Resource: ART Drug-Drug Interactions

April 2023

Table 44: Rifamycins and Other Antituberculosis Medications (also see drug package inserts)		
→ Rifampin, rifabutin, rifapentine [a]; isoniazid [b], pyrazinamide [b], ethambutol [b], rifaximin [b]		
Class or Drug	**Mechanism of Action**	**Clinical Comments**
• Emtricitabine (FTC) • Lamivudine (3TC) • Tenofovir disoproxil fumarate (TDF)	No clinically significant interactions are expected.	No dose adjustments are necessary.
Abacavir (ABC)	• **Rifabutin, rifapentine:** No clinically significant interactions are expected. • **Rifampin** may reduce ABC concentrations.	• **Rifabutin, rifapentine:** No dose adjustments are necessary. • **Rifampin:** No dose adjustments are recommended for concomitant use with ABC.
Tenofovir alafenamide (TAF)	• **Rifabutin:** CYP3A and P-gP induction is expected to decrease TAF levels. • **Rifampin, rifapentine:** CYP3A induction may reduce TAF concentrations.	• **Rifampin:** Do not coadminister with TAF; consider TDF as alternative. • **Rifabutin, rifapentine:** Do not coadminister with TAF unless benefit outweighs risk; monitor closely for virologic response.
Doravirine (DOR)	• **Rifabutin:** CYP3A induction is expected to decrease DOR levels. • **Rifampin, rifapentine:** CYP3A induction reduces DOR bioavailability.	• **Rifabutin:** When used concomitantly, increase DOR to 100 mg twice per day. • **Rifampin, rifapentine:** – Concomitant use is contraindicated. – After stopping rifampin or rifapentine, wait 4 weeks before starting DOR.
Efavirenz (EFV)	• **Rifabutin:** EFV induction of CYP3A reduces rifabutin bioavailability, but coadministration does not affect EFV levels. • **Rifampin, rifapentine**: No clinically significant interactions are expected.	• **Rifabutin:** With concomitant EFV, dose rifabutin at 450 mg to 600 mg daily. • **Rifampin:** – Dose EFV at 600 mg daily when administered concomitantly. – Do not use EFV 400 mg daily. • **Rifapentine:** No dose adjustments are necessary.
Etravirine (ETR)	• **Rifabutin:** When used concomitantly, increased rifabutin levels are expected and decreased ETR levels may occur. • **Rifampin, rifapentine:** CYP3A induction reduces ETR bioavailability.	• **Rifabutin:** – If ETR and rifabutin are used concomitantly, dose rifabutin 300 mg daily, with no changes to ETR dose. Continue rifabutin 300 mg daily dosing until at least 2 weeks after rifabutin is stopped. – Concomitant use of boosted PI with ETR and rifabutin is contraindicated. • **Rifampin, rifapentine:** Concomitant use is contraindicated.

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Class or Drug	**Mechanism of Action**	**Clinical Comments**
Nevirapine (NVP)	• **Rifabutin:** No clinically significant interactions are expected. • **Rifampin, rifapentine:** Coadministration reduces NVP concentrations.	• **Rifabutin:** No dose adjustments are necessary. • **Rifampin, rifapentine:** Do not coadminister.
Rilpivirine (RPV)	**Rifabutin, rifampin, rifapentine:** Coadministration may significantly reduce RPV concentrations through induction of CYP450, UGT1A, and/or P-gP systems.	• **Rifabutin:** – Oral RPV: Increase RPV dose to 50 mg once daily [DHHS 2021]. – Injectable RPV: Concomitant use is contraindicated. • **Rifampin, rifapentine:** Concomitant use with oral and injectable RPV is contraindicated [FDA(b) 2021].
All PIs and boosted PIs	• **Rifabutin** does not affect boosted PI levels, but when used concomitantly, bioavailability of rifabutin and its active metabolite is increased. • **Rifampin, rifapentine:** CYP3A induction reduces bioavailability of *all* PIs.	• **Rifabutin:** – RTV-boosted PIs: When used concomitantly, reduce rifabutin to 150 mg 3 times per week. – COBI-boosted PIs: Do not coadminister. • **Rifampin, rifapentine:** Concomitant use of PIs and rifampin or rifapentine is contraindicated.
Bictegravir (BIC)	• **Rifabutin:** CYP3A and P-gP induction decreases BIC levels. • **Rifampin, rifapentine:** CYP3A induction reduces bioavailability.	• **Rifampin:** Concomitant use is contraindicated. • **Rifabutin, rifapentine:** Concomitant use is not recommended [FDA(a) 2021].
Cabotegravir (CAB)	• **Rifabutin, rifampin, rifapentine:** Coadministration may significantly reduce CAB concentrations through induction of CYP450, UGT1A, and/or P-gP system.	• **Rifampin, rifapentine:** Concomitant use is contraindicated with *oral* CAB. • **Rifabutin:** May be used with *oral* CAB without dosage adjustment. • **Rifabutin, rifampin, rifapentine:** Concomitant use is contraindicated with *injectable* CAB [FDA(b) 2021].
Dolutegravir (DTG)	• **Rifabutin:** No clinically significant interactions expected. • **Rifampin:** CYP3A induction reduces DTG bioavailability. • **Rifapentine:** Reduced rifapentine levels are expected.	• **Rifabutin:** No dose adjustments are necessary. • **Rifampin:** When used concomitantly, dose DTG at 50 mg twice per day instead of 50 mg once per day in patients without suspected or documented INSTI-associated resistance mutations. Consider rifabutin in patients with INSTI resistance. • **Rifapentine, once weekly:** – If using concomitant DTG 50 mg once daily, monitor for virologic efficacy. – Do not coadminister with DTG 50 mg twice daily. • **Rifapentine, once daily:** Do not coadminister.
Elvitegravir (EVG), boosted	• **Rifabutin:** CYP3A induction is expected to decrease EVG levels. • **Rifampin, rifapentine:** CYP3A induction reduces EVG bioavailability.	• **Rifabutin:** Concomitant use is not recommended. When concomitant use cannot be avoided, dose rifabutin at 150 mg 3 times per week and monitor for response to EVG-containing regimen. • **Rifampin, rifapentine:** Concurrent use with boosted EVG is not recommended.

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Raltegravir (RAL)	• **Rifabutin:** No clinically significant interactions are expected. • **Rifampin:** CYP3A induction reduces RAL bioavailability. • **Rifapentine:** Induction of metabolism may reduce RAL metabolism.	• **Rifabutin:** No dose adjustments are necessary. • **Rifampin:** – When used concomitantly, dose RAL at 800 mg twice per day instead of 400 mg twice per day. – Do not use RAL HD. • **Rifapentine:** – For 900 mg once-weekly rifapentine and RAL 400 mg twice daily, no dose adjustments are necessary. – Do not coadminister RAL with once-daily rifapentine.
Fostemsavir (FTR)	• **Rifabutin:** Interaction is not expected. • **Rifampin, rifapentine:** CYP3A4 induction reduces FTR bioavailability.	• **Rifabutin:** No dose adjustments are necessary. • **Rifampin, rifapentine:** Do not coadminister.
Lenacapavir (LEN)	**Rifabutin, rifampin, rifapentine:** CYP3A4 and P-gP induction associated with rifamycins potentially decreases LEN levels.	• **Rifampin:** Concomitant use is contraindicated. • **Rifabutin, rifapentine:** Coadministration is not recommended. • Consider alternatives.

Abbreviations: ARV, antiretroviral; COBI, cobicistat; CYP, cytochrome P450; P-gP, P-glycoprotein; PI, protease inhibitor; RTV, ritonavir; UGT, uridine diphosphate glucuronosyltransferase.

Notes:

a. **Rifapentine:** Has not been studied with many ARVs, but its CYP3A-inducing effects are expected to be lower than those seen with rifampin but higher than those seen with rifabutin. Global research has suggested that rifapentine combined with isoniazid may be safe and effective for patients using EFV (dose adjusted), RAL, or DTG, but additional studies are required before recommendations can be made about the use of this medicine with other ARVs.

b. **Isoniazid, pyrazinamide, ethambutol, rifaximin:** No clinically significant interactions with ARVs are expected; no dose adjustments are necessary. Rifaximin is a rifamycin drug that is not used to treat tuberculosis but may be seen in patients with hepatic encephalopathy or some forms of infectious diarrhea.

References

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