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Rifamycin Drug-Drug Interactions

A Guide for Primary Care Providers Treating Latent Tuberculosis Infection

Rifamycin Drug-Drug Interactions: A Guide for Primary Care Providers Treating Latent Tuberculosis Infection was created through a collaboration of the State of California Department of Public Health, Tuberculosis Control Branch (CDPH), the Rutgers Ernest Mario School of Pharmacy (EMSOP), the Rutgers Global Tuberculosis Institute (GTBI), and the Curry International Tuberculosis Center (CITC).

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Read this section first

Rifampin, rifapentine, and rifabutin (known as "rifamycins") are drugs that can be used in the treatment of tuberculosis disease and latent tuberculosis infection. Rifamycins often have the potential for drug interactions with co-administered drugs.

This guide was created to clarify drug interactions between rifamycins and drugs commonly used in primary care. The content was created by a team of clinical pharmacists using a standardized search strategy and definitions, and subsequently reviewed by clinical experts in TB as well as primary care providers. The primary audience includes medical providers but may also be useful for public health personnel.

This guide summarizes drug-drug interactions (DDI) between drugs commonly used in primary care and rifamycins, in the context of treatment of ***latent*** **tuberculosis infection (LTBI)**. More information on LTBI treatment options can be found here: https://www.cdc.gov/tb/topic/treatment/ltbi.htm. Note that in the 2020 Guidelines for the Treatment of LTBI from the Centers for Disease Control and Prevention, **rifampin** and **rifapentine** are each included in preferred regimens for LTBI. Rifabutin is not included in a preferred regimen for LTBI and is included here only for reference. For treatment of (active) tuberculosis disease, or if you have additional questions regarding LTBI therapy or DDI, please consult an infectious diseases specialist, your local public health department, or your regional TB Center of Excellence: https://www.cdc.gov/tb/education/tb_coe/default.htm.

Many rifamycin DDIs can be managed with clinical monitoring or dosage modifications. In this table form DDI guide, drugs are grouped by class; medical providers can access clinical recommendations for each drug and compare drug options within the same drug class. **This guide is not exhaustive;** many drugs were not included and no conclusions should be made about drugs not included in this guide.

Read this section first
(continued)

General principles:

Rifamycins are inducers of cytochrome P450 isoenzymes (CYP) and some drug transporters, such as P-glycoprotein, and therefore may impact the levels and effects of co-administered drugs. **Drug interactions for rifampin tend to be more significant than for rifapentine/rifabutin, because levels of induction of CYP enzymes and drug transporters are typically higher for rifampin than rifapentine/rifabutin.** Most drug interaction data are based on daily administration of rifamycins; induction may be less with weekly dosing. In most cases when a rifamycin is administered, a decrease in the effect of the co-administered drug is anticipated, although in circumstances where the drug's effect is due to an active metabolite, increased effects may be seen.

Timing of interaction onset and dose adjustments:

This is a complex issue that is dependent on the interplay of the rifamycin, which acts as the **inducing drug**, the dosing regimen, the **object drug** (i.e., the non-rifamycin concomitant drug), and the metabolic/transporter pathway that is induced (e.g., CYP 3A4 vs 2C9). There are two scenarios to consider:

1. **Chronic use of object drug, with new start of rifamycin**
   - Enzyme induction (and the object drug's metabolism) by a rifamycin generally starts a few days after the patient starts rifamycin, with maximal enzyme induction occurring ***1-2 weeks after rifamycin initiation***. Monitoring for declining clinical effect of the object drug may include clinical assessment or drug levels, and should occur ***over approximately the first two weeks from starting a rifamycin.*** An ***increase*** in the object drug's dose may be necessary as a stepped increase over approximately two weeks, rather than an immediate increase on rifamycin initiation.
   - De-induction (induced metabolizing enzymes returning to baseline) can take approximately ***2-4 weeks after the patient stops taking a rifamycin.*** Monitoring for object drug's clinical effect returning to baseline may include clinical assessment or drug levels, and should occur ***over 2-4 weeks from stopping rifamycin.*** A ***decrease*** in the object drug's dose may be necessary.
2. **Maintained on rifamycin for >1-2 weeks, with new start of object drug**
   - If the patient has been on rifamycin continuously for at least one week, the enzyme induction is most likely at or near the peak point; lower drug levels of the object drug and potentially decreased clinical effect will be apparent much faster, if not right away. Empiric dose adjustments may be required.

Disclaimer:

This guide is meant as a reference. Medical providers should exercise their own clinical judgement when caring for patients and seek guidance from an expert, if needed. Links to other clinical guidelines are also meant as a reference and not necessarily endorsed by authors and reviewers.

Interaction

↓ = **decrease** [drug name] concentration or efficacy *expected* (direct pharmacokinetic or clinical data) ***or*** *possible* (based on metabolic/transporter pathway or data from similar drugs)

↑ = **increase** [drug name] concentration or toxicity risk *expected* (direct pharmacokinetic or clinical data) ***or*** *possible* (based on metabolic/transporter pathway or data from similar drugs)

No significant interaction expected

Recommendation Key

Symbol	Risk level	Recommendation	Rationale
	**Very low risk**	**Co-administer without modifications.** No clinically significant interaction likely.	This recommendation is made because either: 1) clinical/pharmacokinetic data exists suggesting there is no clinically significant interaction, *or* 2) no reaction is expected based on drug's mechanism of clearance, wide therapeutic window, *in vitro* data, or published clinical data for a similar drug in the same class.
	**Low to medium risk**	**Co-administer with caution.** If co-administration necessary, consider [dose adjustment, clinical monitoring, addition of another agent (i.e., barrier method in contraception), laboratory monitoring].	This recommendation is made because clinical/pharmacokinetic data exists suggesting a possible clinically significant interaction for the concomitant drug or a mechanistically similar drug; however, the interaction is mild-moderate and can be managed in routine primary care practice, with monitoring and/or dose adjustment of concomitant drug.
	**Medium to high risk**	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	This recommendation is made because clinical/pharmacokinetic data exists suggesting a clinically significant interaction for the concomitant drug or a mechanistically similar drug is possible. This recommendation differs from the yellow category (low to medium risk) in that the clinical implications of the interaction are potentially serious or life-threatening, and extremely close monitoring and probable dosage changes are needed to ensure patient safety. Input from a clinical pharmacist and/or subspecialist is recommended.
	**Highest risk**	**Contraindicated, do not co-administer.**	This recommendation is made because clinical/pharmacokinetic data exists suggesting a clinically significant interaction for the concomitant drug which will: 1) render concomitant drug ineffective (regardless of clinical indication, implications of inactive drug may not be serious or life-threatening) *and/or* 2) have a potentially serious or life-threatening interaction, and patient safety cannot be guaranteed even with monitoring or dose titration.

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CLICK ON THE DRUG/DRUG CLASS OF INTEREST TO SKIP TO THAT SECTION

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
ACID SUPPRESSING MEDICATIONS					
Antacids **Aluminum hydroxide** **Calcium carbonate** **Magnesium hydroxide**	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	US labeling for rifampin products states that because coadministration of rifampin with antacids may reduce rifampin absorption, rifampin should be given 1 hour prior to any antacid. The effect of this dose separation has not been evaluated in a clinical study. In one pharmacokinetic study of healthy volunteers, the AUC and maximum serum concentration (Cmax) of rifampin (600 mg single oral dose) were unchanged when administered with aluminum/magnesium hydroxide (Mylanta 30 mL). In another study of 45 patients with pulmonary tuberculosis, the mean rifampin serum concentrations observed at 2 hours, 3 hours, and 4 hours after rifampin (10-12 mg/kg single oral dose), were similar in patients who received no antacid compared with patients who received aluminum hydroxide (1,220 mg) or aluminum hydroxide/magnesium trisilicate (1,250 mg/2,500 mg) with their rifampin therapy.	9925057 3182711 Package insert
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; based on information with rifampin.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; based on information with rifampin.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
H2 Receptor Antagonists **Cimetidine** **Famotidine** **Nizatidine**	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	In vitro studies indicate that famotidine is a substrate for OAT1 and OAT3, however, no clinical or pharmacokinetic data exists suggesting a clinically relevant drug interaction with rifamycins.	Package insert
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	In vitro studies indicate that famotidine is a substrate for OAT1 and OAT3, however, no clinical or pharmacokinetic data exists suggesting a clinically relevant drug interaction with rifamycins.	Package insert
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	In vitro studies indicate that famotidine is a substrate for OAT1 and OAT3, however, no clinical or pharmacokinetic data exists suggesting a clinically relevant drug interaction with rifamycins.	Package insert

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Proton Pump Inhibitors **Dexlansoprazole** **Esomeprazole** **Lansoprazole** **Omeprazole** **Pantoprazole** **Rabeprazole**	Rifampin	**Pantoprazole** and **rabeprazole**: No significant interaction expected	Pantoprazole and rabeprazole: **Co-administer without modifications**, no clinically significant interaction likely.	Pantoprozole and rabeprazole have less potential for clinically significant drug-drug interactions than other proton pump inhibitors. They are both minor CYP2C19 substrates and less likely to be impacted by strong CYP2C19 inducers, such as rifampin, than other proton pump inhibitors.	10491725 8793602
		↓ **omeprazole, esomeprazole, dexlansoprazole,** and **lansoprazole** concentration or efficacy expected	Omeprazole, esomeprazole, dexlansoprazole, and lansoprazole: **Contraindicated, do not co-administer.**	Implications of inactive proton pump inhibitors may not be serious or life-threatening. However, co-administration with rifampin may render these drugs ineffective due to major reduction in drug levels, and dosage changes will likely not overcome this interaction. Omeprazole prescribing information states that because drugs that are strong inducers of CYP2C19 can substantially decrease omeprazole concentrations, concomitant use should be avoided. In three pharmacokinetic studies of healthy volunteers, rifampin decreased the omeprazole AUC 83% to 90%. Consider use of alternate proton pump inhibitor with less significant interaction expected or an alternative acid suppressing agent, if appropriate.	28408803 30902567 35238961 Package insert (omeprazole, lansoprazole, esomeprazole)
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific data. Reductions in drug levels are expected but are not expected to be clinically significant.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific data. Reductions in drug levels are expected but are not expected to be clinically significant.	

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected* ***or*** *possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected* ***or*** *possible*

Very low risk: Co-administer without modifications. **Low to medium risk:** Co-administer with caution. **Medium to high risk:** Co-administer with extreme caution if benefits outweigh risks. **Highest risk:** Contraindicated, do not co-administer.

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
ALPHA-ADRENERGIC RECEPTOR BLOCKERS FOR BPH					
Alfuzosin	Rifampin	↓ alfuzosin concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for reduced clinical effect and consider increasing alfuzosin dose as needed.	There is a lack of pharmacokinetic or clinical case data reported for rifampin co-administration with alfuzosin. Alfuzosin is a major CYP3A4 substrate and rifampin is a strong CYP3A4 inducer – potential for some reduction in drug levels and efficacy of alfuzosin.	
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with alfuzosin. Reductions in drug levels are not expected when given with rifapentine (once weekly dosing).	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with alfuzosin. Reductions in drug levels are not expected when given with rifabutin.	
Doxazosin	Rifampin	↓ doxazosin concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for reduced clinical effect and consider increasing doxazosin dose as needed.	There is a lack of pharmacokinetic or clinical case data reported for rifampin co-administration with doxazosin. Doxazosin is a major CYP3A4 substrate and rifampin is a strong CYP3A4 inducer – potential for some reduction in drug levels and efficacy of doxazosin.	
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with doxazosin. Reductions in drug levels are not expected when given with rifapentine (once weekly dosing).	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with doxazosin. Reductions in drug levels are not expected when given with rifabutin.	

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Silodosin	Rifampin	↓ silodosin concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for reduced clinical effect and consider increasing silodosin dose as needed.	There is a lack of pharmacokinetic or clinical case data reported for rifampin co-administration with silodosin. Silodosin is a major CYP3A4 substrate and rifampin is a strong CYP3A4 inducer – potential for some reduction in drug levels and efficacy of silodosin.	
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with silodosin. Reductions in drug levels are not expected when given with rifapentine (once weekly dosing).	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with silodosin. Reductions in drug levels are not expected when given with rifabutin.	
Tamsulosin	Rifampin	↓ tamsulosin concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for reduced clinical effect and consider increasing tamsulosin dose as needed.	There is a lack of pharmacokinetic or clinical case data reported for rifampin co-administration with tamsulosin. Tamsulosin is a major CYP3A4 substrate and rifampin is a strong CYP3A4 inducer – potential for some reduction in drug levels and efficacy of tamsulosin.	
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with tamsulosin. Reductions in drug levels are not expected when given with rifapentine (once weekly dosing).	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with tamsulosin. Reductions in drug levels are not expected when given with rifabutin.	

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Terazosin	Rifampin	No significant interaction expected	✓ **Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifampin co-administration with terazosin. Terazosin undergoes hepatic metabolism, but up to 30% excreted unchanged (20% feces; ~10% urine). Significant reduction in terazosin exposure and efficacy not expected.	
	Rifapentine (once weekly dosing)	No significant interaction expected	✓ **Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with tamsulosin. Reductions in drug levels are not expected when given with rifapentine (once weekly dosing).	
	Rifabutin	No significant interaction expected	✓ **Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with tamsulosin. Reductions in drug levels are not expected when given with rifabutin.	
ANGIOTENSIN-CONVERTING ENZYME (ACE) INHIBITORS					
Benazepril **Captopril** **Cilazapril** **Enalapril** **Fosinopril** **Lisinopril** **Moexipril** **Perindopril** **Quinapril** **Ramipril** **Trandolapril**	Rifampin	↓ enalapril concentration or efficacy possible No significant interaction expected for other listed ACE inhibitors	✓ **Co-administer without modifications**, no clinically significant interaction likely.	Rifampin prescribing information states rifampin may decrease exposure to the active metabolite of enalapril. In a single case report in a patient with essential hypertension whose blood pressure rose while on rifampin, rifampin did not alter serum concentrations of enalapril or the area under the curve (AUC) between 0 and 7 h, but it did reduce the AUC of the active metabolite enalaprilat by 31%.	2848708
	Rifapentine (once weekly dosing)	No significant interaction expected	✓ **Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; based on information with rifampin.	
	Rifabutin	No significant interaction expected	✓ **Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; based on information with rifampin.	

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
ANGIOTENSIN II RECEPTOR BLOCKERS (ARB)					
Azilsartan **Candesartan** **Eprosartan** **Irbesartan** **Olmesartan** **Telmisartan**	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	These drugs are not metabolized through CYP pathway; although no clinical data is present, no interaction is anticipated.	
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	These drugs are not metabolized through CYP pathway; although no clinical data are present, no interaction is anticipated.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	These drugs are not metabolized through CYP pathway; although no clinical data are present, no interaction is anticipated.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Losartan	Rifampin	↓ losartan concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for blood pressure control after the addition or withdrawal of rifampin, adjusting the losartan dose to regain control. Substitution of an alternative ARB or a different class of antihypertensive agent can be considered.	Strong CYP3A4 Inducers, such as rifampin, may decrease serum concentrations of losartan and its active metabolite(s). AUC of losartan (50 mg) and E3174 (the more potent active metabolite) decreased 36% and 41%, respectively, following a 7-day course of rifampin (300 mg daily). The half-life of both losartan and E3174 was reduced approximately 50%; clinical significance of these changes is unclear.	9542475 12235444 8653989
	Rifapentine (once weekly dosing)	↓ losartan concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for blood pressure control after the addition or withdrawal of rifapentine, adjusting the losartan dose to regain control. Substitution of an alternative ARB or a different class of antihypertensive agent can be considered.	No drug-specific data; recommendation based on rifampin data.	
	Rifabutin	↓ losartan concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for blood pressure control after the addition or withdrawal of rifabutin adjusting the losartan dose to regain control. Substitution of an alternative ARB or a different class of antihypertensive agent can be considered.	No drug-specific data; recommendation based on rifampin data.	

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Valsartan	Rifampin	↑ valsartan concentration possible	**Co-administer with caution.** If co-administration necessary, monitor patients for increased valsartan adverse events (e.g., dizziness, hypotension, abdominal pain).	Valsartan is a substrate of the hepatic uptake transporter OATP1B1. Concomitant administration with an OATP1B1 uptake transport inhibitor, such as rifampin, may increase the systemic exposure of valsartan. Clinical significance of this interaction has not been demonstrated.	Package Insert 31628668
	Rifapentine (once weekly dosing)	↑ valsartan concentration possible	**Co-administer with caution.** If co-administration necessary, monitor patients for increased valsartan adverse events (e.g., dizziness, hypotension, abdominal pain).	No drug-specific data; recommendation based on rifampin data.	26976869
	Rifabutin	↑ valsartan concentration possible	**Co-administer with caution.** If co-administration necessary, monitor patients for increased valsartan adverse events (e.g., dizziness, hypotension, abdominal pain).	No drug-specific data; recommendation based on rifampin data.	26976869

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected* ***or*** *possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected* ***or*** *possible*

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
ANTIARRHYTHMICS					
Amiodarone	Rifampin	↓ amiodarone concentration or efficacy possible	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If co-administration is necessary, monitor for reduced amiodarone concentrations and effectiveness. Amiodarone doses may need to be increased to maintain therapeutic effects. See page 3 for additional important information on timing.	Strong CYP3A4 inducers, such as rifampin, may decrease serum concentrations of both amiodarone and the active metabolites of amiodarone. In a case report, a 33 y/o women stabilized on amiodarone 400 mg daily saw a 75% decrease in amiodarone and desethylamiodarone (DEA) concentrations, paroxysms of atrial fibrillation, flutter, and ICD shocks after starting rifampin. In another case, a 69 y/o man on amiodarone 200 mg saw a 52% decrease in amiodarone and DEA concentration which required a 3.5-fold increase in amiodarone dose.	29470228 10030779 21941175
	Rifapentine (once weekly dosing)	↓ amiodarone concentration or efficacy possible	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If co-administration is necessary, monitor for reduced amiodarone concentrations and effectiveness. Amiodarone doses may need to be increased to maintain therapeutic effects. See page 3 for additional important information on timing.	No drug-specific information; based on information with rifampin. Strong CYP3A4 inducers may decrease serum concentrations of both amiodarone and the active metabolites of amiodarone.	Package Insert

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Amiodarone	Rifabutin	↓ amiodarone concentration or efficacy possible	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If co-administration is necessary, monitor for reduced amiodarone concentrations and effectiveness. Amiodarone doses may need to be increased to maintain therapeutic effects. See page 3 for additional important information on timing.	No drug-specific information; based on information with rifampin. Strong CYP3A4 inducers may decrease serum concentrations of both amiodarone and the active metabolites of amiodarone.	Package Insert
Digoxin	Rifampin	↓ digoxin concentration or efficacy possible	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If co-administration is necessary, measure digoxin concentrations prior to initiation of rifampin. A total increase of 20-40% in dose may be needed, continue to monitor plasma concentration. See page 3 for additional important information on timing.	Concurrent use may result in decreased digoxin levels. A number of case reports have shown concomitant use of digoxin and rifampin decrease digoxin concentrations to subtherapeutic levels (decreased AUC 15% to 30%).	7397060 6830398 7431585 6734026 6712395 22190694 17079360 16221745 10411543

Key: **See page 4 for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected or possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected or possible*

Very low risk: Co-administer without modifications. **Low to medium risk:** Co-administer with caution. **Medium to high risk:** Co-administer with extreme caution if benefits outweigh risks. **Highest risk:** Contraindicated, do not co-administer.

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Digoxin	Rifapentine (once weekly dosing)	↓ digoxin concentration or efficacy possible	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If co-administration is necessary, measure digoxin concentrations prior to initiation of rifapentine. Increase in digoxin dose maybe necessary; continue to monitor plasma concentration levels to assess dosing needs. See page 3 for additional important information on timing.	No drug-specific data; recommendation based on rifampin data.	
	Rifabutin	↓ digoxin concentration or efficacy possible	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If co-administration is necessary, measure digoxin concentrations prior to initiation of rifabutin. Increase in digoxin dose maybe necessary; continue to monitor plasma concentration levels to assess dosing needs. See page 3 for additional important information on timing.	No drug-specific data; recommendation based on rifampin data.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
ANTICOAGULANTS					
Apixaban	Rifampin	↓ apixaban concentration or efficacy expected	**Contraindicated, do not co-administer.**	Apixaban is substrate of CYP3A4 and P-gp, both of which are significantly induced by rifampin. Approximately 50% decrease in apixaban AUC with rifampin co-administration via induction of P-gp and drug metabolism. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequences; patient safety cannot be guaranteed even with monitoring or dose titration.	Package insert 26749408 35152432
	Rifapentine (once weekly dosing)	↓ apixaban concentration or efficacy possible	**Contraindicated, do not co-administer.**	There is a lack of pharmacokinetic or clinical case data reported for rifapentine-apixaban co-administration. There is potential for significant reduction in apixaban AUC and variability in induction effect with once weekly rifapentine dosing unknown. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequences; patient safety cannot be guaranteed even with monitoring or dose titration.	Package insert 22472995 35152432
	Rifabutin	↓ apixaban concentration or efficacy possible	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin-apixaban co-administration. Apixaban is substrate of CYP3A4 and P-gp. Rifabutin is a moderate inducer of CYP3A4 and a weak inducer of P-gp. There is potential for reduction in apixaban AUC but likely less than with rifampin (strong CYP3A4 inducer and strong P-gp inducer).	Package insert 35152432

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected* ***or*** *possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected* ***or*** *possible*

Very low risk: Co-administer without modifications. **Low to medium risk:** Co-administer with caution. **Medium to high risk:** Co-administer with extreme caution if benefits outweigh risks. **Highest risk:** Contraindicated, do not co-administer.

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Edoxaban	Rifampin	↓ edoxaban concentration or efficacy expected	**Contraindicated, do not co-administer.**	Edoxaban is substrate of P-gp, which is significantly induced by rifampin. Approximately 34% decrease in edoxaban AUC with rifampin co-administration. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequences; patient safety cannot be guaranteed even with monitoring or dose titration.	Package insert 26068927 35152432
	Rifapentine (once weekly dosing)	↓ edoxaban concentration or efficacy possible	**Contraindicated, do not co-administer.**	There is a lack of pharmacokinetic or clinical case data reported for rifapentine-edoxaban co-administration. There is potential for significant reduction in edoxaban AUC and variability in induction effect with once weekly rifapentine dosing unknown. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequences; patient safety cannot be guaranteed even with monitoring or dose titration.	35152432
	Rifabutin	↓ edoxaban concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, consider close clinical monitoring and consultation with clinical pharmacist or subspecialist.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin-edoxaban co-administration. Edoxaban is a substrate of P-gp. Rifabutin is a weak inducer of P-gp. There is potential for modest reduction in edoxaban AUC but likely less than with rifampin (strong P-gp inducer).	35152432

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Dabigatran (administered as prodrug dabigatran etexilate)	Rifampin	↓ dabigatran concentration or efficacy expected	**Contraindicated, do not co-administer.**	Dabigatran is substrate of P-gp, which is significantly induced by rifampin. Approximately 67% decrease in dabigatran AUC with rifampin co-administration via induction of P-gp. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequences; patient safety cannot be guaranteed even with monitoring or dose titration.	Package insert 29569723 35152432
	Rifapentine (once weekly dosing)	↓ dabigatran concentration or efficacy possible	**Contraindicated, do not co-administer.**	There is a lack of pharmacokinetic or clinical case data reported for rifapentine-dabigatran co-administration. There is potential for moderate reduction in dabigatran AUC and variability in induction effect with once weekly rifapentine dosing unknown. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequences; patient safety cannot be guaranteed even with monitoring or dose titration.	35152432
	Rifabutin	↓ dabigatran concentration or efficacy expected	**Co-administer with caution.** If co-administration necessary, consider close clinical monitoring and consultation with clinical pharmacist or subspecialist	Dabigatran is a substrate of P-gp. Rifabutin is a weak inducer of P-gp. Approximately 20% reduction in dabigatran AUC via induction of P-gp.	Package insert 29569712 35152432

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Rivaroxaban	Rifampin	↓ rivaroxaban concentration or efficacy expected	**Contraindicated, do not co-administer.**	Rivaroxaban is substrate of CYP3A4 and P-gp, both of which are significantly induced by rifampin. Approximately 50% decrease in rivaroxaban AUC with rifampin co-administration via induction of P-gp and CYP3A4. Case report of patient with fatal pulmonary embolism associated with low rivaroxaban levels in patient on rifampin. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequences; patient safety cannot be guaranteed even with monitoring or dose titration.	Package insert 24497568 35152432
	Rifapentine (once weekly dosing)	↓ rivaroxaban concentration or efficacy possible	**Contraindicated, do not co-administer.**	There is a lack of pharmacokinetic or clinical case data reported for rifapentine-rivaroxaban co-administration. There is potential for significant reduction in rivaroxaban AUC and variability in induction effect with once weekly rifapentine dosing unknown. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequences; patient safety cannot be guaranteed even with monitoring or dose titration.	35152432
	Rifabutin	↓ rivaroxaban concentration or efficacy possible	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin-rivaroxaban co-administration. Rivaroxaban is substrate of CYP3A4 and P-gp. Rifabutin is a moderate inducer of CYP3A4 and a weak inducer of P-gp. There is potential for reduction in rivaroxaban AUC but likely less than with rifampin (strong CYP3A4 inducer and strong P-gp inducer).	35152432

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected* ***or*** *possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected* ***or*** *possible*

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Warfarin	Rifampin	↓ warfarin concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If co-administration necessary, requires close clinical and increased laboratory (INR) monitoring. Dose adjustment to maintain target INR necessary – dose increases at initiation and dose decreases after cessation of rifampin (see "More Information"). Consider alternatives for short-term anticoagulation or use of rifabutin instead of rifampin, if appropriate.	There is significant reduction in warfarin exposure due to increased metabolism by CYP1A2, 2C9, 3A4. Decreases in warfarin AUC of 50-75% depending on isomer. Anticipate increased dose requirements of warfarin approximately 1 week after initiation of rifampin if on stable warfarin dose. Anticipate dose increases of 2-5 fold from baseline or initial dose in order to maintain goal INR. Careful down-titration of warfarin dose based on INR monitoring is required after rifampin discontinuation; anticipate reducing warfarin dose by up to 50% within 1-2 weeks of rifampin discontinuation to avoid over-anticoagulation. Bleeding episodes reported from failure to decrease warfarin doses after rifampin discontinuation.	Package insert 20703222 35152432
	Rifapentine (once weekly dosing)	↓ warfarin concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If co-administration necessary, requires close clinical and increased laboratory (INR) monitoring. Dose adjustment to maintain target INR necessary – dose increases at initiation and dose decreases after cessation of rifapentine (see "More Information"). Consider alternatives for short-term anticoagulation.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with warfarin. The magnitude of reduction in warfarin AUC is likely significant and variability in induction effect with once-weekly dosing unknown. Anticipate increased dose requirements of warfarin approximately 1 week after initiation of rifapentine if on stable warfarin dose. Anticipate dose increases of up to 2-5 fold from baseline or initial dose in order to maintain goal INR. Careful down-titration of warfarin dose based on INR monitoring is required after rifapentine discontinuation; anticipate reducing warfarin dose by up to 50% within 1-2 weeks of rifapentine discontinuation to avoid over-anticoagulation. Consider monitoring INR twice-weekly to determine induction waning.	Package insert 22472995 35152432

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Warfarin	Rifabutin	↓ warfarin concentration or efficacy expected	**Co-administer with caution.** If co-administration necessary, requires close clinical and increased laboratory (INR) monitoring and consider consultation with clinical pharmacist or subspecialist. Dose adjustment to maintain target INR necessary – dose increases at initiation and dose decreases after cessation of rifabutin (see "More Information"). Consider alternatives for short-term anticoagulation.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with warfarin. The magnitude of reduction in warfarin AUC with rifabutin is likely lower than rifampin but still significant. Anticipate increased dose requirements of warfarin approximately 1 week after initiation of rifabutin if on stable warfarin dose. Anticipate dose increases from baseline or initial dose in order to maintain goal INR. Careful down-titration of warfarin dose based on INR monitoring is required after rifabutin discontinuation; anticipate reducing warfarin dose within 1-2 weeks of rifabutin discontinuation to avoid over-anticoagulation.	Package insert 35152432

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
ANTIDEPRESSANTS AND ANXIOLYTICS					
Buspirone	Rifampin	↓ buspirone concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. Consider alternative treatment; recommend close clinical monitoring and titration of buspirone to clinical effect if concomitant use is deemed necessary. Monitor for psychiatric symptoms including anxiety.	The AUC of buspirone (30 mg) was decreased by about 90% in subjects when administered following a 5-day course of rifampin (600 mg daily) compared to placebo. The Cmax was reduced by 83.7% and half-life was reduced by 52.8%. The AUC of the 1-(2-pyrimidinyl)-piperazine metabolite (possesses roughly 20% of anxiolytic activity of parent drug) was minimally affected. Cmax of the piperazine metabolite was 35% higher. Pharmacodynamic effects appeared to be reduced based on psychomotor testing and subjective drowsiness.	Package insert 9578186 10068153
	Rifapentine (once weekly dosing)	↓ buspirone concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, titrate buspirone dose as needed to maintain clinical effect, monitoring for psychiatric symptoms including anxiety.	No drug-specific data; recommendation based on rifampin data. Reductions in drug levels are expected to be less when given with rifapentine (once weekly dosing) than when given with rifampin.	
	Rifabutin	↓ buspirone concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, titrate of buspirone dose as needed to maintain clinical effect, monitoring for psychiatric symptoms including anxiety.	No drug-specific data; recommendation based on rifampin data. Reductions in drug levels are expected to be less when given with rifabutin than when given with rifampin.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Bupropion	Rifampin	↓ bupropion concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. Bupropion dose may need to be increased but maximum dose should not be exceeded due to risk of seizures.	The AUC of bupropion was decreased by 67.2% with steady state rifampin (600 mg daily) while the AUC of the active metabolite hydroxybupropion was decreased by 42.9%. Half-life of the parent drug and metabolite both decreased 2-fold. Cmax of bupropion decreased by 62.3% while hydroxybupropion increased by 38.7%.	Package insert 16815319 20876786
	Rifapentine (once weekly dosing)	No interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific data available; no expected interaction based on metabolic pathway and lack of CYP2B6 activity with rifapentine.	
	Rifabutin	No interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific data available; no expected interaction based on metabolic pathway and lack of CYP2B6 activity with rifabutin.	
Mirtazapine	Rifampin	↓ mirtazapine concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, titrate mirtazapine dose as needed to maintain clinical effect, monitoring for psychiatric symptoms including depression and anxiety.	No drug-specific data available; based on studies with carbamazepine and phenytoin.	Package insert
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific data. Reductions in drug levels are expected to be less when given with rifapentine (once weekly dosing) than when given with rifampin.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific data. Reductions in drug levels are expected to be less when given with rifabutin than when given with rifampin.	

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected* ***or*** *possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected* ***or*** *possible*

Very low risk: Co-administer without modifications. **Low to medium risk:** Co-administer with caution. **Medium to high risk:** Co-administer with extreme caution if benefits outweigh risks. **Highest risk:** Contraindicated, do not co-administer.

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Trazodone	Rifampin	↓ trazodone concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If co-administration necessary, consider increasing the dose of trazodone when rifampin is initiated and titrate as needed.	No drug-specific information; based on pharmacokinetic data with carbamazepine.	Package insert
	Rifapentine (once weekly dosing)	↓ trazodone concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for reduced clinical effect at initiation of rifapentine and increase dose of trazodone to clinical effect if needed. Monitor for psychiatric symptoms including depression and anxiety.	No drug-specific information; based on pharmacokinetic data with carbamazepine.	
	Rifabutin	↓ trazodone concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for reduced clinical effect at initiation of rifabutin and increase dose of trazodone to clinical effect if needed. Monitor for psychiatric symptoms including depression and anxiety.	No drug-specific information; based on pharmacokinetic data with carbamazepine.	

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected* ***or*** *possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected* ***or*** *possible*

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Selective Serotonin Reuptake Inhibitors (SSRIs)					
Citalopram **Escitalopram**	Rifampin	↓ citalopram/ escitalopram concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, titrate SSRI dose as needed to maintain clinical effect, monitoring for psychiatric symptoms including depression and anxiety.	Two case reports of anxiety exacerbation after starting rifampin. One occurred in a patient stable on citalopram 20 mg daily 5 days after starting rifampin. Symptoms improved after increasing citalopram dose to 40 mg daily. The other occurred in a patient taking citalopram 40 mg daily after taking rifampin for 7 days. Citalopram was changed to escitalopram without symptom improvement. Symptoms improved after discontinuing rifampin and switching back to citalopram.	15843291 23131874
	Rifapentine (once weekly dosing)	↓ citalopram/ escitalopram concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, titrate SSRI dose as needed to maintain clinical effect, monitoring for psychiatric symptoms including depression and anxiety.	No drug-specific information; recommendation based on rifampin and efavirenz data.	
	Rifabutin	↓ citalopram/ escitalopram concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, titrate SSRI dose as needed to maintain clinical effect, monitoring for psychiatric symptoms including depression and anxiety.	No drug-specific information; recommendation based on rifampin and efavirenz data.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Sertraline	Rifampin	↓ sertraline concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, titrate sertraline dose as needed to maintain clinical effect, monitoring for psychiatric symptoms including depression and anxiety.	AUC of sertraline was 50% lower in patients taking rifampin in one observational study. One case report of anxiety exacerbation and symptoms of sertraline withdrawal after 7 days of taking rifampin 600 mg/day. The AUC of sertraline and N-desmethylsertraline were 67% and 54% lower, respectively, than 7 days after discontinuing rifampin.	10653222 28766827
	Rifapentine (once weekly dosing)	↓ sertraline concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, titrate sertraline dose as needed to maintain clinical effect, monitoring for psychiatric symptoms including depression and anxiety.	No drug-specific information; recommendation based on rifampin and efavirenz data.	
	Rifabutin	↓ sertraline concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, titrate sertraline dose as needed to maintain clinical effect, monitoring for psychiatric symptoms including depression and anxiety.	No drug-specific information; recommendation based on rifampin and efavirenz data.	
Fluoxetine **Fluvoxamine** **Paroxetine**	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; no expected interaction based on metabolic pathway.	Package insert
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; no expected interaction based on metabolic pathway.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; no expected interaction based on metabolic pathway.	

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Vilazodone	Rifampin	↓ vilazodone concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If co-administration necessary, increase dose of vilazodone to clinical effect if needed. Do not exceed 80 mg/day.	No drug-specific information; recommendation based on carbamazepine data.	Package insert
	Rifapentine (once weekly dosing)	↓ vilazodone concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, increase dose of vilazodone to clinical effect if needed. Do not exceed 80 mg/day. Monitor for psychiatric symptoms including depression and anxiety.	No drug-specific information; recommendation based on carbamazepine data. Reductions in drug levels are expected to be less when given with rifapentine (once weekly dosing) than when given with rifampin.	
	Rifabutin	↓ vilazodone concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, increase dose of vilazodone to clinical effect if needed. Do not exceed 80 mg/day. Monitor for psychiatric symptoms including depression and anxiety.	No drug-specific information; recommendation based on carbamazepine data. Reductions in drug levels are expected to be less when given with rifabutin than when given with rifampin.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Vortioxetine	Rifampin	↓ vortioxetine concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If co-administration necessary, increase dose of vortioxetine to clinical effect if needed. Do not exceed a maximum of 3 times the original dose.	AUC and Cmax of vortioxetine were 72% and 51% lower, respectively, with coadministration of rifampin 600 mg/day for 11 days.	Package insert 23975654
	Rifapentine (once weekly dosing)	↓ vortioxetine concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, increase dose of vortioxetine to clinical effect if needed. Do not exceed a maximum of 3 times the original dose. Monitor for psychiatric symptoms including depression and anxiety.	No drug-specific information; based on information with rifampin. Reductions in drug levels are expected to be less when given with rifapentine (once weekly dosing) than when given with rifampin.	
	Rifabutin	↓ vortioxetine concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, increase dose of vortioxetine to clinical effect if needed. Do not exceed a maximum of 3 times the original dose. Monitor for psychiatric symptoms including depression and anxiety.	No drug-specific information; based on information with rifampin. Reductions in drug levels are expected to be less when given with rifabutin than when given with rifampin.	

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)					
Levomilnacipran	Rifampin	↓ levomilnacipran concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, titrate levomilnacipran dose as needed to maintain clinical effect, monitoring for psychiatric symptoms including depression and anxiety.	No drug-specific information; based on information with carbamazepine. In a pharmacokinetic study of 27 healthy volunteers, the strong CYP3A4 inducer carbamazepine (200 mg twice daily) decreased the levomilnacipran (120 mg daily) AUC and Cmax 29% and 26%, respectively. The study concluded that no dose adjustment is needed for this combination of drugs. Levomilnacipran prescribing information recommends no clinical action when it is combined with strong CYP3A4 inducers, but due to lack of direct studies with rifampin general caution is advised with clinical monitoring.	Package insert 26315684
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information. Reductions in drug levels are expected to be less when given with rifapentine (once weekly dosing) than when given with rifampin.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information. Reductions in drug levels are expected to be less when given with rifabutin than when given with rifampin.	
Desvenlafaxine **Duloxetine** **Venlafaxine**	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; no expected interaction based on metabolic pathway.	
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; no expected interaction based on metabolic pathway.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; no expected interaction based on metabolic pathway.	

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected or possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected or possible*

Very low risk: Co-administer without modifications. **Low to medium risk:** Co-administer with caution. **Medium to high risk:** Co-administer with extreme caution if benefits outweigh risks. **Highest risk:** Contraindicated, do not co-administer.

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
ANTIFUNGALS (common outpatient use)					
Fluconazole	Rifampin	↓ fluconazole concentration or efficacy expected ↑ rifampin concentration possible	**Co-administer with caution.** If co-administration necessary, monitor clinically for reduced efficacy and consider dose adjustments for fluconazole (increased dosing may be necessary). For serious invasive infections, maximize dosing as appropriate – consider consultation with clinical pharmacist or subspecialist if needed.	Pharmacokinetic and clinical studies have observed a 22-56% decrease in fluconazole AUC. Clinical events: clinical relapse of cryptococcal meningitis has been reported with concomitant usage in case series. In contrast, a pharmacokinetic study of patients being treated for cryptococcal meningitis observed unchanged fluconazole concentrations in the presence of rifampin. Fluconazole may be less effective in treating oral candidiasis with concomitant rifampin use. Increase in rifampin exposure with fluconazole seen in one study but not in a separate study. The mechanism of this possible interaction is not well described.	2037709 2224282 2837559 Package insert 2330488 8845561 15301576 8876848 8961059
	Rifapentine (once weekly dosing)	↓ fluconazole concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor clinically for reduced efficacy and dose adjust as needed.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with fluconazole. Modest decreases in fluconazole exposure may be seen with rifapentine based on observed data with rifampin-fluconazole co-administration.	Package insert
	Rifabutin	No interaction for fluconazole expected ↑ rifabutin concentration expected	**Co-administer with caution.** If co-administration necessary, monitor clinically for rifabutin-related adverse reactions (e.g., neutropenia, uveitis). Rifabutin dose reductions may be required particularly for prolonged concomitant therapy. Consider monitoring rifabutin peak level.	There are minimal effects on fluconazole exposure when given with rifabutin. No changes to fluconazole dosing required. In contrast, the effect of fluconazole on rifabutin exposure is potentially significant. Pharmacokinetic and clinical studies have observed an increase in rifabutin exposure (AUC) by 76% - 82%; Cmax increase by up to 90% via CYP3A4 inhibition by fluconazole. Clinical events: rifabutin associated uveitis has been reported. Rifabutin should be withdrawn if uveitis develops, consult appropriate subspecialist and apply therapeutic management (e.g., topical corticosteroids and mydriatic agents).	Package insert 10898693 8145794 7695673 8597321 8573961

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
ANTIMICROBIALS (common outpatient use)					
Azithromycin	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	In vitro, azithromycin has been shown to interact minimally with CYP450 system. Azithromycin has not been implicated in clinically significant drug-drug interactions.	11012550
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	In vitro, azithromycin has been shown to interact minimally with CYP450 system. Azithromycin has not been implicated in clinically significant drug-drug interactions.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	A multicenter study evaluated the tolerance and potential pharmacokinetic interactions between azithromycin and rifabutin in volunteers with or without HIV infection. The study evaluated high-dose regimen of azithromycin 1200 mg daily and rifabutin 600 mg daily (n = 9) and a lower-dose regimen of azithromycin 600 mg daily and rifabutin at 300 mg daily (n = 17). One group received azithromycin on days 1 to 14 and the combination of azithromycin and rifabutin on days 15 to 42. The other group received rifabutin on days 1 to 14 and the combination on days 15 to 42. The 14-day mean azithromycin AUC in the high-dose regimen was 10.6 +/- 2.6 with a Cmax of 1.2 +/- 0.6 and a Tmax of 2.79 +/- 0.98. None of the mean percentage changes in AUC_{0-24}, Cmax, and Tmax values between study days 14 and 42 for azithromycin, rifabutin, or 25-O-desacetyl-rifabutin (an active metabolite) between the high or low-dose group were significantly different. Only one of the 8 individuals receiving the low-dose regimen had an AUC_{0-24} increase > 25% (45%) between days 14 and 42.	11302832

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Ciprofloxacin	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	Prescribing label states that concurrent use of ciprofloxacin and rifampin may result in decreased ciprofloxacin effectiveness. Probable mechanism of interaction is that rifamycins can accelerate ciprofloxacin metabolism through increased hepatic elimination through induction of CYP450 3A4. However, in a study of 12 nursing home patients colonized with MRSA were randomized to receive a 14-day course of PO ciprofloxacin (750 mg every 12 hours) or PO ciprofloxacin (750 mg every 12 hours) and PO rifampin (300 mg every 12 hours), no significant differences were observed in any pharmacokinetic parameter (Cmax, Tmax, B, AUC, and CL_o) for either ciprofloxacin or rifampin at any of the tested time points. This study supports that ciprofloxacin and rifampin may be given together in standard clinical dosing regimens. An open-label study including 14 injection drug users with *S aureus* bacteremia and mitral or aortic valve infections found no difference in the efficacy of ciprofloxacin when combined with rifampin or used along. Subjects received ciprofloxacin 300 mg IV for 7 days followed by 750 mg PO for 28 days. Rifampin was given as 300 mg every 12 hours PO with ciprofloxacin. Peak ciprofloxacin concentrations were 5-7 times the MIC when ciprofloxacin was used in combination. However, 5 patients were lost to follow up but were considered cured. No other pharmacokinetic parameters were evaluated other than peak and trough antimicrobial concentrations. Pharmacokinetic and serum bactericidal activity (SBA) of ciprofloxacin when co-administered with rifampin were compared in 6 healthy elderly patients > 65 years with normal renal function. The authors found that PO ciprofloxacin in doses of 750 mg twice daily can be co-administered with PO rifampin at a dose of 600 mg daily without significantly altering peak ciprofloxacin concentrations and other pharmacokinetic parameters. CONTINUES	10466918 2185691 2572799 1804008

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Ciprofloxacin				CONTINUED A review of pharmacokinetic studies on fluoroquinolones and rifampin suggests that total plasma clearance may be increased in some instances, but may not be significant enough to change the efficacy of either agents. This review also comments on how results from time-kill studies have shown significant differences in animal and in vitro models. However, transition to human models and clinical significance remains unknown.	
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	Prescribing label states that concurrent use of ciprofloxacin and rifapentine may result in decreased ciprofloxacin effectiveness. Probable mechanism of interaction is that rifamycin can accelerate ciprofloxacin metabolism through increased hepatic elimination through induction of CYP450 3A4. In vitro and in vivo enzyme inductions have suggested that rifapentine induction potential may be less than rifampin but more potent than rifabutin. However, rifampin and ciprofloxacin have not been shown to have a clinically significant interaction in clinical studies. Extrapolating from these studies, rifapentine is unlikely to have a clinically significant interaction with ciprofloxacin.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	Prescribing label states that concurrent use of ciprofloxacin and rifabutin may result in decreased ciprofloxacin effectiveness. Probable mechanism of interaction is that rifamycin can accelerate ciprofloxacin metabolism through increased hepatic elimination through induction of CYP450 3A4. However, rifampin and ciprofloxacin have not been shown to have a clinically significant interaction in clinical studies. Extrapolating from these studies, rifabutin is unlikely to have a clinically significant interaction with ciprofloxacin.	

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Trimethoprim-sulfamethoxazole	Rifampin	↓ sulfamethoxazole concentration or efficacy possible ↑ hydroxylamine (metabolite of sulfamethoxazole) concentration possible ↑ rifampin concentration possible	**Co-administer with caution** for outpatient indications such as UTI, skin/soft tissue infection. If co-administration necessary, monitor for reduced sulfamethoxazole efficacy and increased rifampin adverse effects. For severe infections and/or immune-compromised patients, **co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	The mechanism of this reaction is likely due rifampin inducing sulfamethoxazole metabolism leading to decreased sulfamethoxazole efficacy and increased toxicity from accumulation of hydroxylamine from sulfamethoxazole metabolism. Increased trimethoprim metabolism is likely due to rifampin-mediated enzyme induction. The mechanism of increased rifampin concentrations during coadministration with trimethoprim-sulfamethoxazole is unknown. In a study of HIV patients (n = 10), sulfamethoxazole AUC was decreased 23% when TMP-SMX (160-800 mg 1 tablet daily for at least 1 month) was co-administered with rifampin (600 mg for 12 days). Trimethoprim AUC was decreased by 47% when co-administered with rifampin (600 mg for 12 days) in the same study. No significant changes in Cmax or Tmax occurred with co-administration of TMP-SMX and rifampin. Study did not comment on clinical implications of these reductions. A case-control study of 32 patients with toxoplasmosis and 64 patients without toxoplasmosis aimed to evaluate the optimal dose of TMP-SMX for toxoplasmosis prophylaxis. The authors identified that receiving concomitant rifampin therapy was a risk factor for toxoplasmosis. For patients receiving rifampin, the OR for low doses of co-trimoxazole was 10.83 (95% CI 1.77-84.36; p = 0.0064) whereas for patients not receiving rifampin, it was 3.63 (95% CI 0.95-17.29; p = 0.055). For patients receiving high doses of co-trimoxazole, the OR for rifampin exposure was 1.41 (95% CI 0.15-11.11; p = 0.55) whereas for patients receiving low doses, the OR for rifampin exposure was 4.17 (95% CI 1.28-14.29; p = 0.013).	11600390 10585796

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Trimethoprim-sulfamethoxazole	Rifapentine (once weekly dosing)	↓ sulfamethoxazole concentration or efficacy possible ↑ hydroxylamine (metabolite of sulfamethoxazole) concentration possible	**Co-administer with caution** for outpatient indications such as UTI, skin/soft tissue infection. If co-administration necessary, monitor for reduced sulfamethoxazole efficacy and increased sulfamethoxazole toxicity. For severe infections and/or immune-compromised patients, **co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	Rifapentine is a known inducer of CYP3A4 and CYP2C8/9. In vitro and in vivo enzyme inductions have suggested that rifapentine induction potential may be less than rifampin but more potent than rifabutin. The magnitude of enzyme induction also seems to be dose and dosing frequency dependent with less induction occurring when 600 mg oral doses were given once every 72 hours versus daily. Although there is no pharmacokinetic data available on the interaction with rifapentine specifically, other studies have postulated that sulfamethoxazole metabolism to its hydroxylamine formulation is mediated via CYP3A4 or 2C89. Therefore, there is a possibility of increased concentrations of this active metabolite that can result in sulfamethoxazole-hydroxylamine related adverse effects.	

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Trimethoprim-sulfamethoxazole	Rifabutin	↓ sulfamethoxazole concentration or efficacy possible ↑ hydroxylamine (metabolite of sulfamethoxazole) concentration possible	**Co-administer with caution** for outpatient indications such as UTI, skin/soft tissue infection. If co-administration necessary, monitor for reduced sulfamethoxazole efficacy and increased sulfamethoxazole toxicity. For severe infections and/or immune-compromised patients, **co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	Rifabutin increased the apparent formulation of hydroxylamine in HIV-infected subjects. Rifabutin likely increases hydroxylamine concentration through induction of CYP3A4 or CYP2C9-mediated sulfamethoxazole metabolism. Co-administration of rifabutin (300 mg/day) and sulfamethoxazole-trimethoprim (double strength) in 12 HIV-infected patients decreased the AUC of sulfamethoxazole-trimethoprim by about 15% to 20%. When trimethoprim was given alone, the AUC of trimethoprim was decreased by 14% and the Cmax by 6%. Sulfamethoxazole-trimethoprim did not alter the pharmacokinetics of rifabutin. Sulfamethoxazole has a biologically reactive metabolite, hydroxylamine, that may play a key role in sulfamethoxazole-related adverse reactions. In a pharmacokinetic study of HIV-infected patients, 9 received TMP-SMX (800 mg sulfamethoxazole/160 mg trimethoprim daily) alone for 2 weeks followed by cotrimoxazole with rifabutin 300 mg daily for 2 weeks. At 2 weeks, rifabutin significantly increased the AUC and urinary recovery for hydroxylamine by 50% and 45% respectively ($p < 0.05$). Rifabutin therefore may increase adverse reactions to sulfamethoxazole through induction of CYP3A4 or CYP2C9 and increased amounts of hydroxylamine formulation.	15470330

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
ANTIPLATELET MEDICATIONS					
Clopidogrel	Rifampin	↑ clopidogrel concentration expected	**Contraindicated, do not co-administer.**	Avoid co-administration if possible due to increased risk of bleeding. Pharmacokinetic studies have observed an increase in AUC of clopidogrel active metabolite of >350% with rifampin co-administration. There is also an increase in maximal inhibition of platelet aggregation 3-10 fold with rifampin co-administration. Effects may vary by patient CYP2C19 genotype. Do not co-administer recommendation made because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	Package insert 20492465 14707025 35152432
	Rifapentine (once weekly dosing)	↑ clopidogrel concentration possible	**Contraindicated, do not co-administer.**	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with clopidogrel. There is potential for increase in AUC of clopidogrel active metabolite through rifapentine-mediated induction of CYP2C19. Do not co-administer recommendation made because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	35152432
	Rifabutin	↑ clopidogrel concentration possible	**Contraindicated, do not co-administer.**	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with clopidogrel. There is potential for increase in AUC of clopidogrel active metabolite through rifabutin-mediated induction of CYP2C19. Do not co-administer recommendation made because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	35152432 34228545

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Prasugrel	Rifampin	No significant interaction expected	**Co-administer with caution.** If co-administration necessary, standard clinical monitoring for prasugrel recommended.	In a pharmacokinetic study, there was minimal impact on AUC of prasugrel active metabolite and minimal change in platelet aggregation with rifampin co-administration. Given no known clinical data of agents given together and general risk of subtherapeutic antiplatelet therapy, caution and clinical monitoring is recommended.	Package insert 19530977 35152432
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer with caution.** If co-administration necessary, standard clinical monitoring for prasugrel recommended.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with prasugrel. Based on studies with rifampin, impacts of rifapentine on prasugrel exposure are likely to be minimal. Manufacturer states that prasugrel can be co-administered with inducers or inhibitors of CYP enzymes. Given no known clinical data of agents given together and general risk of subtherapeutic antiplatelet therapy, caution and clinical monitoring is recommended.	Package insert 35152432
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with prasugrel. Based on studies with rifampin, impacts of rifabutin on prasugrel exposure are likely to be minimal. Manufacturer states that prasugrel can be co-administered with inducers or inhibitors of CYP enzymes.	Package insert 35152432

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Ticagrelor	Rifampin	↓ ticagrelor concentration or efficacy expected	**Contraindicated, do not co-administer.**	In a pharmacokinetic study, ticagrelor AUC decreased 86%, Cmax decreased 73%, active metabolite AUC decreased 46% and area under effect curve decreased 27% with rifampin co-administration. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	Package insert 23093043 35152432
	Rifapentine (once weekly dosing)	↓ ticagrelor concentration or efficacy possible	**Contraindicated, do not co-administer.**	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with ticagrelor. Ticagrelor is a major substrate of CYP3A4. There is potential for decreased drug exposure and antiplatelet effect due to CYP enzyme induction by rifapentine. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	35152432
	Rifabutin	↓ ticagrelor concentration or efficacy possible	**Contraindicated, do not co-administer.**	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with ticagrelor. Ticagrelor is a major substrate of CYP3A4. There is potential for decreased drug exposure and antiplatelet effect due to CYP enzyme induction by rifabutin. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	35152432

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Vorapaxar	Rifampin	↓ vorapaxar concentration or efficacy expected	**Contraindicated, do not co-administer.**	In a pharmacokinetic study, AUC of vorapaxar decreased by approximately 50% with rifampin co-administration. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	Package insert 23426761
	Rifapentine (once weekly dosing)	↓ vorapaxar concentration or efficacy possible	**Contraindicated, do not co-administer.**	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with vorapaxar. Vorapaxar is a major substrate of CYP3A4. There is potential for decreased drug exposure and antiplatelet effect due to CYP enzyme induction by rifapentine. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	
	Rifabutin	↓ vorapaxar concentration or efficacy possible	**Contraindicated, do not co-administer.**	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with vorapaxar. Vorapaxar is a major substrate of CYP3A4. There is potential for decreased drug exposure and antiplatelet effect due to CYP enzyme induction by rifabutin. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
ANTIRETROVIRALS					
Integrase strand transfer inhibitor (INSTI) **Non-nucleoside reverse transcriptase inhibitor (NNRTI)** **Protease inhibitors (PI)**	Rifampin Rifapentine Rifabutin	**Refer to DHHS Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV, Drug-Drug Interactions tables** (click here for overview page) • Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs – click here • Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs – click here • Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) – click here • Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs – click here			
BETA BLOCKERS					
Carvedilol	Rifampin	↓ carvedilol concentration or efficacy expected	**Co-administer with caution.** If co-administration is necessary, monitor for reduced clinical effect and dose adjust beta-blocker as needed.	Various pharmacokinetic studies have observed reduction in AUC by 57%, 63%, and 70% via CYP enzyme induction – likely 2D6 (varies by genotype), 2C9 and intestinal transporters (P-gp).	15001973
	Rifapentine (once weekly dosing)	↓ carvedilol concentration or efficacy possible	**Co-administer with caution.** If co-administration is necessary, monitor for reduced clinical effect and dose adjust beta-blocker as needed.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with carvedilol. Carvedilol is metabolized CYP2C9. Rifapentine package insert mentions potential for dose adjustment for drugs metabolized via CYP2C9.	Package insert (rifapentine)
	Rifabutin	↓ carvedilol concentration or efficacy possible	**Co-administer with caution.** If co-administration is necessary, monitor for reduced clinical effect and dose adjust beta-blocker as needed.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with carvedilol. Carvedilol is metabolized CYP2C9. Rifabutin is a weak CYP2C9 inducer. Minimal interaction expected.	

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Bisoprolol **Metoprolol**	Rifampin	↓ beta blocker concentration or efficacy expected	**Co-administer with caution.** If co-administration is necessary, monitor for reduced clinical effect and dose adjust beta-blocker as needed.	Pharmacokinetic studies have observed decreased bisoprolol exposure – 34% AUC and 23% Cmax reductions; likely secondary to CYP3A4 induction (partial metabolic pathway). Also, decreased metoprolol exposure – 14% (7-day rifampin course) and 33% (15-day rifampin course) reduction in AUC. Bisoprolol package insert: strong CYP3A4 inducers such as rifampin decrease bisoprolol exposure, but initial dose modifications are usually not necessary.	2877885 7059439 26123704 6639842 Package insert
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with these beta-blockers. Significant reductions in drug exposure are not expected; based on rifampin and propranolol pharmacokinetic data, rifapentine package insert states “drugs metabolized by CYP3A4 or P450 2C8/9” may require dose adjustments but likely doesn’t extrapolate to rifapentine and other beta-blockers. Significant reductions in drug exposure are not expected.	6639842 Package insert
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with these beta-blockers. Significant reductions in drug exposure are not expected.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Nadolol	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	Although rifampin is a strong P-gp inducer and nadolol is a major P-gp substrate, rifampin (450 mg daily for 6 days) only decreased the nadolol (30 mg single dose) AUC 29%, and this decrease did not reach statistical significance. Significant reduction in drug levels not expected.	23677858
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with this beta-blocker. Reductions in drug levels are not expected when given with rifapentine (once weekly dosing).	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with this beta-blocker. Reductions in drug levels are not expected when given with rifabutin.	
Nebivolol	Rifampin	↓ nebivolol concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for reduced clinical effect and dose adjust beta-blocker as needed.	There is a lack of pharmacokinetic or clinical case data reported for rifampin co-administration with nebivolol. Nebivolol is a major CYP2D6 substrate and rifampin is CYP2D6 inducer, thus there is potential for some reduction in drug levels of nebivolol.	Package insert
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with nebivolol. Reductions in drug levels are not expected when given with rifapentine (once weekly dosing).	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with nebivolol. Reductions in drug levels are not expected when given with rifabutin.	

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected or possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected or possible*

Very low risk: Co-administer without modifications. **Low to medium risk:** Co-administer with caution. **Medium to high risk:** Co-administer with extreme caution if benefits outweigh risks. **Highest risk:** Contraindicated, do not co-administer.

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Acebutolol **Atenolol** **Betaxolol** **Esmolol**	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifampin co-administration with these beta-blockers. Reductions in drug levels are not expected. These beta-blockers are either not a CYP substrate or only minor CYP substrate.	
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with these beta-blockers. Reductions in drug levels are not expected. These beta-blockers are either not a CYP substrate or only minor CYP substrate.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with these beta-blockers. Reductions in drug levels are not expected. These beta-blockers are either not a CYP substrate or only minor CYP substrate.	
BIOLOGICS					
Adalimumab **Bevacizumab** **Etanercept** **Infliximab** **Rituximab** **Trastuzumab**	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	These drugs are not metabolized through CYP pathway; although no clinical data are present, no interaction is anticipated.	23855593
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	These drugs are not metabolized through CYP pathway; although no clinical data are present, no interaction is anticipated.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	These drugs are not metabolized through CYP pathway; although no clinical data are present, no interaction is anticipated.	

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
CALCIUM CHANNEL BLOCKERS					
Nicardipine	Rifampin	↓ nicardipine concentration or efficacy possible	**Co-administer with caution** for indication of hypertension. If co-administration necessary, monitor for loss of nicardipine effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required. For other indications including acute aortic syndromes, acute ischemic syndromes, or hypertensive emergency, **co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	Case studies have reported decreased serum concentrations of nicardipine with rifamycin use.	28407303 1345893

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Very low risk: Co-administer without modifications. **Low to medium risk:** Co-administer with caution. **Medium to high risk:** Co-administer with extreme caution if benefits outweigh risks. **Highest risk:** Contraindicated, do not co-administer.

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Nicardipine	Rifapentine (once weekly dosing)	↓ nicardipine concentration or efficacy possible	**Co-administer with caution** for indication of hypertension. If co-administration necessary, monitor for loss of nicardipine effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required. For other indications including acute aortic syndromes, acute ischemic syndromes, or hypertensive emergency, **co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	No drug-specific data; recommendation based on rifampin data.	Package insert

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Nicardipine	Rifabutin	↓ nicardipine concentration or efficacy possible	**Co-administer with caution** for indication of hypertension. If co-administration necessary, monitor for loss of nicardipine effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required. For other indications including acute aortic syndromes, acute ischemic syndromes, or hypertensive emergency, **co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	No drug-specific data; recommendation based on rifampin data.	
Nifedipine	Rifampin	↓ nifedipine concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. Consider alternatives to nifedipine for patients who are using strong CYP3A4 inducers. If co-administration is needed, monitor patients closely for clinical signs of diminished nifedipine response.	In a pharmacokinetic study of 6 healthy volunteers, rifampin (600 mg daily for 7 days) decreased the nifedipine (20 mg single dose) AUC 92%. The AUC of nifedipine was also reduced 64% after just a single dose of rifampin (1,200 mg) in another study of healthy volunteers. In one report, a patient with previously controlled hypertension on nifedipine experienced a loss of blood pressure control after starting rifampin. Another patient who was taking nifedipine for control of angina also experienced a loss of nifedipine effectiveness shortly after starting concurrent rifampin.	8894514 9226591 1345893 1345893 3453828 31047967 24530864

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Very low risk: Co-administer without modifications. **Low to medium risk:** Co-administer with caution. **Medium to high risk:** Co-administer with extreme caution if benefits outweigh risks. **Highest risk:** Contraindicated, do not co-administer.

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Nifedipine	Rifapentine (once weekly dosing)	↓ nifedipine concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. Consider alternatives to nifedipine for patients who are using strong CYP3A4 inducers. If co-administration is needed, monitor patients closely for clinical signs of diminished nifedipine response.	Rifapentine may increase the metabolism of nifedipine due to increased metabolism by CYP3A4.	Package insert
	Rifabutin	↓ nifedipine concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. Consider alternatives to nifedipine for patients who are using strong CYP3A4 inducers. If co-administration is needed, monitor patients closely for clinical signs of diminished nifedipine response.	No drug-specific data; recommendation based on rifampin data.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Felodipine	Rifampin	↓ felodipine concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If used concurrently, monitor for loss of felodipine effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	CYP3A4 inducers (strong) may decrease serum concentrations of felodipine. In pharmacokinetic studies, the maximum plasma concentrations of felodipine were considerably lower in epileptic patients on long-term anticonvulsant therapy (strong 3A4 inducers phenytoin, carbamazepine, or phenobarbital) than in healthy volunteers; the mean felodipine AUC was reduced by ~6%.In an additional study of healthy volunteers, a weak CYP3A4 inducer (oxcarbazepine) decreased felodipine AUC 28%.	Package insert 8451779 16480505 19951720
	Rifapentine (once weekly dosing)	↓ felodipine concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for loss of felodipine effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	No studies have been conducted for moderate CYP3A4 inducers on felodipine but strong inducers have decreased felodipine concentrations. Reductions in drug levels are expected to be less when given with rifapentine (once weekly dosing) than when given with rifampin.	Package insert
	Rifabutin	↓ felodipine concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for loss of felodipine effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	No studies have been conducted for moderate CYP3A4 inducers on felodipine but strong inducers have decreased felodipine concentrations. Reductions in drug levels are expected to be less when given with rifabutin than when given with rifampin.	Package Insert

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Nisoldipine	Rifampin	↓ nisoldipine concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If used concurrently, monitor for loss of nisoldipine effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	Strong CYP3A4 inducers may decrease the serum concentrations of nisoldipine. Concomitant use of rifampin and some calcium channel blockers has caused loss of control of hypertension due to decreased serum concentrations of the Ca channel blocker. In patients with epilepsy who were using phenytoin (a strong CYP3A4 inducer), the AUC for nisoldipine was decreased by 90%. A 75 y/o hypertensive woman had been well controlled with nifedipine. After she developed tuberculosis and was treated with rifampin, both peak plasma concentration and AUC of nifedipine decreased to about 40% of previous levels; control of the hypertension was significantly affected. Another calcium channel blocker, nisoldipine, was administered concurrently with rifampin, but it also was unable to lower her blood pressure.	Package insert 1345893 9784933
	Rifapentine (once weekly dosing)	↓ nisoldipine concentration or efficacy possible	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If used concurrently, monitor for loss of nisoldipine effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	Moderate CYP3A4 inducers may decrease the serum concentrations of nisoldipine No formal interaction studies have been done to evaluate for the effects of moderate inducers on nisoldipine. However, in patients with epilepsy who were using phenytoin (a strong CYP3A4 inducer), the AUC for nisoldipine was decreased by 90%.	Package insert

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Nisoldipine	Rifabutin	↓ nisoldipine concentration or efficacy possible	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If used concurrently, monitor for loss of nisoldipine effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	Moderate CYP3A4 inducers may decrease the serum concentrations of nisoldipine No formal interaction studies have been done to evaluate for the effects of moderate inducers on nisoldipine. However, in patients with epilepsy who were using phenytoin (a strong CYP3A4 inducer), the AUC for nisoldipine was decreased by 90%.	Package insert

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Amlodipine	Rifampin	↓ amlodipine concentration or efficacy expected	**Co-administer with caution** for indication of hypertension. If co-administration necessary, monitor for loss of amlodipine effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	Changes in amlodipine drug levels may occur, but can likely be managed in a primary care setting by dose titration and/or addition of additional antihypertensive agents. Strong CYP3A4 inducers decrease the serum concentration of amlodipine. In a cohort study, patients using amlodipine with rifampin saw a mean decrease of 81.7% in amlodipine levels. In 8 patients, levels were undetectable. In a single case report, a 67 y/o man taking amlodipine 10 mg experienced increased blood pressure requiring treatment with six additional antihypertensive agents after initiation of rifampin. After rifampin was stopped, blood pressure control improved.	26009790 32918434 27795624
	Rifapentine (once weekly dosing)	↓ amlodipine concentration or efficacy possible	**Co-administer with caution** for indication of hypertension. If co-administration necessary, monitor for loss of amlodipine effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	No drug-specific data; recommendation based on amlodipine interaction with strong CYP3A4 inducer carbamazepine.	Package Insert
	Rifabutin	↓ amlodipine concentration or efficacy possible	**Co-administer with caution** for indication of hypertension. If co-administration necessary, monitor for loss of amlodipine effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	No drug-specific data; recommendation based on amlodipine interaction with strong CYP3A4 inducer carbamazepine.	Package Insert

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Isradipine	Rifampin	↓ isradipine concentration or efficacy possible	**Co-administer with caution** for indication of hypertension. If co-administration necessary, monitor for loss of isradipine effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	Changes in drug levels are possible, but can likely be managed in a primary care setting by dose titration and/or addition of additional antihypertensive agents. Strong CYP3A4 inducers may decrease the serum concentration of isradipine. The strong CYP3A4 inducer rifampin (600 mg daily for 6 days) co-administered with isradipine (5 mg single dose) resulted in a reduction in isradipine serum levels to below detectable limits.	Package insert 33030266
	Rifapentine (once weekly dosing)	↓ isradipine concentration or efficacy possible	**Co-administer with caution** for indication of hypertension. If co-administration necessary, monitor for loss of isradipine effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	Moderate CYP3A4 inducers may decrease the serum concentration of isradipine. No formal interaction studies have been done to evaluate for the effects of moderate inducers on isradipine. However, in patients using strong CYP3A4 inducers, isradipine serum levels were reduced to below detectable levels.	Package insert
	Rifabutin	↓ isradipine concentration or efficacy possible	**Co-administer with caution** for indication of hypertension. If co-administration necessary, monitor for loss of isradipine effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	Moderate CYP3A4 inducers may decrease the serum concentration of isradipine. No formal interaction studies have been done to evaluate for the effects of moderate inducers on isradipine. However, in patients using strong CYP3A4 inducers, isradipine serum levels were reduced to below detectable levels.	Package insert

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Clevidipine	Rifampin	↓ clevidipine concentration or efficacy possible	**Co-administer without modifications** for indication of hypertension, no clinically significant interaction likely.	Rifampin use may decrease levels of calcium channel blockers. Clevidipine is metabolized by blood and tissue esterases, no clinically significant interactions likely.	
	Rifapentine (once weekly dosing)	↓ clevidipine concentration or efficacy possible	**Co-administer without modifications** for indication of hypertension, no clinically significant interaction likely.	Rifapentine use may decrease levels of calcium channel blockers. Clevidipine is metabolized by blood and tissue esterases, no clinically significant interactions likely.	
	Rifabutin	↓ clevidipine concentration or efficacy possible	**Co-administer without modifications** for indication of hypertension, no clinically significant interaction likely.	Rifabutin use may decrease levels of calcium channel blockers. Clevidipine is metabolized by blood and tissue esterases, no clinically significant interactions likely.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Nimodipine	Rifampin	↓ nimodipine concentration or efficacy expected	**Contraindicated, do not co-administer.**	Strong CYP3A4 inducers may decrease the serum concentrations of nimodipine. No drug-specific information; however, when nimodipine (60 mg) was combined with strong CYP3A4 inducers, the Cmax and AUC were decreased 89% and 86%, respectively. Due to potential for significant consequences of reduced nimodipine exposure when used for indication of subarachnoid hemorrhage, concomitant use of a strong CYP3A4 inducer such as rifampin should be avoided.	1777370 Package Insert
	Rifapentine (once weekly dosing)	↓ nimodipine concentration or efficacy possible	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If used concurrently, monitor for loss of nimodipine effects. Dose increases of calcium channel blocker or use other antihypertensives may be required.	Moderate CYP3A4 inducers may decrease the serum concentrations of nimodipine. Due to potential for significant consequences of reduced nimodipine exposure when used for indication of subarachnoid hemorrhage, recommend close monitoring and possible dose increase of nimodipine with input from a subspecialist and/or clinical pharmacist.	
	Rifabutin	↓ nimodipine concentration or efficacy possible	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If used concurrently, monitor for loss of nimodipine effects. Dose increases of calcium channel blocker or use other antihypertensives may be required.	Moderate CYP3A4 inducers may decrease the serum concentrations of nimodipine. Due to potential for significant consequences of reduced nimodipine exposure when used for indication of subarachnoid hemorrhage, recommend close monitoring and possible dose increase of nimodipine with input from a subspecialist and/or clinical pharmacist.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Diltiazem	Rifampin	↓ diltiazem concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If used concurrently, monitor for loss of diltiazem effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	Diltiazem prescribing information states that rifampin has been shown to reduce diltiazem concentrations to undetectable levels.	Package Insert 2792166
	Rifapentine (once weekly dosing)	↓ diltiazem concentration or efficacy expected	**Co-administer with caution.** If co-administration necessary, monitor for loss of diltiazem effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	CYP3A4 inducers (moderate) may decrease the serum concentration of diltiazem. While no data specifically known for rifapentine, a pharmacokinetic study of another moderate CYP3A4 inducer, efavirenz, showed a decrease in diltiazem AUC by 69%.	Package insert (efavirenz)
	Rifabutin	↓ diltiazem concentration or efficacy expected	**Co-administer with caution.** If co-administration necessary, monitor for loss of diltiazem effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	CYP3A4 inducers (moderate) may decrease the serum concentration of diltiazem. While no data specifically known for rifabutin, a pharmacokinetic study of another moderate CYP3A4 inducer, efavirenz, showed a decrease in diltiazem AUC by 69%.	Package insert (efavirenz)

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Verapamil	Rifampin	↓ verapamil concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If used concurrently, monitor for loss of verapamil effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	Two pharmacokinetic studies, rifampin (600 mg daily) co-administered with oral verapamil (120 mg twice daily) decreased the total verapamil AUC 93%, increased the R-verapamil clearance 32-fold, and increased the S-verapamil clearance 57-fold. The effects of strong CYP3A4 inducers appear smaller when combined with IV verapamil. In a pharmacokinetic study, rifampin (600 mg daily) co-administered with IV verapamil (10 mg single dose) decreased the total verapamil AUC 18%, increased R-verapamil clearance 1.3-fold, and increased S-verapamil clearance 1.9-fold. Verapamil prescribing information states that use of a CYP3A4 inducer can decrease verapamil exposure.	8855178 3180898 3974676 4028962 1891033
	Rifapentine (once weekly dosing)	↓ verapamil concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for loss of verapamil effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	Concurrent use of rifapentine and calcium channel blockers may result in decreased calcium channel blocker effectiveness.	Package Insert
	Rifabutin	↓ verapamil concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for loss of verapamil effects, including clinical signs or symptoms of hypertension or angina. Dose increases of calcium channel blocker or use other antihypertensives may be required.	CYP3A4 inducers (moderate) may decrease the serum concentration of Verapamil.	

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
CONTRACEPTIVE MEDICATIONS					
Combined oral contraceptives	Rifampin	↓ ethinyl estradiol concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifampin.	Reported 64-66% reduction in ethinyl estradiol AUC with rifampin co-administration, reported 42% reduction in ethinyl estradiol Cmax with rifampin co-administration, reported 51-60% reduction in norethindrone AUC with rifampin co-administration. Some studies demonstrate increased ovulation. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	32275771 10223781 9824786 29130574
	Rifapentine (once weekly dosing)	↓ ethinyl estradiol concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifapentine.	No direct pharmacokinetic or clinical case data reported, extrapolation from rifampin and rifabutin data. Potential for significant reduction in combined oral contraceptive AUC and Cmax. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	
	Rifabutin	↓ ethinyl estradiol concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifabutin.	Reported 35% reduction in ethinyl estradiol AUC with rifabutin co-administration, reported 20% reduction in ethinyl estradiol Cmax with rifabutin co-administration, reported 13-46% reduction in norethindrone AUC with rifabutin co-administration. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	10223781 9824786 29130574 Package insert

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Levonorgestrel (oral) emergency contraceptive	Rifampin	↓ levonorgestrel concentration or efficacy expected	**Contraindicated, do not co-administer.** Other emergency contraceptives are preferred, such as copper IUD, due to expected reductions in levonorgestrel concentrations. If concomitant use is required, some experts outside the U.S. recommend doubling the dose to 3 mg if enzyme inducers were used in the previous 4 weeks.	Reported AUC ratio (with rifampin/no rifampin) for levonorgestrel was 0.292 for unbound and 0.427 for bound drug. CDC USMEC rates this interaction as category 2: "Advantages generally outweigh theoretical/proven risk." However, the Medicines and Healthcare products Regulatory Agency recommends against concomitant use. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	32275771 CDC US Medical Eligibility Criteria (US MEC) for Contraceptive Use
	Rifapentine (once weekly dosing)	↓ levonorgestrel concentration or efficacy expected	**Contraindicated, do not co-administer.** Other emergency contraceptives are preferred, such as copper IUD, due to expected reductions in levonorgestrel concentrations. If concomitant use is required, some experts outside the U.S. recommend doubling the dose to 3 mg if enzyme inducers were used in the previous 4 weeks.	No pharmacokinetic or clinical case data reported. Potential for significant reduction given ethinyl estradiol and etonogestrel are major substrates of CYP3A4. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Levonorgestrel (oral) emergency contraceptive	Rifabutin	↓ levonorgestrel concentration or efficacy expected	**Contraindicated, do not co-administer.** Other emergency contraceptives are preferred, such as copper IUD, due to expected reductions in levonorgestrel concentrations. If concomitant use is required, some experts outside the U.S. recommend doubling the dose to 3 mg if enzyme inducers were used in the previous 4 weeks.	No pharmacokinetic or clinical case data reported. Potential for significant reduction given ethinyl estradiol and etonogestrel are major substrates of CYP3A4. CDC USMEC rates this interaction as category 2: "Advantages generally outweigh theoretical/proven risk." However, the Medicines and Healthcare products Regulatory Agency recommends against concomitant use. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	CDC US Medical Eligibility Criteria (US MEC) for Contraceptive Use

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Progestin only pills (Norethindrone)	Rifampin	↓ norethindrone concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifampin.	Reported 51-60% reduction in norethindrone AUC with rifampin co-administration. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	32275771 10223781 9824786
	Rifapentine (once weekly dosing)	↓ norethindrone concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifapentine.	No pharmacokinetic or clinical case data reported. Potential for significant reduction given norethindrone is a major substrate of CYP3A4. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	
	Rifabutin	↓ norethindrone concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifabutin.	Reported 13-46% reduction in norethindrone AUC with rifabutin co-administration. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	10223781 9824786 Package insert

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Depot medroxyprogesterone acetate (DMPA) injectable	Rifampin	↓ MPA concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, consider using a backup method (e.g., condoms) during concomitant use and for 28 days after discontinuation of rifampin.	In a pharmacokinetic study of women taking DMPA, rifampin-based TB treatment AND efavirenz-based ARVs, 12% of women had MPA levels < 0.1ng/mL at week 12 and 1 had MPA < 0.1 ng/mL at week 10. Median clearance of MPA was 1.6x faster compared to historical controls. Though, progesterone levels remained < 1ng/mL suggesting ovulation did NOT occur. A pooled pharmacokinetic study of the same population suggested dosing every 8-10 weeks, vs. q13 weeks could overcome the subtherapeutic levels.	31504342 34151439
	Rifapentine (once weekly dosing)	↓ MPA concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, consider using a backup method (e.g., condoms) during concomitant use and for 28 days after discontinuation of rifapentine.	No pharmacokinetic or clinical case data reported, extrapolated based on rifampin data.	
	Rifabutin	↓ MPA concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, consider using a backup method (e.g., condoms) during concomitant use and for 28 days after discontinuation of rifabutin.	No pharmacokinetic or clinical case data reported, extrapolated based on rifampin data.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Etonogestrel subdermal implant (Nexplanon, Implanon)	Rifampin	↓ etonogestrel concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifampin.	Case report: 29 y/o F who received Implanon 2002, started rifampin 300 mg PO BID for HS in March 2004 and became pregnant in August 2004. Review of post-marketing surveillance data indicated 25% of method failures were associated with interacting drugs-majority carbamazepine, but also phenytoin, phenobarbital, and rifampicin. CDC USMEC rates this interaction as category 2: Advantages generally outweigh theoretical/proven risk, but also state: "…the interaction of rifampin or rifabutin with POPs and etonogestrel implants…is likely to reduce the effectiveness of POPs and etonogestrel implants. Use of other contraceptives should be encouraged for women who are long-term users of any of these drugs." Medicines and Healthcare products regulatory agency rates this as category X—avoid use and advise alternative method. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	16371312 18330813 CDC US Medical Eligibility Criteria (US MEC) for Contraceptive Use
	Rifapentine (once weekly dosing)	↓ etonogestrel concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifapentine.	No pharmacokinetic or clinical case data reported. Potential for significant reduction given ethinyl estradiol and etonogestrel are major substrates of CYP3A4. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Etonogestrel subdermal implant (Nexplanon, Implanon)	Rifabutin	↓ etonogestrel concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifabutin.	No pharmacokinetic or clinical case data reported. CDC USMEC rates this interaction as category 2: Advantages generally outweigh theoretical/proven risk, but also state: "…the interaction of rifampin or rifabutin with POPs and etonogestrel implants…is likely to reduce the effectiveness of POPs and etonogestrel implants. Use of other contraceptives should be encouraged for women who are long-term users of any of these drugs." Medicines and Healthcare products regulatory agency rates this as category X—avoid use and advise alternative method. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	CDC US Medical Eligibility Criteria (US MEC) for Contraceptive Use
Ethinyl Estradiol/ Norelgestromin transdermal patch	Rifampin	↓ ethinyl estradiol concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifampin.	No pharmacokinetic or clinical case data reported. Potential for significant reduction given ethinyl estradiol and etonogestrel are major substrates of CYP3A4. Per CDC USMEC: "Evidence indicates that the combined hormonal patch and the combined vaginal ring provide comparable safety and pharmacokinetic profiles to COCs with similar hormone formulations. Pending further studies, the evidence available for recommendations about COCs applies to the recommendations for the combined hormonal patch and vaginal ring." Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	CDC US Medical Eligibility Criteria (US MEC) for Contraceptive Use

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Ethinyl Estradiol/ Norelgestromin transdermal patch	Rifapentine (once weekly dosing)	↓ ethinyl estradiol concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifapentine.	No pharmacokinetic or clinical case data reported. Potential for significant reduction given ethinyl estradiol and etonogestrel are major substrates of CYP3A4. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	
	Rifabutin	↓ ethinyl estradiol concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifabutin.	No pharmacokinetic or clinical case data reported. Potential for significant reduction given ethinyl estradiol and etonogestrel are major substrates of CYP3A4. Per CDC USMEC: "Evidence indicates that the combined hormonal patch and the combined vaginal ring provide comparable safety and pharmacokinetic profiles to COCs with similar hormone formulations. Pending further studies, the evidence available for recommendations about COCs applies to the recommendations for the combined hormonal patch and vaginal ring." Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	CDC US Medical Eligibility Criteria (US MEC) for Contraceptive Use

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Etonogestrel / Ethinyl Estradiol vaginal ring	Rifampin	↓ ethinyl estradiol concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifampin.	No pharmacokinetic or clinical case data reported. Potential for significant reduction given ethinyl estradiol and etonogestrel are major substrates of CYP3A4. Per CDC USMEC: "Evidence indicates that the combined hormonal patch and the combined vaginal ring provide comparable safety and pharmacokinetic profiles to COCs with similar hormone formulations. Pending further studies, the evidence available for recommendations about COCs applies to the recommendations for the combined hormonal patch and vaginal ring." Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	CDC US Medical Eligibility Criteria (US MEC) for Contraceptive Use
	Rifapentine (once weekly dosing)	↓ ethinyl estradiol concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifapentine.	No pharmacokinetic or clinical case data reported. Potential for significant reduction given ethinyl estradiol and etonogestrel are major substrates of CYP3A4. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Etonogestrel / Ethinyl Estradiol vaginal ring	Rifabutin	↓ ethinyl estradiol concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifabutin.	No pharmacokinetic or clinical case data reported. Potential for significant reduction given ethinyl estradiol and etonogestrel are major substrates of CYP3A4. Per CDC USMEC: "Evidence indicates that the combined hormonal patch and the combined vaginal ring provide comparable safety and pharmacokinetic profiles to COCs with similar hormone formulations. Pending further studies, the evidence available for recommendations about COCs applies to the recommendations for the combined hormonal patch and vaginal ring." Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	CDC US Medical Eligibility Criteria (US MEC) for Contraceptive Use
Segesterone/ Ethinyl Estradiol vaginal ring	Rifampin	↓ ethinyl estradiol concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifampin.	No pharmacokinetic or clinical case data reported. Potential for significant reduction given ethinyl estradiol and segesterone are major substrates of CYP3A4. Per CDC USMEC: "Evidence indicates that the combined hormonal patch and the combined vaginal ring provide comparable safety and pharmacokinetic profiles to COCs with similar hormone formulations. Pending further studies, the evidence available for recommendations about COCs applies to the recommendations for the combined hormonal patch and vaginal ring." Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	CDC US Medical Eligibility Criteria (US MEC) for Contraceptive Use

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Segesterone/ Ethinyl Estradiol vaginal ring	Rifapentine (once weekly dosing)	↓ ethinyl estradiol concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifapentine.	No pharmacokinetic or clinical case data reported. Potential for significant reduction given ethinyl estradiol and segesterone are major substrates of CYP3A4. Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	
	Rifabutin	↓ ethinyl estradiol concentration or efficacy expected	**Contraindicated, do not co-administer.** Use alternate method of contraception (e.g., condoms or IUD) if concomitant use is necessary. Alternate contraceptive method should be continued for 28 days after discontinuation of rifabutin.	No pharmacokinetic or clinical case data reported. Potential for significant reduction given ethinyl estradiol and segesterone are major substrates of CYP3A4. Per CDC USMEC: "Evidence indicates that the combined hormonal patch and the combined vaginal ring provide comparable safety and pharmacokinetic profiles to COCs with similar hormone formulations. Pending further studies, the evidence available for recommendations about COCs applies to the recommendations for the combined hormonal patch and vaginal ring." Do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	CDC US Medical Eligibility Criteria (US MEC) for Contraceptive Use

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Copper IUD	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No pharmacokinetic or clinical case data reported; however, contraceptive effect of copper IUD unlikely to be impacted by rifamycins.	
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No pharmacokinetic or clinical case data reported; however, contraceptive effect of copper IUD unlikely to be impacted by rifamycins.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No pharmacokinetic or clinical case data reported; however, contraceptive effect of copper IUD unlikely to be impacted by rifamycins.	
Levonorgestrel IUD	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	Drugs or herbal products that induce or inhibit LNG metabolizing enzymes, including CYP3A4, may decrease or increase, respectively, the serum concentrations of LNG during the use of Mirena. However, the contraceptive effect of Mirena is mediated via the direct release of LNG into the uterine cavity and is unlikely to be affected by drug interactions via enzyme induction or inhibition.	Package insert
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific data; recommendation based on rifampin and rifabutin data. Contraceptive effect of Mirena is mediated via the direct release of LNG into the uterine cavity and is unlikely to be affected by drug interactions via enzyme induction or inhibition.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	In an observational study of 56 Mirena users, only one Mirena failure was documented; this patient was also taking primidone and phenytoin. Rifabutin was included as one of the enzyme inducer drugs studied in the population, though no pregnancies were reported.	12396777

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected* ***or*** *possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected* ***or*** *possible*

Very low risk: Co-administer without modifications. **Low to medium risk:** Co-administer with caution. **Medium to high risk:** Co-administer with extreme caution if benefits outweigh risks. **Highest risk:** Contraindicated, do not co-administer.

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
CORTICOSTEROIDS					
Systemic **Betamethasone** **Prednisolone** **Prednisone** **Triamcinolone**	Rifampin	↓ steroid concentration or efficacy expected	⚠ **Co-administer with caution.** If co-administration necessary, monitor for reduced efficacy, consider dose increase.	Decreased prednisolone exposure with a 28-66% and 39-45% decrease in AUC and half-life, respectively; primarily due to CYP3A4 induction. Other studies of coadministration with carbamazepine, phenytoin or phenobarbital, show a 41-79% increase in clearance; numerous case reports of decrease prednisone/prednisolone effects with CYP3A4 inducers.	8276057 6349444 6403136 6880856 6878255 8018008 8290748 11273129 421090
	Rifapentine (once weekly dosing)	↓ steroid concentration or efficacy expected	⚠ **Co-administer with caution.** If co-administration necessary, monitor for reduced efficacy, consider dose increase.	No drug-specific data with these corticosteroids; potential reduction in corticosteroid exposure secondary to CYP3A4 induction (recommendation cites rifampin data, as well as studies with carbamazepine, phenytoin or phenobarbital co-administration).	
	Rifabutin	↓ steroid concentration or efficacy expected	⚠ **Co-administer with caution.** If co-administration necessary, monitor for reduced efficacy, consider dose increase.	No drug-specific data with these corticosteroids; potential reduction in corticosteroid exposure secondary to CYP3A4 induction (recommendation cites rifampin data, as well as studies with carbamazepine, phenytoin or phenobarbital co-administration).	
Inhaled/intranasal **Beclomethasone** **Budesonide** **Ciclesonide** **Fluticasone** **Mometasone**	Rifampin	No significant interaction expected	✓ **Co-administer without modifications**, no clinically significant interaction likely.		
	Rifapentine (once weekly dosing)	No significant interaction expected	✓ **Co-administer without modifications**, no clinically significant interaction likely.		
	Rifabutin	No significant interaction expected	✓ **Co-administer without modifications**, no clinically significant interaction likely.		

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected* ***or*** *possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected* ***or*** *possible*

✓ **Very low risk:** Co-administer without modifications. ⚠ **Low to medium risk:** Co-administer with caution. ! **Medium to high risk:** Co-administer with extreme caution if benefits outweigh risks. ✗ **Highest risk:** Contraindicated, do not co-administer.

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
DIABETES MEDICATIONS					
Metformin	Rifampin	↑ metformin concentration possible	**Co-administer without modifications**, no clinically significant interaction likely.	Study in TB-DM (TANDEM cohort): rifampin increases metformin exposure via inducing transporter (e.g., OCT1) expression (increased gut absorption). Metformin AUC increased by 28%. Glucose-lowering effect is minimal and likely not clinically significant. Potential increase GI effects when taken together (mostly nausea/vomiting). Study in healthy volunteers: rifampin yielded slight increase in metformin exposure with enhanced glucose-lowering effect after OGTT.	21270793 30222857 30606312
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with metformin. Significant reductions in drug exposure are not expected – extrapolated from rifampin data.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with metformin. Significant reductions in drug exposure are not expected – extrapolated from rifampin data.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
DPP-4 Inhibitors					
Linagliptin	Rifampin	↓ linagliptin concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. Consider use of alternative DPP-4 inhibitor as appropriate.	Linagliptin mostly renally excreted unchanged but in pharmacokinetic study, rifampin decreased linagliptin Cmax and AUC 44% and 40%, respectively.	Package Insert
	Rifapentine (once weekly dosing)	↓ linagliptin concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, consider close clinical and laboratory (blood glucose) monitoring.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with linagliptin. Reductions in drug exposure are possible but unknown – extrapolated from rifampin data.	
	Rifabutin	↓ linagliptin concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, consider close clinical and laboratory (blood glucose) monitoring.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with linagliptin. Reductions in drug exposure are possible but unknown – extrapolated from rifampin data.	

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Very low risk: Co-administer without modifications. **Low to medium risk:** Co-administer with caution. **Medium to high risk:** Co-administer with extreme caution if benefits outweigh risks. **Highest risk:** Contraindicated, do not co-administer.

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Saxagliptin	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	In a pharmacokinetic study, sitagliptin Cmax and AUC were reduced by 53% and 76%, respectively. But active metabolite, 5-hydroxy-saxagliptin (active metabolite) Cmax increased 39% while the AUC was not significantly altered. Plasma DPP-4 activity inhibition was not affected. Manufacturer doesn't recommend any dose adjustment given no change in active metabolite AUC and no effect on PD measure of DPP-4 inhibition.	21651615 Package Insert
		No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with saxagliptin. Significant reductions in drug exposure are not expected – extrapolated from rifampin data.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with saxagliptin. Significant reductions in drug exposure are not expected – extrapolated from rifampin data.	
Alogliptin **Sitagliptin**	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifampin co-administration with listed DPP-4 inhibitors. Significant reductions in drug exposure are not expected as these are mostly renally excreted or only minor CYP enzyme substrates.	20690781 Package Insert
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with listed DPP-4 inhibitors. Significant reductions in drug exposure are not expected as these are mostly renally excreted or only minor CYP enzyme substrates.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with listed DPP-4 inhibitors. Significant reductions in drug exposure are not expected as these are mostly renally excreted or only minor CYP enzyme substrates.	

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected* ***or*** *possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected* ***or*** *possible*

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Sulfonylureas **Gliclazide** **Glimepiride** **Glipizide** **Glyburide**	Rifampin	↓ sulfonylurea concentration or efficacy expected	**Co-administer with caution.** If co-administration necessary, consider close clinical and laboratory (blood glucose) monitoring. Adjust dose if needed or use/add alternative antihyperglycemic agent as appropriate.	In pharmacokinetic studies, rifampin has decreased the gliclazide AUC 70%, the glyburide AUC 39% to 63%, the glipizide AUC 22%, and the glimepiride AUC 34%; mechanism is likely via CYP2C9 induction. Clinical data consistent with potential loss of efficacy (glycemic control).	11136298 11406737 18843263 14534520 10937528 2510976 30606312 27516382
	Rifapentine (once weekly dosing)	↓ sulfonylurea concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, consider close clinical and laboratory (blood glucose) monitoring. Adjust dose if needed or use/add alternative antihyperglycemic agent as appropriate.	While there is no direct pharmacokinetic or clinical data, manufacturer of rifapentine states may need dose adjustment for CYP 3A4 or 2C9 substrates (which includes sulfonylureas) co-administered with rifapentine.	Package insert
	Rifabutin	↓ sulfonylurea concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, consider close clinical and laboratory (blood glucose) monitoring. Adjust dose if needed or use/add alternative antihyperglycemic agent as appropriate.	There is no pharmacokinetic or clinical data for co-administration with rifabutin. Rifabutin is a weak CYP2C9 inducer. Co-administration is an option with clinical and laboratory monitoring.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Thiazolidinedione **Pioglitazone** **Rosiglitazone**	Rifampin	↓ thiazolidinedione concentration or efficacy expected	**Co-administer with caution.** If co-administration necessary, consider close clinical and laboratory (blood glucose) monitoring. Dose adjust as needed based on reduced clinical effect (do not exceed 45 mg/day for pioglitazone).	Pharmacokinetic studies have observed decreased pioglitazone AUC by 54%; decreased rosiglitazone AUC by 65% - both via CYP2C8 induction.	16390353 15001966 15371985
	Rifapentine (once weekly dosing)	↓ thiazolidinedione concentration or efficacy possible	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with thiazolidinediones. Significant reductions in drug exposure are not expected – extrapolated from rifampin data.	
	Rifabutin	↓ thiazolidinedione concentration or efficacy possible	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with thiazolidinediones. Significant reductions in drug exposure are not expected – extrapolated from rifampin data.	
GLP-1 Receptor Agonists **Albiglutide** **Dulaglutide** **Exenatide** **Liraglutide** **Lixisenatide** **Semaglutide**	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	GLP-1 RA are peptides subject to degradation to amino acids by protein catabolism pathways.	
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	GLP-1 RA are peptides subject to degradation to amino acids by protein catabolism pathways.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	GLP-1 RA are peptides subject to degradation to amino acids by protein catabolism pathways.	

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected* ***or*** *possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected* ***or*** *possible*

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
SGL2 Inhibitors					
Canagliflozin	Rifampin	↓ canagliflozin concentration or efficacy expected	**Co-administer with caution.** If co-administration necessary, consider close clinical and laboratory (blood glucose) monitoring. Dosing increase likely necessary to maintain glycemic control. See "More Information" for dosing recommendations.	A pharmacokinetic study observed decreased canagliflozin AUC by 51% and Cmax by 28% - via induction of UGT enzymes. May result in decreased efficacy. *Per Canagliflozin package insert:* Increase dose to 200 mg daily in patients currently tolerating 100 mg daily. eGFR ≥60 – in patients requiring additional glycemic control, may increase dose to 300 mg daily in patients currently tolerating 200 mg daily. eGFR <60 – in patients requiring additional glycemic control, may consider adding an additional antihyperglycemic agent in patients receiving 200 mg daily.	Package insert 25407255
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with canagliflozin. Significant reductions in drug exposure are not expected – extrapolated from rifampin data.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with canagliflozin. Significant reductions in drug exposure are not expected – extrapolated from rifampin data.	
Dapagliflozin	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	Studies show a decrease in dapagliflozin AUC of 22%, Cmax of 7%, urinary glucose excretion of 10% but no dose adjustment required per manufacturer.	Package insert 23061428
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with dapagliflozin. Significant reductions in drug exposure are not expected – extrapolated from rifampin data.	
	Rifabutin	No significant interaction expecte	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with dapagliflozin. Significant reductions in drug exposure are not expected – extrapolated from rifampin data.	

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected or possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected or possible*

Very low risk: Co-administer without modifications. **Low to medium risk:** Co-administer with caution. **Medium to high risk:** Co-administer with extreme caution if benefits outweigh risks. **Highest risk:** Contraindicated, do not co-administer.

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Empagliflozin	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	Empagliflozin is a substrate of various transporters and non-CYP enzymes (OAT, P-gp, UGT). There is no clinical or pharmacokinetic data of multiple daily rifampin dosing; single dose rifampin increased AUC 35% and Cmax 75% likely via inhibition of OATP. There is no data for rifapentine or rifabutin. Minimal concern for significant interaction with any rifamycin and empagliflozin.	Package insert 24491572
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	Empagliflozin is a substrate of various transporters and non-CYP enzymes (OAT, P-gp, UGT). There is no clinical or pharmacokinetic data of multiple daily rifampin dosing; single dose rifampin increased AUC 35% and Cmax 75% likely via inhibition of OATP. There is no data for rifapentine or rifabutin. Minimal concern for significant interaction with any rifamycin and empagliflozin.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	Empagliflozin is a substrate of various transporters and non-CYP enzymes (OAT, P-gp, UGT). There is no clinical or pharmacokinetic data of multiple daily rifampin dosing; single dose rifampin increased AUC 35% and Cmax 75% likely via inhibition of OATP. There is no data for rifapentine or rifabutin. Minimal concern for significant interaction with any rifamycin and empagliflozin.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Ertugliflozin	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a decrease in ertugliflozin AUC of 39% and Cmax of 15% likely via UGT induction - not considered clinically relevant per manufacturer and dose-response model.	Package insert 30170758
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with ertugliflozin. Significant reductions in drug exposure are not expected (not known inducer of UGT) – extrapolated from rifampin data.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with ertugliflozin. Significant reductions in drug exposure are not expected (not known inducer of UGT) – extrapolated from rifampin data.	
DIURETICS					
Hydrochlorothiazide	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	Hydrochlorothiazide is not metabolized hepatically, a majority is excreted unchanged in the urine. Although no clinical data are present, no interaction is anticipated.	NBK430766
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	Hydrochlorothiazide is not metabolized hepatically, a majority is excreted unchanged in the urine. Although no clinical data are present, no interaction is anticipated.	NBK430766
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	Hydrochlorothiazide is not metabolized hepatically, a majority is excreted unchanged in the urine. Although no clinical data are present, no interaction is anticipated.	NBK430766

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Furosemide	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	This drug is minimally metabolized hepatically. Majority is excreted unchanged in the urine along with glucuronidation pathway (UGT1A9) mainly in the kidneys. Although no clinical data are present, no significant interaction is anticipated.	Package insert 33237382 18541222
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	This drug is minimally metabolized hepatically. Majority is excreted unchanged in the urine along with glucuronidation pathway (UGT1A9) mainly in the kidneys. Although no clinical data are present, no significant interaction is anticipated.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	This drug is minimally metabolized hepatically. Majority is excreted unchanged in the urine along with glucuronidation pathway (UGT1A9) mainly in the kidneys. Although no clinical data are present, no significant interaction is anticipated.	
ERECTILE DYSFUNCTION MEDICATIONS					
Sildenafil	Rifampin	↓ sildenafil concentration or efficacy expected	**Co-administer with caution** for indication of erectile dysfunction. If co-administration necessary, monitor for decreased sildenafil effects. For other indications including pulmonary arterial hypertension, **co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	Rifampin (strong CYP3A4 inducer) may decrease the serum concentration of sildenafil. No studies have evaluated the effects of strong CYP3A4 inducers on sildenafil. However, in a study of healthy male volunteers, the moderate CYP3A4 inducer bosentan (125 mg twice daily) decreased the sildenafil (80 mg 3 times daily) AUC and Cmax 63% and 55%, respectively.	Package Insert

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected or possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected or possible*

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Sildenafil	Rifapentine (once weekly dosing)	↓ sildenafil concentration or efficacy possible	**Co-administer with caution** for indication of erectile dysfunction. If co-administration necessary, monitor for decreased sildenafil effects. For other indications including pulmonary arterial hypertension, **co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	Rifapentine (moderate CYP3A4 inducer) may decrease the serum concentration of sildenafil.	
	Rifabutin	↓ sildenafil concentration or efficacy possible	**Co-administer with caution** for indication of erectile dysfunction. If co-administration necessary, monitor for decreased sildenafil effects. For other indications including pulmonary arterial hypertension, **co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	Rifabutin (moderate CYP3A4 inducer) may decrease the serum concentration of Sildenafil.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Tadalafil	Rifampin	↓ tadalafil concentration or efficacy expected	**Co-administer with caution** for indication of erectile dysfunction. If co-administration necessary, monitor for decreased tadalafil effects. For other indications including pulmonary arterial hypertension, **contraindicated, do not co-administer.**	Rifampin (strong CYP3A4 inducer) may decrease the serum concentration of tadalafil. In a pharmacokinetic study, co-administration of rifampin 600 mg daily decreased tadalafil AUC and Cmax by 88% and 46%, respectively. For indication of pulmonary hypertension, do not co-administer recommendation made because co-administration may render this drug ineffective, and because of potentially serious or life-threatening consequence; patient safety cannot be guaranteed even with monitoring or dose titration.	18305126 31222765 28494463 27038140 24872209
	Rifapentine (once weekly dosing)	↓ tadalafil concentration or efficacy possible	**Co-administer with caution** for indication of erectile dysfunction. If co-administration necessary, monitor for decreased tadalafil effects. For other indications including pulmonary arterial hypertension, **co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	Rifapentine (moderate CYP3A4 inducer) may decrease the serum concentration tadalafil.	18305126 31222765 28494463 27038140 24872209

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Tadalafil	Rifabutin	↓ tadalafil concentration or efficacy possible	**Co-administer with caution** for indication of erectile dysfunction. If co-administration necessary, monitor for decreased tadalafil effects. For other indications including pulmonary arterial hypertension, **co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	Rifabutin (moderate CYP3A4 inducer) may decrease the serum concentration tadalafil.	18305126 31222765 28494463 27038140 24872209

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected or possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected or possible*

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Avanafil	Rifampin	↓ avanafil concentration or efficacy expected	**Contraindicated, do not co-administer.**	Avanafil metabolism occurs primarily through the CYP3A4 pathway and use with CYP3A4 inducers is expected to reduce avanafil concentrations and effects. Implications of inactive avanafil may not be serious or life-threatening. However, co-administration with rifampin may render this drug ineffective due to major reduction in drug levels, and dosage changes will likely not overcome this interaction.	Package insert
	Rifapentine (once weekly dosing)	↓ avanafil concentration or efficacy expected	**Contraindicated, do not co-administer.**	Avanafil metabolism occurs primarily through the CYP3A4 pathway and use with CYP3A4 inducers is expected to reduce avanafil concentrations and effects. Implications of inactive avanafil may not be serious or life-threatening. However, co-administration with rifapentine may render this drug ineffective due to major reduction in drug levels, and dosage changes will likely not overcome this interaction.	
	Rifabutin	↓ avanafil concentration or efficacy expected	**Contraindicated, do not co-administer.**	Avanafil metabolism occurs primarily through the CYP3A4 pathway and use with CYP3A4 inducers is expected to reduce avanafil concentrations and effects. Implications of inactive avanafil may not be serious or life-threatening. However, co-administration with rifabutin may render this drug ineffective due to major reduction in drug levels, and dosage changes will likely not overcome this interaction.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Vardenafil	Rifampin	↓ vardenafil concentration or efficacy possible	**Co-administer with caution** for indication of erectile dysfunction. If co-administration necessary, monitor for decreased vardenafil effects. For other indications including pulmonary arterial hypertension, **co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	No drug-specific data; recommendation is based on rifampin and sildenafil interaction data, as well as efavirenz (moderate CYP inducer) and vardenafil interaction data.	
	Rifapentine (once weekly dosing)	↓ vardenafil concentration or efficacy possible	**Co-administer with caution** for indication of erectile dysfunction. If co-administration necessary, monitor for decreased vardenafil effects. For other indications including pulmonary arterial hypertension, **co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	No drug-specific data; recommendation is based on rifampin and sildenafil interaction data, as well as efavirenz (moderate CYP inducer) and vardenafil interaction data.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Vardenafil	Rifabutin	↓ vardenafil concentration or efficacy possible	**Co-administer with caution** for indication of erectile dysfunction. If co-administration necessary, monitor for decreased vardenafil effects. For other indications including pulmonary arterial hypertension, **co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended.	No drug-specific data; recommendation is based on rifampin and sildenafil interaction data, as well as efavirenz (moderate CYP inducer) and vardenafil interaction data.	
HEPATITIS B ANTIVIRALS					
Tenofovir disoproxil fumarate (TDF) and **Tenofovir alafenamide (TAF)** *only*	Rifampin	**Refer to DHHS Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV, Drug-Drug Interactions tables** (click here for overview page) • Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) – click here • Note that TDF has no need for dose adjustment when used with rifamycins			
	Rifapentine (once weekly dosing)				
	Rifabutin				
HEPATITIS C ANTIVIRALS					
Ledipasvir/ Sofosbuvir **Sofosbuvir/ Velpatasvir** **Glecaprevir/ Pibrentasvir** **Elbasvir/ Grazoprevir**	Rifampin	Due to significant interactions within this drug class, as well as the limited duration of both HCV and LTBI therapies, we recommend sequential treatment, rather than concurrent therapy.			
	Rifapentine (once weekly dosing)				
	Rifabutin				

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected or possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected or possible*

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
IMMUNOSUPPRESSANTS					
Cyclosporine **Everolimus** **Sirolimus** **Tacrolimus**	Rifampin Rifapentine (once weekly dosing) Rifabutin	Due to significant interactions within this drug class, as well as clinical importance of immunosuppressant therapies, we recommend input from clinical pharmacist and transplant team if concurrent use is needed.			
NEUROPATHIC AGENTS					
Gabapentin	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; no expected interaction based on metabolic pathway.	
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; no expected interaction based on metabolic pathway.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; no expected interaction based on metabolic pathway.	
Pregabalin	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; no expected interaction based on metabolic pathway.	
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; no expected interaction based on metabolic pathway.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; no expected interaction based on metabolic pathway.	

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
OPIOIDS					
WARNING: Discontinuation of a concomitantly used CYP3A4 inducer, such as a rifamycin, may result in an increase in opioid drug plasma concentration, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression. Close monitoring is required when discontinuing a rifamycin and managing probable need for opioid dose reduction as a result of CYP3A4 de-induction. See page 3 for additional important information on timing.					
Hydrocodone	Rifampin	↓ hydrocodone concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for decreased effects and withdrawal symptoms; if rifampin is discontinued, extremely important to monitor for respiratory depression and consider a hydrocodone dose reduction until stable drug effects are achieved.	No drug-specific data with hydrocodone; potential reduction in hydrocodone exposure secondary to CYP3A4 induction.	
	Rifapentine (once weekly dosing)	↓ hydrocodone concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for decreased effects and withdrawal symptoms; if rifapentine is discontinued, extremely important to monitor for respiratory depression and consider a hydrocodone dose reduction until stable drug effects are achieved.	No drug-specific data with hydrocodone; potential reduction in hydrocodone exposure secondary to CYP3A4 induction.	
	Rifabutin	↓ hydrocodone concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for decreased effects and withdrawal symptoms; if rifabutin is discontinued, extremely important to monitor for respiratory depression and consider a hydrocodone dose reduction until stable drug effects are achieved.	No drug-specific data with hydrocodone; potential reduction in hydrocodone exposure secondary to CYP3A4 induction.	

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected or possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected or possible*

Very low risk: Co-administer without modifications. **Low to medium risk:** Co-administer with caution. **Medium to high risk:** Co-administer with extreme caution if benefits outweigh risks. **Highest risk:** Contraindicated, do not co-administer.

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Oxycodone	Rifampin	↓ oxycodone concentration or efficacy expected	⚠ **Co-administer with caution.** If co-administration necessary, monitor for decreased effects and withdrawal symptoms; if rifampin is discontinued, extremely important to monitor for respiratory depression and consider an oxycodone dose reduction until stable drug effects are achieved.	Co-administration of rifampin significantly decreased the AUC values of 0.1 mg/kg IV and oral oxycodone 15 mg by 53% and 86%, respectively, reduced oral bioavailability of oxycodone from 69% to 21%.	28579821
	Rifapentine (once weekly dosing)	↓ oxycodone concentration or efficacy possible	⚠ **Co-administer with caution.** If co-administration necessary, monitor for decreased effects and withdrawal symptoms; if rifapentine is discontinued, extremely important to monitor for respiratory depression and consider a oxycodone dose reduction until stable drug effects are achieved.	No drug-specific data with oxycodone; potential reduction in oxycodone exposure secondary to CYP3A4 induction.	
	Rifabutin	↓ oxycodone concentration or efficacy possible	⚠ **Co-administer with caution.** If co-administration necessary, monitor for decreased effects and withdrawal symptoms; if rifabutin is discontinued, extremely important to monitor for respiratory depression and consider an oxycodone dose reduction until stable drug effects are achieved.	No drug-specific data with oxycodone; potential reduction in oxycodone exposure secondary to CYP3A4 induction.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Tramadol	Rifampin	↓ tramadol concentration or efficacy expected	⚠ **Co-administer with caution.** If co-administration necessary, monitor for decreased effects and withdrawal symptoms; if rifampin is discontinued, extremely important to monitor for respiratory depression, seizures, and serotonin toxicity and consider a tramadol dose reduction until stable drug effects are achieved.	Rifampicin significantly decreased the exposure to tramadol and active metabolite by 43%–59% after both oral and IV administration, increased the clearance of IV tramadol by 67%, and reduced bioavailability of oral tramadol from 66% to 49%.	28579821
	Rifapentine (once weekly dosing)	↓ tramadol concentration or efficacy possible	⚠ **Co-administer with caution.** If co-administration necessary, monitor for decreased effects and withdrawal symptoms; if rifapentine is discontinued, extremely important to monitor for respiratory depression, seizures, and serotonin toxicity and consider a tramadol dose reduction until stable drug effects are achieved.	No drug-specific data with tramadol; potential reduction in tramadol exposure secondary to CYP3A4 induction.	
	Rifabutin	↓ tramadol concentration or efficacy possible	⚠ **Co-administer with caution.** If co-administration necessary, monitor for decreased effects and withdrawal symptoms; if rifabutin is discontinued, extremely important to monitor for respiratory depression, seizures, and serotonin toxicity and consider a tramadol dose reduction until stable drug effects are achieved.	No drug-specific data with tramadol; potential reduction in tramadol exposure secondary to CYP3A4 induction.	

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected* ***or*** *possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected* ***or*** *possible*
✓ **Very low risk:** Co-administer without modifications. ⚠ **Low to medium risk:** Co-administer with caution. ! **Medium to high risk:** Co-administer with extreme caution if benefits outweigh risks. ✗ **Highest risk:** Contraindicated, do not co-administer.

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
OPIOID USE DISORDER THERAPY					
Buprenorphine	Rifampin	↓ buprenorphine concentration or efficacy expected	**Co-administer with caution.** If co-administration necessary, monitor for decreased buprenorphine effects (e.g., pain, opioid withdrawal). Buprenorphine dose increase may be needed.	Concomitant use of buprenorphine and CYP3A4 inducers may decrease plasma concentrations and lead to opioid withdrawal symptoms. In a pharmacokinetic study, co-administration of rifampin 600mg daily produced a 70% reduction in AUC and onset of opiate withdrawal symptoms. Most participants experienced resolution of withdrawal with a buprenorphine dose increase of 25–50%. These increased doses remained within the dose range approved by the FDA for this drug (up to 24 mg daily).	21596492
	Rifapentine (once weekly dosing)	↓ buprenorphine concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for decreased buprenorphine effects (e.g., pain, opioid withdrawal). Buprenorphine dose increase may be needed.	No direct pharmacokinetic studies with buprenorphine; potential reduction in buprenorphine exposure secondary to CYP3A4 induction.	
	Rifabutin	↓ buprenorphine concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, monitor for decreased buprenorphine effects (e.g., pain, opioid withdrawal). Buprenorphine dose increase may be needed.	Concomitant use of buprenorphine and CYP3A4 inducers may decrease plasma concentrations and lead to opioid withdrawal symptoms. In a pharmacokinetic study, co-administration of rifabutin 300 mg daily decreased buprenorphine AUC by 35% but did not precipitate opioid withdrawal.	21596492

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected* ***or*** *possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected* ***or*** *possible*

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Methadone	Rifampin	↓ methadone concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If co-administration necessary, monitor for decreased methadone effects (e.g., pain, opioid withdrawal). Methadone dose increase may be needed. If rifampin is discontinued, extremely important to monitor for respiratory depression and consider a methadone dose reduction until stable drug effects are achieved.	Rifampin decreased bioavailability and plasma concentrations of methadone, and increased oral (1.7-fold) and IV (3.2-fold) clearance. Pharmacokinetic models predict need for dose increases of methadone during rifampin treatment due to reductions in methadone drug levels. Clinical cases of patient experiencing withdrawal symptoms have been reported.	28579821 31122724 68314 2286719 8876100
	Rifapentine (once weekly dosing)	↓ methadone concentration or efficacy possible	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If co-administration necessary, monitor for decreased methadone effects (e.g., pain, opioid withdrawal). Methadone dose increase may be needed. If rifampin is discontinued, extremely important to monitor for respiratory depression and consider a methadone dose reduction until stable drug effects are achieved.	No drug-specific data with methadone; potential reduction in methadone exposure secondary to CYP3A4 induction.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Methadone	Rifabutin	↓ methadone concentration or efficacy expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. If co-administration necessary, monitor for decreased methadone effects (e.g., pain, opioid withdrawal). Methadone dose increase may be needed. If rifampin is discontinued, extremely important to monitor for respiratory depression and consider a methadone dose reduction until stable drug effects are achieved.	Rifabutin in persons living with HIV who formerly used IV drugs showed that while there were no significant differences in peak concentrations or AUC of methadone when co-administered with rifabutin, 75% of patients experienced at least one symptom of opioid withdrawal; however, symptoms were mild. Concurrent administration of rifabutin and methadone appeared to be safe in HIV infected former injecting drug users maintained on stable doses of methadone.	8957145
Naltrexone	Rifampin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; no expected interaction based on metabolic pathway.	
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; no expected interaction based on metabolic pathway.	
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	No drug-specific information; no expected interaction based on metabolic pathway.	

Key: See page 4 **for full description.** ↓ = **decrease** [drug name] concentration or efficacy *expected* ***or*** *possible* ↑ = **increase** [drug name] concentration or toxicity risk *expected* ***or*** *possible*

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Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
STATINS					
Lovastatin **Simvastatin**	Rifampin	↓ statin concentration or efficacy expected	**Co-administer with caution.** If co-administration necessary, consider close clinical and laboratory monitoring for decreased statin effect and adjust dose as needed. Consider increasing statin dose or switching to alternative statin (e.g., atorvastatin or rosuvastatin) if appropriate.	Pharmacokinetic studies in 10 healthy volunteers taking rifampin 600 mg daily for 5 days then a single 40 mg dose of simvastatin on day 6, saw that rifampin reduced simvastatin's AUC by 87%. This is likely due to induction of the CYP3A4 mediated first-pass metabolism of simvastatin in the intestine and the liver causing lower bloodstream drug concentration. No pharmacokinetic studies on rifampin effect on OATP1B1/1B3 in individuals taking simvastatin. No pharmacokinetic data with lovastatin, however given lovastatin is a major CYP3A4 substrate like simvastatin, its drug concentration is likely similarly affected by rifampin.	11180018
	Rifapentine (once weekly dosing)	↓ statin concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, consider close clinical and laboratory monitoring for decreased statin effect and adjust dose as needed.	There are no direct pharmacokinetic or clinical studies evaluating co-administration of these agents. Rifapentine and rifabutin are both considered moderate CYP3A4 inducers and may reduce drug levels of these statin agents.	
	Rifabutin	↓ statin concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, consider close clinical and laboratory monitoring for decreased statin effect and adjust dose as needed.	There are no direct pharmacokinetic or clinical studies evaluating co-administration of these agents. Rifapentine and rifabutin are both considered moderate CYP3A4 inducers and may reduce drug levels of these statin agents.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Atorvastatin	Rifampin	↓ or ↑ statin concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, consider administration schedule as recommended in "More Information."	If initiating rifampin in person already on atorvastatin: • Recommend holding atorvastatin for 5-7 days, then restart at regular dose. When resuming atorvastatin, atorvastatin and rifampin should be administered together simultaneously based on pharmacokinetic studies. If initiating statin in person already on rifampin (at steady state): • No dose adjustment needed. Atorvastatin and rifampin should be administered together simultaneously based on pharmacokinetic studies. Pharmacokinetic studies evaluating co-administration of these two agents found these outcomes: • A single dose of rifampin 600 mg IV co-administered with atorvastatin 40 mg caused atorvastatin and its metabolites' plasma concentration to be elevated for up to 24 h after dosing. Rifampin significantly increased AUC of atorvastatin acid by 6.8-fold due to significant reduction in atorvastatin's hepatobiliary elimination mediated by hepatic transporters (OATP1B1). Rifampin inhibits OATP transporter and this inhibition occurs rapidly (and does not appear to be sustained) compared to CYP induction which is delayed. • In a study with volunteers who took 600 mg rifampin once daily for 5 days, and a single 40-mg dose of atorvastatin on day 6 (not administered simultaneously), rifampin reduced the AUC of unchanged atorvastatin and its metabolites by 80% and 43% - 81% respectively. This effect is likely due to CYP3A4 induction. However, with simultaneous administration of atorvastatin and rifampin, atorvastatin AUC was increased by 30% (not considered clinically significant).	17192770 32705692 16084850

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Atorvastatin	Rifapentine (once weekly dosing)	↓ statin concentration or efficacy possible	**Co-administer with caution**. If co-administration necessary, consider close clinical and laboratory monitoring for decreased statin effect and adjust dose as needed.	No direct pharmacokinetic studies with atorvastatin; potential reduction in atorvastatin exposure secondary to CYP3A4 induction (recommendation cites pharmacokinetic studies of co-administration with moderate CYP3A4 inducing agents like efavirenz, bexarotene and St. John's wort where they found atorvastatin AUC to be 43% lower when atorvastatin (10 mg/day) was co-administered for 4 days with efavirenz (600 mg/day for 15 days). Rifapentine and rifabutin are both considered moderate CYP3A4 inducers and may reduce drug levels of these statin agents.	15980690 22057855 17701167
	Rifabutin	↓ statin concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, consider close clinical and laboratory monitoring for decreased statin effect and adjust dose as needed.	No direct pharmacokinetic studies with atorvastatin; potential reduction in atorvastatin exposure secondary to CYP3A4 induction (recommendation cites pharmacokinetic studies of co-administration with moderate CYP3A4 inducing agents like efavirenz, bexarotene and St. John's wort where they found atorvastatin AUC to be 43% lower when atorvastatin (10 mg/day) was co-administered for 4 days with efavirenz (600 mg/day for 15 days). Rifapentine and rifabutin are both considered moderate CYP3A4 inducers and may reduce drug levels of these statin agents.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Pravastatin **Rosuvastatin**	Rifampin	↓ or ↑ statin concentration or efficacy possible	⚠ **Co-administer with caution.** If co-administration necessary, consider administration schedule as recommended in "More Information."	If initiating rifampin in person already on rosuvastatin or pravastatin: • Recommend holding statin for 5-7 days, then restart at regular dose. If initiating statin in person already on rifampin (at steady state): • No dose adjustment needed. Monitor clinical response and make adjustment to statin dose as needed. Single dose rifampin (600 mg) co-administered with single dose rosuvastatin (100 mcg) increased the rosuvastatin AUC and Cmax by 3.1-3.9 fold and 8.5 -10.9 fold, respectively. This is likely due to OATP1 inhibition by rifampin. A pharmacokinetic study found rifampin (600 mg daily) decreased the rosuvastatin (10 mg single dose) AUC and Cmax 63% and 30%, respectively. Another study in 18 healthy volunteers found rifampin (450 mg daily) for 6 days had variable effect on rosuvastatin (20 mg single dose), with 8 subjects experiencing slight increase in rosuvastatin AUC (majority had increase of <30%; not considered clinically significant) and 10 experiencing a slight decrease (majority <30%) in AUC. Pharmacokinetics of rosuvastatin were not significantly changed by co-administration of rifampin. One study found co-administration of a single rifampin 600 mg dose increased pravastatin's mean AUC by 127% and decreased its oral clearance by 60% compared to placebo likely due to OATP1B1 inhibition. In a study with 10 healthy volunteers who received a 5-day pretreatment with rifampicin (600 mg daily) and single 40 mg dose of pravastatin on day 6, AUC and Cmax were reduced by 31% and 21%, respectively (not clinically significant).	29569723 32705692 18691987 19695392 29569723 14748817

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Pravastatin **Rosuvastatin**	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with rosuvastatin or pravastatin. Significant reductions in drug exposure are not expected – extrapolated from rifampin data. In vitro studies demonstrate rifapentine may be an inhibitor of OATP1B1 but significantly less potent than rifampin.	24060875 26976869
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with rosuvastatin or pravastatin. Significant reductions in drug exposure are not expected – extrapolated from rifampin data. In vitro studies demonstrate rifabutin may be an inhibitor of OATP1B1 but significantly less potent than rifampin.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Pitavastatin	Rifampin	↑ statin concentration expected	**Co-administer with extreme caution if benefits outweigh risks.** Input from a clinical pharmacist or subspecialist recommended. Consider use of alternative statin as appropriate. Avoid dosing pitavastatin and rifampin at the same time. If concurrent therapy is required, lower the first dose of pitavastatin. Limit pitavastatin dose to a maximum of 2 mg/day with concurrent rifampin use.	Pitavastatin plasma concentration monitoring and dose adjustments may be required with long-term therapy. Pitavastatin AUC and max concentration were increased by an average of 1.3- and 2-fold, respectively, when pitavastatin (4 mg daily) and rifampin (600 mg daily) were co-administered for 5 days. Pitavastatin disposition is largely dependent on uptake transporter (OATP1B1), and rifampin is a known OATP1B1 inhibitor, resulting in increased pitavastatin concentration. Also, pitavastatin does not undergo metabolism by CYP3A4 enzymes and thus is not affected by CYP3A4 induction by rifampin.	18408565 15159445
	Rifapentine (once weekly dosing)	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifapentine co-administration with pitavastatin. Significant reductions in drug exposure are not expected – extrapolated from rifampin data. In vitro studies demonstrate rifapentine may be an inhibitor of OATP1B1 but significantly less potent than rifampin.	24060875 26976869
	Rifabutin	No significant interaction expected	**Co-administer without modifications**, no clinically significant interaction likely.	There is a lack of pharmacokinetic or clinical case data reported for rifabutin co-administration with pitavastatin. Significant reductions in drug exposure are not expected – extrapolated from rifampin data. In vitro studies demonstrate rifabutin may be an inhibitor of OATP1B1 but significantly less potent than rifampin.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
Fluvastatin	Rifampin	↓ or ↑ statin concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, consider administration schedule as recommended in "More Information."	If initiating rifampin in person already on fluvastatin: • Recommend holding statin for 5-7 days, then restart at regular dose. Adjust dose based on clinical response (e.g., lipid panel levels) and tolerance. If initiating statin in person already on rifampin (at steady state): • No dose adjustment needed. May adjust/ increase dose based on clinical response (e.g., lipid panel levels) and tolerance. Single dose rifampin (300 mg or 600 mg) co-administered with single dose fluvastatin (20 mg) increased the fluvastatin AUC 2.2-fold to 2.6-fold and increased the Cmax 2-fold to 2.9-fold likely due to rifampin-mediated inhibition of OATP1B1/1B3. Another pharmacokinetic study found rifampin (600 mg daily for 6 days) decreased the fluvastatin (20 mg single dose) AUC and Cmax 53% and 42%, respectively. Rifampin-mediated induction of CYP2C9, and possibly CYP3A4 is likely responsible for reduced fluvastatin concentrations with prolonged co-administration.	8198019 29748935 33880760
	Rifapentine (once weekly dosing)	↓ statin concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, consider close clinical and laboratory monitoring for decreased statin effect and adjust dose as needed.	No direct pharmacokinetic studies done, but fluvastatin is a CYP2C9 substrate and rifapentine has been shown to induce CYP2C9 in vitro. Also because rifapentine is structurally related to rifampin, a known CYP2C9 inducer, prescribing information warns that rifapentine may reduce concentrations and effects of CYP2C9 substrates. Rifabutin is a weak CYP2C9 inducer and may reduce statin levels but likely not to a significant extent.	9402947 35152432
	Rifabutin	↓ statin concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, consider close clinical and laboratory monitoring for decreased statin effect and adjust dose as needed.	No direct pharmacokinetic studies done, but fluvastatin is a CYP2C9 substrate and rifapentine has been shown to induce CYP2C9 in vitro. Also because rifapentine is structurally related to rifampin, a known CYP2C9 inducer, prescribing information warns that rifapentine may reduce concentrations and effects of CYP2C9 substrates. Rifabutin is a weak CYP2C9 inducer and may reduce statin levels but likely not to a significant extent.	

Concomitant Drug or Drug Class	Rifamycin	Interaction	Recommendations and Clinical Comments	More information	References and Pubmed ID
THYROID MEDICATIONS					
Levothyroxine	Rifampin	↓ levothyroxine concentration or efficacy possible	**Co-administer with caution.** If co-administration necessary, consider monitoring TSH every 4-8 weeks and adjusting levothyroxine dose following initiation and cessation of rifampin.	Concentrations of levothyroxine have mostly been reported as decreased in clinical data/case reports. A single study of eight participants reported increased levothyroxine levels after a single dose of rifampin (600 mg), the clinical significance of this study is unclear. The mechanism for rifampin altering thyroid hormone concentrations is uncertain, but evidence suggests that increased levothyroxine metabolism is at least partially responsible.	10342905 16957414 6800809 3584854
	Rifapentine (once weekly dosing)	↓ levothyroxine concentration or efficacy possible	**Co-administer with caution**, although clinically significant interaction is unlikely. Consider checking a single TSH 4-8 weeks after rifapentine initiation.	No drug-specific data; because the mechanism for rifampin altering thyroid hormone concentrations is uncertain, it is difficult to extrapolate from rifampin data.	
	Rifabutin	↓ levothyroxine concentration or efficacy possible	**Co-administer with caution**, although clinically significant interaction is unlikely. Consider checking a single TSH 4-8 weeks after rifabutin initiation.	No drug-specific data; because the mechanism for rifampin altering thyroid hormone concentrations is uncertain, it is difficult to extrapolate from rifampin data.	