitor for therapeutic effectiveness of atovaquone.
Antivirals—Orthopoxviruses (Smallpox, Mpox)			
Brincidofovir	All NNRTIs	↔ brincidofovir expected	No dose adjustment needed.
Cidofovir	All NNRTIs	↔ cidofovir expected	No dose adjustment needed.
Tecovirimat	DOR, RPV PO	↓ DOR or RPV expected but not likely to be clinically relevant	No dose adjustment needed.
	EFV, ETR, NVP	↔ EFV, ETR, or NVP expected	No dose adjustment needed.
	RPV IM	↓ RPV expected but not likely to be clinically relevant	No dose adjustment needed. If there is a concern for suboptimal RPV exposure, seek expert consultation. Do not initiate CAB/RPV IM during and within 2 weeks after tecovirimat treatment. (Refer to Table 24d for interaction with CAB.)
Cardiac Medications			
Bosentan	DOR	↓ DOR possible	Consider alternative ARV or alternative to bosentan. If coadministration is necessary, monitor virologic response.
	EFV, ETR, NVP	↓ NNRTI possible ↓ bosentan possible	Consider alternative ARV or alternative to bosentan. If coadministration is necessary, monitor bosentan efficacy and virologic response.
	RPV IM, RPV PO	↓ RPV possible	Consider alternative ARV or alternative to bosentan. If coadministration is necessary, monitor virologic response.
Dihydropyridine CCBs	DOR, RPV IM, RPV PO	↔ CCBs expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ CCBs possible	Titrate CCB dose based on clinical response.
Diltiazem, Verapamil	DOR, RPV IM, RPV PO	↔ CCBs expected ↑ NNRTI possible	No dose adjustment needed.
	EFV	Diltiazem AUC ↓ 69% ↓ verapamil possible	Titrate diltiazem or verapamil dose based on clinical response.
	ETR, NVP	↓ diltiazem or verapamil possible	

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Corticosteroids			
Dexamethasone	DOR, EFV, ETR, NVP	↓ NNRTI possible	Consider alternative corticosteroid for long-term use. If dexamethasone is used with NNRTI, monitor virologic response.
	RPV IM, RPV PO	Significant ↓ RPV possible	Contraindicated with more than a single dose of dexamethasone.
Glucose-Lowering Agents			
Canagliflozin, Dapagliflozin, Empagliflozin, Sitagliptin	All NNRTIs	↔ antihyperglycemic expected	No dose adjustment needed.
Linagliptin, Saxagliptin	DOR, RPV IM, RPV PO	↔ antihyperglycemic expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antihyperglycemic possible	Monitor glycemic control.
Metformin	DOR	↔ metformin AUC DOR AUC ↓ 26% and C_{max} ↓ 24%	No dose adjustment needed.
	EFV, ETR, NVP	↔ metformin expected	No dose adjustment needed.
	RPV IM	↔ metformin expected	No dose adjustment needed.
	RPV PO	↔ metformin AUC	No dose adjustment needed.
Hepatitis C Direct-Acting Antiviral Agents			
Daclatasvir	DOR, RPV IM, RPV PO	No data	No dose adjustment needed.
	EFV, ETR, NVP	Daclatasvir 120 mg Once Daily plus EFV 600 mg Daily Compared to Daclatasvir 60 mg Alone Daclatasvir C_{min} ↓ 17% and AUC ↑ 37%	The recommended dose is daclatasvir 90 mg once daily.
Dasabuvir plus Paritaprevir/ Ombitasvir/RTV	DOR	↑ DOR possible	No dose adjustment needed.
	EFV	No data	Contraindicated.
	ETR, NVP	↓ DAAs possible	Do not coadminister.
	RPV IM	↑ RPV expected	Do not coadminister due to the potential for QTc prolongation with higher concentrations of RPV.
	RPV PO	RPV AUC ↑ 150% to 225%	Do not coadminister due to the potential for QTc prolongation with higher concentrations of RPV.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Elbasvir/Grazoprevir	DOR	↔ elbasvir and grazoprevir DOR AUC ↑ 56% and C_{min} ↑ 41%	No dose adjustment needed.
	EFV	Elbasvir AUC ↓ 54% Grazoprevir AUC ↓ 83% ↔ EFV	Contraindicated.
	ETR, NVP	↓ elbasvir and grazoprevir expected	Do not coadminister.
	RPV IM	↔ elbasvir and grazoprevir expected ↔ RPV expected	No dose adjustment needed.
	RPV PO	↔ elbasvir and grazoprevir ↔ RPV AUC and C_{min}	No dose adjustment needed.
Glecaprevir/Pibrentasvir	DOR	↑ DOR expected	No dose adjustment needed.
	EFV	↓ glecaprevir and pibrentasvir expected	Do not coadminister.
	ETR	↓ glecaprevir and pibrentasvir possible	Do not coadminister.
	NVP	↓ glecaprevir and pibrentasvir possible	Consider alternative ARV or HCV regimen. If coadministration is necessary, monitor for HCV treatment efficacy.
	RPV IM	↔ glecaprevir and pibrentasvir expected ↑ RPV expected	No dose adjustment needed.
	RPV PO	↔ glecaprevir and pibrentasvir RPV AUC ↑ 84%	No dose adjustment needed.
Ledipasvir/Sofosbuvir	DOR	↔ ledipasvir and sofosbuvir ↔ DOR	No dose adjustment needed.
	EFV	Ledipasvir AUC, C_{min}, and C_{max} ↓ 34% ↔ sofosbuvir	
	ETR, NVP	No significant effect expected	
	RPV IM	↔ ledipasvir, sofosbuvir, and RPV expected	
	RPV PO	↔ ledipasvir and sofosbuvir ↔ RPV	

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Sofosbuvir/Velpatasvir	DOR, RPV IM, RPV PO	No significant effect expected	No dose adjustment needed.
	EFV	Velpatasvir AUC ↓ 43%, C_{max} ↓ 37%, and C_{min} ↓ 47%	Do not coadminister.
	ETR, NVP	↓ velpatasvir expected	Do not coadminister.
Sofosbuvir/Velpatasvir/ Voxilaprevir	DOR, RPV IM, RPV PO	No significant effect expected	No dose adjustment needed.
	EFV	Velpatasvir AUC ↓ 43%, C_{max} ↓ 37%, and C_{min} ↓47% ↓ voxilaprevir expected	Do not coadminister.
	ETR, NVP	↓ voxilaprevir expected ↓ velpatasvir expected	Do not coadminister.
Herbal Products			
St. John's Wort	DOR	↓ DOR expected	Contraindicated. After stopping St. John's Wort, wait 4 weeks before initiating DOR.
	EFV, ETR, NVP	↓ EFV, ETR, and NVP expected	Do not coadminister.
	RPV IM, RPV PO	↓ RPV expected	Contraindicated.
Hormonal Therapies			
Contraceptives—Injectable Depot MPA	DOR, ETR, RPV IM, RPV PO	↔ MPA expected	No dose adjustment needed.
	EFV, NVP	↔ MPA	No dose adjustment needed.
Contraceptives—Oral	DOR	↔ ethinyl estradiol ↔ levonorgestrel	No dose adjustment needed.
	EFV	↔ ethinyl estradiol Etonogestrel (metabolite of oral desogestrel) C_{min} ↓ 61% Levonorgestrel (metabolite of oral norgestimate) AUC ↓ 83% Norelgestromin (metabolite of oral norgestimate) AUC ↓ 64%	When Used for Contraception Use alternative ARV or contraceptive methods. When Used for Other Clinical Indications (e.g., Acne, Menstrual Cycle Regulation) Monitor for clinical effectiveness of hormonal therapy.
	ETR	Ethinyl estradiol AUC ↑ 22% ↔ norethindrone	No dose adjustment needed.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	NVP	Ethinyl estradiol AUC ↓ 29% and C_{min} ↓ 58% Norethindrone AUC ↓ 18% Etonogestrel (metabolite of oral desogestrel) C_{min} ↓ 22%	No dose adjustment needed based on clinical data that demonstrated no change in effectiveness.
	RPV IM	↔ ethinyl estradiol expected ↔ norethindrone expected	No dose adjustment needed.
	RPV PO	↔ ethinyl estradiol ↔ norethindrone	No dose adjustment needed.
Contraceptives—Subdermal Implant Etonogestrel	DOR, RPV IM, RPV PO	↔ etonogestrel expected	No dose adjustment needed.
	EFV	Etonogestrel AUC ↓ 63% to 82%	Use alternative ARV or contraceptive methods.
	ETR	↓ etonogestrel possible	No data available to make dose recommendation.
	NVP	↔ etonogestrel	No dose adjustment needed.
Contraceptives—Subdermal Implant Levonorgestrel	DOR, RPV IM, RPV PO	↔ levonorgestrel expected	No dose adjustment needed.
	EFV	Levonorgestrel AUC ↓ 42% to 47%	Use alternative ARV or contraceptive methods. Unintended pregnancies were observed in women who used EFV and levonorgestrel implant concomitantly.
	ETR	↓ levonorgestrel possible	No data available to make dose recommendation.
	NVP	Levonorgestrel AUC ↑ 35%	No dose adjustment needed.
Contraceptives—Transdermal Ethinyl Estradiol/ Norelgestromin	DOR, RPV IM, RPV PO	↔ ethinyl estradiol or norelgestromin expected	No dose adjustment needed.
	EFV	↓ ethinyl estradiol or norelgestromin expected	No data available to make dose recommendation.
	ETR, NVP	↓ ethinyl estradiol or norelgestromin possible	No data available to make dose recommendation.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Contraceptives—Vaginal Ring Etonogestrel/Ethinyl Estradiol	DOR, RPV IM, RPV PO	↔ etonogestrel and ethinyl estradiol expected	No dose adjustment needed.
	EFV	Ethinyl estradiol (intravaginal ring) AUC ↓ 56% Etonogestrel (intravaginal ring) AUC ↓ 81%	Consider alternative ARV or contraceptive method.
	ETR, NVP	↓ etonogestrel and ethinyl estradiol possible	No data available to make dose recommendation.
Contraceptives—Vaginal Ring Segesterone/Ethinyl Estradiol	DOR, RPV IM, RPV PO	↔ segesterone and ethinyl estradiol expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ segesterone and ethinyl estradiol possible	No data available to make dose recommendation.
Emergency Contraceptives Levonorgestrel (oral)	DOR, RPV IM, RPV PO	↔ levonorgestrel expected	No dose adjustment needed.
	EFV	Levonorgestrel AUC ↓ 58%	Effectiveness of emergency postcoital contraception may be diminished.
	NVP, ETR	↓ levonorgestrel possible	No data available to make dose recommendation.
Gender-Affirming Therapy	DOR, RPV IM, RPV PO	↔ hormonal concentrations expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ estradiol possible ↓ cyproterone and progestogens possible ↔ goserelin, leuprolide acetate, and spironolactone expected ↓ dutasteride and finasteride possible	Monitor feminizing effects of estrogen and antiandrogen therapy. Titrate dose as necessary to achieve therapeutic goals.
	EFV, ETR, NVP	↓ testosterone possible	Monitor masculinizing effects of testosterone. Titrate testosterone dose as necessary to achieve therapeutic goals.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Menopausal Replacement Therapy	DOR, RPV IM, RPV PO	↔ hormonal concentrations expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ estrogen possible with estradiol or conjugated estrogen (equine and synthetic) ↓ medroxyprogesterone possible ↓ micronized progesterone possible ↓ drospirenone possible See Contraceptives—Oral above for other progestin-NNRTI interactions	Monitor menopausal symptoms. Titrate to the dose of hormonal therapy that achieves menopausal symptom relief.
Immunosuppressants			
Cyclosporine	DOR, RPV IM, RPV PO	↔ cyclosporine expected ↑ NNRTI possible	No dose adjustment needed.
	EFV, ETR, NVP	↓ cyclosporine possible	Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.
Everolimus, Sirolimus, Tacrolimus	DOR, RPV IM, RPV PO	↔ immunosuppressant expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ immunosuppressant possible	Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.
Lipid-Modifying Agents			
Atorvastatin	DOR	↔ atorvastatin AUC	No dose adjustment needed.
	EFV, ETR	Atorvastatin AUC ↓ 32% to 43%	Adjust atorvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
	NVP	↓ atorvastatin possible	Adjust atorvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
	RPV IM	↔ atorvastatin expected	No dose adjustment needed.
	RPV PO	↔ atorvastatin AUC	No dose adjustment needed.
Fluvastatin	DOR, NVP, RPV IM, RPV PO	↔ fluvastatin expected	No dose adjustment needed.
	EFV, ETR	↑ fluvastatin possible	Dose adjustments for fluvastatin may be necessary. Monitor for fluvastatin toxicity.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lovastatin, Simvastatin	DOR, RPV IM, RPV PO	↔ lovastatin and simvastatin expected	No dose adjustment needed.
	EFV	Simvastatin AUC ↓ 60% to 68% Simvastatin active metabolite AUC ↓ 60%	Adjust simvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
	ETR, NVP	↓ lovastatin possible ↓ simvastatin possible	Adjust lovastatin or simvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
Pitavastatin	DOR, ETR, NVP, RPV IM, RPV PO	↔ pitavastatin expected	No dose adjustment needed.
	EFV	↔ pitavastatin AUC	No dose adjustment needed.
Pravastatin	DOR, NVP, RPV IM, RPV PO	↔ pravastatin expected	No dose adjustment needed.
	EFV	Pravastatin AUC ↓ 44%	Adjust statin dose according to lipid responses, but do not exceed the maximum recommended dose.
	ETR	↓ pravastatin possible	
Rosuvastatin	DOR, EFV, ETR, NVP, RPV IM, RPV PO	↔ rosuvastatin expected	No dose adjustment needed.
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual or buccal	DOR, RPV IM, RPV PO	↔ buprenorphine expected	No dose adjustment needed.
	EFV	Buprenorphine AUC ↓ 50% Norbuprenorphine (active metabolite) AUC ↓ 71%	No dose adjustment needed, monitor for withdrawal symptoms.
	ETR	Buprenorphine AUC ↓ 25%	No dose adjustment needed.
	NVP	No significant effect	No dose adjustment needed.
Buprenorphine Implant	DOR, RPV IM, RPV PO	↔ buprenorphine expected	No dose adjustment needed.
	EFV, ETR, NVP	No data	Clinical monitoring is recommended when NNRTI is initiated after insertion of buprenorphine implant.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lofexidine	DOR, EFV, ETR, NVP, RPV IM, RPV PO	↔ lofexidine expected	No dose adjustment needed.
Methadone	DOR	↔ methadone AUC DOR AUC ↓ 26%	No dose adjustment needed.
	EFV	Methadone AUC ↓ 52%	Opioid withdrawal common; monitor and increase methadone dose as necessary.
	ETR	↔ methadone AUC	No dose adjustment needed.
	NVP	Methadone AUC ↓ 37% to 51% ↔ NVP	Opioid withdrawal common; monitor and increase methadone dose as necessary.
	RPV IM	↓ methadone AUC expected	No dose adjustment needed, but monitor for withdrawal symptoms.
	RPV PO	R-methadone[a] AUC ↓ 16%	No dose adjustment needed, but monitor for withdrawal symptoms.
PDE5 Inhibitors			
Sildenafil	DOR	↔ sildenafil expected	No dose adjustment needed.
	EFV, NVP	↓ sildenafil possible	May need to titrate sildenafil dose based on clinical effect.
	ETR	Sildenafil AUC ↓ 57%	May need to titrate sildenafil dose based on clinical effect.
	RPV IM	↔ sildenafil expected	No dose adjustment needed.
	RPV PO	↔ sildenafil AUC and C_{max}	No dose adjustment needed.
Tadalafil	DOR, RPV IM, RPV PO	↔ tadalafil expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ tadalafil possible	May need to titrate tadalafil dose based on clinical effect.
Avanafil, Vardenafil	DOR, RPV IM, RPV PO	↔ avanafil or vardenafil expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ avanafil or vardenafil possible	May need to increase PDE5 inhibitor dose based on clinical effect.
Sedative/Hypnotics			
Alprazolam, Triazolam	DOR, RPV IM, RPV PO	↔ alprazolam or triazolam expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ alprazolam or triazolam possible	Monitor for therapeutic effectiveness of benzodiazepine.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Diazepam	DOR, RPV IM, RPV PO	↔ diazepam expected	No dose adjustment needed.
	EFV, NVP	↓ diazepam possible	Monitor for therapeutic effectiveness of diazepam.
	ETR	↑ diazepam possible	Decreased dose of diazepam may be necessary. Monitor for diazepam toxicity.
Lorazepam	DOR, ETR, NVP, RPV IM, RPV PO	↔ lorazepam expected	No dose adjustment needed.
	EFV	↔ lorazepam AUC	No dose adjustment needed.
Midazolam	DOR	↔ midazolam AUC	No dose adjustment needed.
	EFV	↑ or ↓ midazolam possible	Monitor for therapeutic effectiveness and toxicity of midazolam.
	ETR	Midazolam AUC ↓ 31% Midazolam active metabolite C_{max} ↑ 57%	Monitor for therapeutic effectiveness of midazolam.
	NVP	↓ midazolam possible	Monitor for therapeutic effectiveness of midazolam.
	RPV IM, RPV PO	↔ midazolam expected	No dose adjustment needed.

[a] R-methadone is the active form of methadone.

Key to Symbols

↑ = increase
↓ = decrease
↔ = no change

Key: ARV = antiretroviral; AUC = area under the curve; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; CAB = cabotegravir; CCB = calcium channel blocker; DAA = direct-acting antiviral; DHA = dihydroartemisinin; DOR = doravirine; EFV = efavirenz; ETR = etravirine; HCV = hepatitis C virus; IM = intramuscular; INR = international normalized ratio; isoniazid = isonicotinic acid hydrazide; MAC = *Mycobacterium avium* complex; MPA = medroxyprogesterone acetate; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; OH-itraconazole = active metabolite of itraconazole; PCP = *Pneumocystis jirovecii* pneumonia; PDE5 = phosphodiesterase type 5; PI/r = protease inhibitor/ritonavir; PO = orally; QTc = QT corrected for heart rate; RPV = rilpivirine; RTV = ritonavir.