Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 1 of 15) (Last updated October 22, 2019; last reviewed October 13, 2021)

This table lists the known, predicted, or suspected PK interactions between drugs used for the treatment or prevention of HIV-associated OIs. Many of the drugs listed in this table may also interact with ARV drugs. Clinicians should see the Drug-Drug Interactions tables in the most current Adult and Adolescent Antiretroviral Guidelines to assess interaction potentials between OI drugs and ARV drugs.

Throughout the table, three recommendations are commonly used when concomitant administration of two drugs may lead to untoward consequences. The rationale for these recommendations are summarized below:

Do not coadminister.

There is either strong evidence or strong likelihood that the drug-drug interaction cannot be managed with a dose modification of one or both drugs, and will or may result in either:

- Increase in concentrations of one or both drugs, which may lead to excessive risk of toxicity; *or*
- Decrease in concentrations of one or both drugs, which may render one or both drugs ineffective.

Coadministration should be avoided, if possible.

There is a potential for significant PK interactions. If other more favorable options exist, clinicians are advised to consider changing components of the regimen to accommodate a safer or more effective regimen. However, coadministration of the drugs may be necessary when there are no other acceptable therapeutic options that provide a more favorable benefit-to-risk ratio.

Use with caution.

Drug combinations are recommended to be used with caution when:

- PK studies have shown a moderate degree of interaction of unknown clinical significance; *or*
- Based on the known metabolic pathway of the two drugs, there is a potential for PK interaction of unknown clinical significance.

Rifamycin Antibiotics-Related Interactions

Rifamycin antibiotics are potent inducers of Phase 1 and Phase 2 drug metabolizing reactions. Studies have demonstrated that with daily doses of rifampin, enzyme induction increases over a week or more. Based on limited data, larger doses of rifampin (e.g., 1,200 mg) appear to produce the same maximum induction as lower doses, but more rapidly. Single doses of rifampin may not produce significant induction. In general, rifabutin as a CYP3A4 inducer is about 40% of the potency of rifampin, but this can vary by substrate and enzymatic reaction. In general, daily rifapentine (for active TB disease) is at least as potent an inducer as rifampin. However, the potential of drug interactions with once weekly rifapentine (prescribed with isoniazid for latent TB infection) is not well studied, and may result in reduced exposure of drugs that are CYP3A4 substrates. When using a rifamycin antibiotic with a potential interacting drug is necessary, close monitoring for clinical efficacy of the coadministered agent is advised.

Note: To avoid redundancy, drug-drug interactions are listed only once by primary drug (listed alphabetically). Subsequently, when an interacting agent becomes the primary drug, guideline users are referred to the entry for the initial primary drug. See the Clarithromycin row for the first example of this format.

Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 2 of 15)

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Artemether/ Lumefantrine	Clarithromycin	↑ lumefantrine expected	Coadministration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
	Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	↑ artemether and lumefantrine possible	Use with caution. Monitor for artemether and lumefantrine toxicities.
	Erythromycin	↑ lumefantrine possible	**Do not coadminister.** Consider azithromycin in place of erythromycin.
	Fluconazole	↑ lumefantrine possible	Coadministration should be avoided, if possible. If coadministered, monitor for lumefantrine toxicities.
	Isavuconazole	↑ lumefantrine possible	Coadministration should be avoided, if possible. If coadministered, monitor for lumefantrine toxicities.
	Itraconazole	↑ lumefantrine expected	Coadministration should be avoided, if possible. If coadministered, monitor for lumefantrine toxicities.
	Mefloquine	↓ lumefantrine possible	If mefloquine is administered immediately before artemether/lumefantrine, monitor for decreased efficacy of artemether/lumefantrine and encourage food intake.
	Posaconazole	↑ lumefantrine expected	Coadministration should be avoided, if possible. If coadministered, monitor for lumefantrine toxicities.
	Rifabutin[a]	↓ artemether, DHA, and lumefantrine expected	Use with caution. Monitor for antimalarial efficacy.
	Rifampin[a]	Artemether AUC ↓ 89% DHA AUC ↓ 85% Lumefantrine AUC ↓ 68%	**Do not coadminister.**
	Rifapentine[a]	↓ artemether, DHA, and lumefantrine expected	**Do not coadminister.**
	Voriconazole	↑ lumefantrine expected	Coadministration should be avoided, if possible. If coadministered, monitor for lumefantrine toxicities.
Atovaquone	Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	↔ atovaquone (based on interaction data for atovaquone oral solution with ATV/r)	No dosage adjustment necessary.
	Doxycycline	Atovaquone concentration ↓ approximately equal to 40% with tetracycline No interaction study with doxycycline	Dose adjustment not established; if coadministered, instruct patient to take atovaquone with fatty meal and monitor for decreased atovaquone efficacy.
	Rifabutin[a]	Atovaquone C_{SS} ↓ 34% Rifabutin C_{SS} ↓ 19%	Dose adjustment not established; if coadministered, instruct patient to take atovaquone with fatty meal and monitor for decreased atovaquone efficacy.
	Rifampin[a]	Atovaquone C_{SS} ↓ 52% Rifampin C_{SS} ↑ 37%	**Do not coadminister.**
	Rifapentine[a]	↓ atovaquone expected	**Do not coadminister.**

Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 3 of 15)

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Atovaquone/ Proguanil	Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	↓ atovaquone and proguanil AUC (when coadministered with ATV/r or LPV/r)	Consider alternative drug for malaria prophylaxis.
Bedaquiline	Clarithromycin	↑ bedaquiline expected	**Do not coadminister.** Consider azithromycin in place of clarithromycin.
	Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	↑ bedaquiline expected	Coadministration should be avoided, if possible. Consider alternative HCV regimen.
	Erythromycin	↑ bedaquiline possible	**Do not coadminister.** Consider azithromycin in place of erythromycin.
	Fluconazole	↑ bedaquiline possible	Coadministration should be avoided, if possible. If coadministered, monitor for bedaquiline toxicities.
	Isavuconazole	↑ bedaquiline possible	Coadministration should be avoided, if possible. If coadministered, monitor for bedaquiline toxicities.
	Itraconazole	↑ bedaquiline expected	Coadministration should be avoided, if possible. If coadministration is required for >14 days, weigh the benefits of therapy against the risks of bedaquiline toxicities. If coadministered, monitor for bedaquiline toxicities.
	Posaconazole	↑ bedaquiline expected	Coadministration should be avoided, if possible. If coadministered, monitor for bedaquiline toxicities.
	Rifabutin[a]	↔ bedaquiline	If coadministered, monitor for rifabutin toxicities.
	Rifampin[a]	Bedaquiline AUC ↓ 53%	**Do not coadminister.**
	Rifapentine[a]	Bedaquiline AUC ↓ 55% (with daily rifapentine)	**Do not coadminister.**
	Voriconazole	↑ bedaquiline expected	Coadministration should be avoided, if possible. If coadministered, monitor for bedaquiline toxicities.
Caspofungin	Rifabutin[a]	No data ↓ caspofungin possible	Monitor for antifungal efficacy. Dose not established. Consider increasing caspofungin dose to 70 mg/day or switch to another echinocandin (e.g., micafungin or anidulafungin).
	Rifampin[a]	Caspofungin C_{min} ↓ 30%	If coadministered, caspofungin dose should be increased to 70 mg/day. Consider alternative echinocandin (e.g., micafungin or anidulafungin).
	Rifapentine[a]	No data ↓ caspofungin possible	Monitor for antifungal efficacy. Dose not established. Consider increasing caspofungin dose to 70 mg/day or switch to another echinocandin (e.g., micafungin or anidulafungin).

Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 4 of 15)

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Chloroquine	Clarithromycin	↑ chloroquine expected	**Do not coadminister.** Consider azithromycin in place of clarithromycin.
	Erythromycin	↑ chloroquine possible	**Do not coadminister.** Consider azithromycin in place of erythromycin.
	Fluconazole	↑ chloroquine possible	Coadministration should be avoided, if possible. If co-administered, monitor for chloroquine toxicities.
	Isavuconazole	↑ chloroquine possible	Coadministration should be avoided, if possible. If coadministered, monitor for chloroquine toxicities.
	Itraconazole	↑ chloroquine expected	Coadministration should be avoided, if possible. If coadministered, monitor for chloroquine toxicities.
	Posaconazole	↑ chloroquine expected	Coadministration should be avoided, if possible. If coadministered, monitor for chloroquine toxicities.
	Rifabutin[a]	↓ chloroquine expected	Monitor for chloroquine efficacy.
	Rifampin[a]	↓ chloroquine expected	Monitor for chloroquine efficacy.
	Rifapentine[a]	↓ chloroquine expected	Monitor for chloroquine efficacy.
	Voriconazole	↑ chloroquine expected	Coadministration should be avoided, if possible. If coadministered, monitor for chloroquine toxicities.
Clarithromycin	Artemether/Lumefantrine	See Artemether/Lumefantrine	See Artemether/Lumefantrine
	Bedaquiline	See Bedaquiline	See Bedaquiline
	Chloroquine	See Chloroquine	See Chloroquine
	Daclatasvir	↑ daclatasvir expected	Decrease daclatasvir dose to 30 mg once daily.
	Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir	↑ clarithromycin and paritaprevir expected ↑ ombitasvir and dasabuvir possible	Coadministration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
	Elbasvir/Grazoprevir	↑ elbasvir and grazoprevir expected	Coadministration should be avoided, if possible. If coadministered, monitor closely for hepatotoxicity. Consider azithromycin in place of clarithromycin.
	Fluconazole	Clarithromycin AUC ↑ 18% and C_{min} ↑ 33%	No dose adjustment necessary in patients with normal renal function. Monitor for clarithromycin toxicity.
	Isavuconazole	↑ isavuconazole and clarithromycin expected	Coadministration should be avoided, if possible. Consider azithromycin in place of clarithromycin. If coadministered, monitor for toxicities of both isavuconazole and clarithromycin. Role of isavuconazole TDM has not been established.

Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 5 of 15)

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Clarithromycin, continued	Itraconazole	↑ itraconazole and clarithromycin expected	Coadministration should be avoided, if possible. Consider azithromycin in place of clarithromycin. If coadministered, monitor for toxicities of both itraconazole and clarithromycin); consider monitoring itraconazole concentration and adjust dose accordingly.
	Mefloquine	↑ mefloquine expected	Use with caution. Consider azithromycin in place of clarithromycin. If coadministered, monitor for mefloquine toxicity.
	Posaconazole	↑ clarithromycin expected	Coadministration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
	Quinine	↑ quinine expected ↑ clarithromycin possible	**Do not coadminister.** Consider azithromycin in place of clarithromycin.
	Rifabutin[a]	Clarithromycin AUC ↓ 44% 14-OH AUC ↑ 57% Rifabutin AUC ↑ 76% to 99% des-Rbt AUC ↑ 375%	Use with caution. Consider azithromycin in place of clarithromycin. If coadministered, consider reducing rifabutin dose, monitoring clarithromycin and rifabutin concentrations, and monitoring for rifabutin toxicities.
	Rifampin[a]	Clarithromycin concentration ↓ 87% Rifampin AUC ↑ 60%	**Do not coadminister.** Use azithromycin in place of clarithromycin.
	Rifapentine[a]	↓ clarithromycin expected ↑ 14-OH and rifapentine expected	Use with caution. Consider azithromycin in place of clarithromycin. If coadministered, monitor for rifapentine toxicities; consider monitoring clarithromycin and rifapentine concentrations and adjusting doses accordingly.
	Voriconazole	↑ clarithromycin expected	Coadministration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
Daclatasvir	Clarithromycin	See Clarithromycin	See Clarithromycin
	Erythromycin	↑ daclatasvir possible	No dosage adjustment. Monitor for daclatasvir toxicities.
	Fluconazole	↑ daclatasvir possible	No dosage adjustment. Monitor for daclatasvir toxicities.
	Isavuconazole	↑ daclatasvir possible	Dose not established. Monitor for daclatasvir toxicities.
	Itraconazole	↑ daclatasvir expected	Reduce daclatasvir dose to 30 mg once daily.
	Posaconazole	↑ daclatasvir expected	Reduce daclatasvir dose to 30 mg once daily.
	Rifabutin[a]	↓ daclatasvir expected	Dose not established. Consider increasing daclatasvir dose to 90 mg once daily and monitor for therapeutic efficacy.
	Rifampin[a]	Daclatasvir AUC ↓ 79%	**Do not coadminister.**
	Rifapentine[a]	↓ daclatasvir expected	Dose not established. Consider increasing daclatasvir dose to 90 mg once daily and monitor for therapeutic efficacy.

Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 6 of 15)

Primary Drug	Interacting Agent	Effect on Primary and/ or Concomitant Drug Concentrations	Recommendations
Daclatasvir, continued	TDF	TFV AUC ↑ 10%	No dosage adjustment.
	Voriconazole	↑ daclatasvir expected	Reduce daclatasvir dose to 30 mg once daily.
Dapsone	Rifabutin[a]	Dapsone AUC ↓ 27% to 40%	Coadministration should be avoided, if possible. Consider alternatives for dapsone.
	Rifampin[a]	Dapsone concentration ↓ 7-fold to 10-fold and $t_{1/2}$ ↓ from 24 hours to 11 hours	Coadministration should be avoided, if possible. Consider alternatives for dapsone.
	Rifapentine[a]	↓ dapsone expected	Coadministration should be avoided, if possible. Consider alternatives for dapsone.
Dasabuvir/ Ombitasvir/ Paritaprevir/ Ritonavir	Artemether/ Lumefantrine	See Artemether/lumefantrine	See Artemether/Lumefantrine
	Atovaquone (oral solution)	See Atovaquone (oral solution)	See Atovaquone (oral solution)
	Atovaquone/ Proguanil	See Atovaquone/Proguanil	See Atovaquone/Proguanil
	Bedaquiline	See Bedaquiline	See Bedaquiline
	Clarithromycin	See Clarithromycin	See Clarithromycin
	Erythromycin	↑ erythromycin and paritaprevir expected ↑ ombitasvir and dasabuvir possible	Coadministration should be avoided, if possible. Consider azithromycin in place of erythromycin.
	Isavuconazole	Isavuconazole ↑ 96% and RTV AUC ↓ 31% (when studied with LPV/r) ↑ or ↓ paritaprevir, ombitasvir, and dasabuvir possible	Coadministration should be avoided, if possible. If coadministered, monitor for isavuconazole toxicity and HCV regimen-associated toxicities and efficacy.
	Itraconazole	↑ itraconazole and paritaprevir expected ↑ ombitasvir and dasabuvir possible	Itraconazole doses >200 mg/day are not recommended unless dosing is guided by itraconazole concentration. Monitor for itraconazole- and HCV regimen-associated toxicities.
	Mefloquine	RTV AUC ↓ 31% (based on study with RTV 200 mg twice daily)	Monitor for HCV antiviral activity.
	Posaconazole	↑ posaconazole and paritaprevir expected ↑ ombitasvir and dasabuvir possible	Monitor for posaconazole- and HCV regimen-associated toxicities. Monitor posaconazole concentration and adjust dose if necessary.
	Rifabutin[a]	↑ rifabutin expected ↓ paritaprevir possible	Coadministration should be avoided, if possible. With coadministration, decrease rifabutin dose to 150 mg/day and monitor rifabutin concentration. Monitor HCV regimen for efficacy.
	Rifampin[a]	↓ paritaprevir, ritonavir, ombitasvir, and dasabuvir expected	**Do not coadminister.**
	Rifapentine[a]	↓ paritaprevir, ritonavir, ombitasvir, and dasabuvir expected	**Do not coadminister.**
	Voriconazole	Voriconazole AUC ↓ 39% (when given with RTV 100 mg twice daily) ↑ paritaprevir expected	Coadminister only if the benefits outweigh the risk. Monitor voriconazole concentration to guide dosage adjustments.

Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 7 of 15)

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Doxycycline	Atovaquone	See Atovaquone	See Atovaquone
	Rifabutin[a]	No data ↓ doxycycline possible	Monitor closely for doxycycline efficacy or consider alternative therapy.
	Rifampin[a]	Doxycycline AUC ↓ 59%	Use with caution. Monitor closely for doxycycline efficacy or consider alternative therapy.
	Rifapentine[a]	No data ↓ doxycycline possible	Monitor closely for doxycycline efficacy or consider alternative therapy.
Elbasvir/ Grazoprevir	Clarithromycin	See Clarithromycin	See Clarithromycin
	Erythromycin	↑ elbasvir and grazoprevir expected	Coadministration should be avoided, if possible. If coadministered, monitor closely for hepatotoxicity. Consider azithromycin in place of erythromycin.
	Isavuconazole	↑ elbasvir and grazoprevir expected	Coadministration should be avoided, if possible. If coadministered, monitor closely for hepatotoxicity.
	Itraconazole	↑ elbasvir and grazoprevir expected	Coadministration should be avoided, if possible. If coadministered, monitor closely for hepatotoxicity.
	Posaconazole	↑ elbasvir and grazoprevir expected	Coadministration should be avoided, if possible. If coadministered, monitor closely for hepatotoxicity.
	Rifabutin[a]	↓ elbasvir and grazoprevir possible	Coadministration should be avoided if possible. Consider alternative HCV regimen.
	Rifampin[a]	Grazoprevir AUC ↓ 7% and C_{24h} ↓ 90% ↓ elbasvir expected	**Do not coadminister.**
	Rifapentine[a]	↓ elbasvir and grazoprevir expected	**Do not coadminister.**
	Voriconazole	↑ elbasvir and grazoprevir expected	Coadministration should be avoided if possible. If coadministered, monitor closely for hepatotoxicity.
Erythromycin	Artemether/ Lumefantrine	See Artemether/Lumefantrine	See Artemether/Lumefantrine
	Bedaquiline	See Bedaquiline	See Bedaquiline
	Chloroquine	See Chloroquine	See Chloroquine
	Daclatasvir	See Daclatasvir	See Daclatasvir
	Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/Paritaprevir/ Ritonavir
	Elbasvir/Grazoprevir	See Elbasvir/Grazoprevir	See Elbasvir/Grazoprevir
	Fluconazole	↑ erythromycin possible	**Do not coadminister.** Consider azithromycin in place of erythromycin.
	Isavuconazole	↑ erythromycin and isavuconazole possible	**Do not coadminister.** Consider azithromycin in place of erythromycin.
	Itraconazole	Itraconazole AUC ↑ 36% ↑ erythromycin possible	**Do not coadminister.** Consider azithromycin in place of erythromycin.

Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 8 of 15)

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Erythromycin, continued	Mefloquine	↑ mefloquine possible	**Do not coadminister.** Consider azithromycin in place of erythromycin.
	Posaconazole	↑ erythromycin expected	**Do not coadminister.** Consider azithromycin in place of erythromycin.
	Quinine	↑ quinine expected ↑ erythromycin possible	**Do not coadminister.** Consider azithromycin in place of erythromycin.
	Rifabutin[a]	↓ erythromycin possible ↑ rifabutin possible	Use with caution. Consider azithromycin in place of erythromycin. If coadministered, monitor for erythromycin efficacy or rifabutin toxicities.
	Rifampin[a]	↓ erythromycin expected	Consider azithromycin in place of erythromycin. If co-coadministered, monitor for erythromycin efficacy.
	Rifapentine[a]	↓ erythromycin expected	Consider azithromycin in place of erythromycin. If coadministered, monitor for erythromycin efficacy.
	Voriconazole	↑ erythromycin expected	**Do not coadminister.** Consider azithromycin in place of erythromycin.
Fluconazole	Artemether/Lumefantrine	See Artemether/Lumefantrine	See Artemether/Lumefantrine
	Bedaquiline	See Bedaquiline	See Bedaquiline
	Chloroquine	See Chloroquine	See Chloroquine
	Clarithromycin	See Clarithromycin	See Clarithromycin
	Daclatasvir	See Daclatasvir	See Daclatasvir
	Erythromycin	See Erythromycin	See Erythromycin
	Mefloquine	↑ mefloquine possible	Coadministration should be avoided, if possible. If coadministered, monitor for mefloquine toxicities.
	Quinine	↑ quinine expected ↑ fluconazole possible	Coadministration should be avoided, if possible. If coadministered, monitor for quinine and fluconazole toxicity.
	Rifabutin[a]	Rifabutin AUC ↑ 80% ↔ fluconazole	Use with caution. Monitor for rifabutin toxicities. Consider monitoring rifabutin concentration; may need to decrease rifabutin dose to 150 mg/day.
	Rifampin[a]	Fluconazole AUC ↓ 23% to 56%	Monitor for antifungal efficacy; may need to increase fluconazole dose.
	Rifapentine[a]	↓ fluconazole expected	Monitor for antifungal efficacy; may need to increase fluconazole dose.
Glecaprevir/Pibrentasvir	Rifabutin[a]	↓ glecaprevir and pibrentasvir possible	Coadminsitration should be avoided, if possible. Consider alternative agents.
	Rifampin[a]	Glecaprevir AUC ↓ 88% Pibrentasvir AUC ↓ 87%	**Do not coadminister.**
	Rifapentine[a]	↓ glecaprevir and pibrentasvir possible	**Do not coadminister.** Consider alternative agents.
	TDF	TFV AUC ↑ 29% when coadministered as EFV/TDF/FTC	Use usual dose. Monitor renal function or consider TAF.

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Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Glecaprevir/ Pibrentasvir, continued	TAF	↔ TFV concentration when coadministered as EVG/c/TAF/FTC	No dose adjustment.
Isavuconazole	Artemether/ Lumefantrine	See Artemether/Lumefantrine	See Artemether/Lumefantrine
	Bedaquiline	See Bedaquiline	See Bedaquiline
	Chloroquine	See Chloroquine	See Chloroquine
	Clarithromycin	See Clarithromycin	See Clarithromycin
	Daclatasvir	See Daclatasvir	See Daclatasvir
	Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/Paritaprevir/ Ritonavir
	Elbasvir/Grazoprevir	See Elbasvir/Grazoprevir	See Elbasvir/Grazoprevir
	Erythromycin	See Erythromycin	See Erythromycin
	Mefloquine	↑ mefloquine expected	Coadministration should be avoided, if possible. If coadministered, monitor for mefloquine toxicities.
	Quinine	↑ quinine expected ↑ isavuconazole possible	Coadministration should be avoided, if possible. If coadministered, monitor for quinine and isavuconazole toxicities.
	Rifabutin[a]	↓ isavuconazole expected ↑ rifabutin expected	Consider alternative agent(s). If alternative agents are not available, use with close monitoring for isavuconazole anti-fungal activity and rifabutin toxicity.
	Rifampin[a]	Isavuconazole AUC ↓ 97%	**Do not coadminister.** Consider alternative antifungal and/or antimycobacterial agent(s).
	Rifapentine[a]	Significant ↓ isavuconazole expected	**Do not coadminister.** Consider alternative antifungal and/or antimycobacterial agent(s).
Itraconazole	Artemether/ Lumefantrine	See Artemether/Lumefantrine	See Artemether/Lumefantrine
	Bedaquiline	See Bedaquiline	See Bedaquiline
	Chloroquine	See Chloroquine	See Chloroquine
	Clarithromycin	See Clarithromycin	See Clarithromycin
	Daclatasvir	See Daclatasvir	See Daclatasvir
	Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/Paritaprevir/ Ritonavir
	Elbasvir/Grazoprevir	See Elbasvir/Grazoprevir	See Elbasvir/Grazoprevir
	Erythromycin	See Erythromycin	See Erythromycin
	Mefloquine	↑ Mefloquine expected	Coadministration should be avoided, if possible. If coadministered, monitor for mefloquine toxicities.
	Quinine	↑ quinine expected ↑ itraconazole possible	Coadministration should be avoided, if possible. If coadministered, monitor for quinine and itraconazole toxicities; monitor itraconazole concentration and adjust dose accordingly.

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Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Itraconazole, continued	Rifabutin[a]	Itraconazole AUC ↓ 70% ↑ rifabutin expected	**Do not coadminister.** Consider alternative antifungal and/or antimycobacterial agent(s).
	Rifampin[a]	Itraconazole AUC ↓ 64% to 88%	**Do not coadminister.** Consider alternative antifungal and/or antimycobacterial agent(s).
	Rifapentine[a]	↓ itraconazole expected	**Do not coadminister.** Consider alternative antifungal and/or antimycobacterial agent(s).
Ledipasvir/ Sofosbuvir	Rifabutin[a]	↓ ledipasvir and sofosbuvir expected	**Do not coadminister.**
	Rifampin[a]	Ledipasvir AUC ↓ 59% Sofosbuvir AUC ↓ 72%	**Do not coadminister.**
	Rifapentine[a]	↓ ledipasvir and sofosbuvir expected	**Do not coadminister.**
	TAF	Ledipasvir AUC ↑ 79% (when given with EVG/c/TAF/FTC)	No dosage adjustment.
	TDF	TFV AUC ↑ 98% (when given with EFV/FTC) TFV AUC ↑ 40% (when given with RPV/FTC) TFV AUC ↑ 50% (when given with DRV/r/FTC)	Monitor for TDF toxicities. Consider TAF in place of TDF.
Linezolid	Rifabutin[a]	↓ linezolid possible	Monitor for linezolid efficacy.
	Rifampin[a]	Linezolid AUC ↓ 32%	Monitor for linezolid efficacy.
	Rifapentine[a]	↓ linezolid possible	Monitor for linezolid efficacy.
Mefloquine	Artemether/ Lumefantrine	See Artemether/Lumefantrine	See Artemether/Lumefantrine
	Clarithromycin	See Clarithromycin	See Clarithromycin
	Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/Paritaprevir/ Ritonavir
	Erythromycin	See Erythromycin	See Erythromycin
	Fluconazole	See Fluconazole	See Fluconazole
	Isavuconazole	See Isavuconazole	See Isavuconazole
	Itraconazole	See Itraconazole	See Itraconazole
	Posaconazole	↑ mefloquine expected	Coadministration should be avoided, if possible. If coadministered, monitor for mefloquine toxicities.
	Rifabutin[a]	↓ mefloquine possible	Monitor for mefloquine efficacy.
	Rifampin[a]	Mefloquine AUC ↓ 68%	**Do not coadminister.** Use alternative antimalarial drug or rifabutin.
	Rifapentine[a]	↓ mefloquine expected	**Do not coadminister.** Use alternative antimalarial drug or rifabutin.
	Voriconazole	↑ mefloquine expected	Coadministration should be avoided, if possible. If coadministered, monitor for mefloquine toxicities.
Posaconazole	Artemether/ Lumefantrine	See Artemether/Lumefantrine	See Artemether/Lumefantrine
	Bedaquiline	See Bedaquiline	See Bedaquiline

Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 11 of 15)

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Posaconazole, continued	Chloroquine	See Chloroquine	See Chloroquine
	Clarithromycin	See Clarithromycin	See Clarithromycin
	Daclatasvir	See Daclatasvir	See Daclatasvir
	Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/Paritaprevir/ Ritonavir
	Elbasvir/Grazoprevir	See Elbasvir/Grazoprevir	See Elbasvir/Grazoprevir
	Erythromycin	See Erythromycin	See Erythromycin
	Mefloquine	See Mefloquine	See Mefloquine
	Quinine	↑ quinine expected ↑ posaconazole possible	Coadministration should be avoided, if possible. If coadministered, monitor for quinine toxicities.
	Rifabutin[a]	Posaconazole AUC ↓ 49% Rifabutin AUC ↑ 72%	Coadministration should be avoided, if possible. If coadministered, monitor posaconazole and rifabutin concentrations and adjust doses accordingly; monitor for clinical response to posaconazole and rifabutin toxicities.
	Rifampin[a]	Significant ↓ posaconazole expected	**Do not coadminister when treating invasive fungal infections.** If coadministered for treatment of non-invasive fungal infections, monitor posaconazole concentration and adjust dose accordingly; monitor for clinical response.
	Rifapentine[a]	↓ posaconazole expected	Coadministration should be avoided, if possible. If coadministered, monitor posaconazole concentration and adjust dose accordingly; monitor clinical response.
Quinine	Clarithromycin	See Clarithromycin	See Clarithromycin
	Erythromycin	See Erythromycin	See Erythromycin
	Fluconazole	See Fluconazole	See Fluconazole
	Itraconazole	See Itraconazole	See Itraconazole
	Posaconazole	See Posaconazole	See Posaconazole
	Rifabutin[a]	↓ quinine possible ↑ rifabutin possible	Monitor for quinine efficacy. Monitor rifabutin concentration and toxicity.
	Rifampin[a]	Quinine AUC ↓ 75% to 85%	**Do not coadminister.**
	Rifapentine[a]	↓ quinine expected	**Do not coadminister.**
	Voriconazole	↑ quinine expected	Coadministration should be avoided, if possible. If coadministered, monitor for quinine toxicities.
Rifabutin[a]	Artemether/ Lumefantrine	See Artemether/Lumefantrine	See Artemether/Lumefantrine
	Atovaquone	See Atovaquone	See Atovaquone
	Bedaquiline	See Bedaquiline	See Bedaquiline
	Caspofungin	See Caspofungin	See Caspofungin
	Chloroquine	See Chloroquine	See Chloroquine

Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 12 of 15)

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Rifabutin[a], continued	Clarithromycin	See Clarithromycin	See Clarithromycin
	Daclatasvir	See Daclatasvir	See Daclatasvir
	Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/Paritaprevir/ Ritonavir
	Dapsone	See Dapsone	See Dapsone
	Doxycycline	See Doxycycline	See Doxycycline
	Elbasvir/Grazoprevir	See Elbasvir/Grazoprevir	See Elbasvir/Grazoprevir
	Erythromycin	See Erythromycin	See Erythromycin
	Fluconazole	See Fluconazole	See Fluconazole
	Glecaprevir/Pibrentasvir	See Glecaprevir/Pibrentasvir	See Glecaprevir/Pibrentasvir
	Isavuconazole	See Isavuconazole	See Isavuconazole
	Itraconazole	See Itraconazole	See Itraconazole
	Ledipasvir/Sofosbuvir	See Ledipasvir/Sofosbuvir	See Ledipasvir/Sofosbuvir
	Linezolid	See Linezolid	See Linezolid
	Mefloquine	See Mefloquine	See Mefloquine
	Posaconazole	See Posaconazole	See Posaconazole
	Quinine	See Quinine	See Quinine
	Sofosbuvir	↓ sofosbuvir expected	**Do not coadminister.**
	Sofosbuvir/Velpatasvir +/- Voxilaprevir	↓ velpatasvir, voxilaprevir, and sofosbuvir expected	**Do not coadminister.**
	TAF	↓ TAF expected	**Do not coadminister.**
	Voriconazole	Voriconazole AUC ↓ 79% Rifabutin AUC ↑ 4-fold	**Do not coadminister.** Consider alternative antifungal and/or antimycobacterial agent(s). If coadministration is absolutely necessary, monitor voriconazole and rifabutin concentrations to guide therapy.
Rifampin[a]	Artemether/ Lumefantrine	See Artemether/Lumefantrine	See Artemether/Lumefantrine
	Atovaquone	See Atovaquone	See Atovaquone
	Bedaquiline	See Bedaquiline	See Bedaquiline
	Caspofungin	See Caspofungin	See Caspofungin
	Chloroquine	See Chloroquine	See Chloroquine
	Clarithromycin	See Clarithromycin	See Clarithromycin
	Daclatasvir	See Daclatasvir	See Daclatasvir
	Dapsone	See Dapsone	See Dapsone
	Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/Paritaprevir/ Ritonavir
	Doxycycline	See Doxycycline	See Doxycycline
	Elbasvir/Grazoprevir	See Elbasvir/Grazoprevir	See Elbasvir/Grazoprevir
	Erythromycin	See Erythromycin	See Erythromycin
	Fluconazole	See Fluconazole	See Fluconazole
	Glecaprevir/Pibrentasvir	See Glecaprevir/Pibrentasvir	See Glecaprevir/Pibrentasvir

Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 13 of 15)

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Rifampin[a], continued	Isavuconazole	See Isavuconazole	See Isavuconazole
	Itraconazole	See Itraconazole	See Itraconazole
	Ledipasvir/Sofosbuvir	See Ledipasvir/Sofosbuvir	See Ledipasvir/Sofosbuvir
	Linezolid	See Linezolid	See Linezolid
	Mefloquine	See Mefloquine	See Mefloquine
	Posaconazole	See Posaconazole	See Posaconazole
	Quinine	See Quinine	See Quinine
	Sofosbuvir	Sofosbuvir AUC ↓ 72%	**Do not coadminister.**
	Sofosbuvir/Velpatasvir +/- Voxilaprevir	Sofosbuvir AUC ↓ 72% Velpatasvir AUC ↓ 82% Voxilaprevir AUC ↓ 73%	**Do not coadminister.**
	TAF	**TAF plus Rifampin:** • TAF AUC ↓ 56%, • TFV AUC ↓ 53% • TFV-DP AUC ↓ 36% Intracellular TFV-DP concentration is 4.2-fold greater than with TDF alone.	If coadministered, monitor for HIV and HBV efficacy. **Note:** FDA labeling recommends not to coadminister.
	Voriconazole	Voriconazole AUC ↓ 96%	**Do not coadminister.** Consider alternative antifungal and/or antimycobacterial agent(s).
Rifapentine[a]	Artemether/ Lumefantrine	See Artemether/Lumefantrine	See Artemether/Lumefantrine
	Atovaquone	See Atovaquone	See Atovaquone
	Bedaquiline	See Bedaquiline	See Bedaquiline
	Caspofungin	See Caspofungin	See Caspofungin
	Chloroquine	See Chloroquine	See Chloroquine
	Clarithromycin	See Clarithromycin	See Clarithromycin
	Daclatasvir	See Daclatasvir	See Daclatasvir
	Dapsone	See Dapsone	See Dapsone
	Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/Paritaprevir/ Ritonavir
	Doxycycline	See Doxycycline	See Doxycycline
	Elbasvir/Grazoprevir	See Elbasvir/Grazoprevir	See Elbasvir/Grazoprevir
	Erythromycin	See Erythromycin	See Erythromycin
	Fluconazole	See Fluconazole	See Fluconazole
	Glecaprevir/Pibrentasvir	See Glecaprevir/Pibrentasvir	See Glecaprevir/Pibrentasvir
	Isavuconazole	See Isavuconazole	See Isavuconazole
	Itraconazole	See Itraconazole	See Itraconazole
	Ledipasvir/Sofosbuvir	See Ledipasvir/Sofosbuvir	See Ledipasvir/Sofosbuvir
	Linezolid	See Linezolid	See Linezolid
	Mefloquine	See Mefloquine	See Mefloquine
	Posaconazole	See Posaconazole	See Posaconazole

Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 14 of 15)

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Rifapentine[a], continued	Quinine	See Quinine	See Quinine
	Sofosbuvir	↓ sofosbuvir expected	**Do not coadminister.**
	TAF	↓ TAF expected	**Do not coadminister.**
	Sofosbuvir/Velpatasvir +/- Voxilaprevir	↓ sofosbuvir, velpatasvir, and voxilaprevir expected	**Do not coadminister.**
	Voriconazole	↓ voriconazole expected	**Do not coadminister.** Consider alternative antifungal and/or antimycobacterial agent(s).
Sofosbuvir	Rifabutin[a]	See Rifabutin	See Rifabutin
	Rifampin[a]	See Rifampin	See Rifampin
	Rifapentine[a]	See Rifapentine	See Rifapentine
Sofosbuvir/ Velpatasvir +/- Voxilaprevir	Rifabutin[a]	See Rifabutin	See Rifabutin
	Rifampin[a]	See Rifampin	See Rifampin
	Rifapentine[a]	See Rifapentine	See Rifapentine
	TAF	TFV AUC ↑ 52% (when RPV/TAF/FTC given with SOF/VEL/VOX)	No dosage adjustment.
	TDF	TFV AUC ↑ 35% to 40% (when given with EVG/c/FTC or RPV/FTC) TFV AUC ↑ 81% (when given with EFV/FTC and SOF/VEL) TFV AUC ↑ 39% (when given with DRV/r/FTC and SOF/VEL/VOX)	Monitor for TDF toxicities. Consider TAF in place of TDF.
Tenofovir Alafenamide	Ledipasvir/Sofosbuvir	See Ledipasvir/Sofosbuvir	See Ledipasvir/Sofosbuvir
	Glecaprevir/Pibrentasvir	See Glecaprevir/Pibrentasvir	See Glecaprevir/Pibrentasvir
	Rifabutin[a]	See Rifabutin	See Rifabutin
	Rifampin[a]	See Rifampin	See Rifampin
	Rifapentine[a]	See Rifapentine	See Rifapentine
	Sofosbuvir/Velpatasvir +/- Voxilaprevir	See Sofosbuvir/Velpatasvir +/- Voxilaprevir	See Sofosbuvir/Velpatasvir +/- Voxilaprevir
Tenofovir Disoproxil Fumarate	Daclatasvir	See Daclatasvir	See Daclatasvir
	Glecaprevir/Pibrentasvir	See Glecaprevir/Pibrentasvir	See Glecaprevir/Pibrentasvir
	Ledipasvir/Sofosbuvir	See Ledipasvir/Sofosbuvir	See Ledipasvir/Sofosbuvir
	Sofosbuvir/Velpatasvir	See Sofosbuvir/Velpatasvir +/- Voxilaprevir	See Sofosbuvir/Velpatasvir +/- Voxilaprevir
Voriconazole	Artemether/ Lumefantrine	See Artemether/Lumefantrine	See Artemether/Lumefantrine
	Bedaquiline	See Bedaquiline	See Bedaquiline
	Chloroquine	See Chloroquine	See Chloroquine
	Clarithromycin	See Clarithromycin	See Clarithromycin
	Daclatasvir	See Daclatasvir	See Daclatasvir
	Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir	See Dasabuvir/Ombitasvir/Paritaprevir/ Ritonavir
	Elbasvir/Grazoprevir	See Elbasvir/Grazoprevir	See Elbasvir/Grazoprevir

Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 15 of 15)

Primary Drug	Interacting Agent	Effect on Primary and/ or Concomitant Drug Concentrations	Recommendations
Voriconazole, continued	Erythromycin	See Erythromycin	See Erythromycin
	Mefloquine	See Mefloquine	See Mefloquine
	Quinine	See Quinine	See Quinine
	Rifabutin[a]	See Rifabutin	See Rifabutin
	Rifampin[a]	See Rifampin	See Rifampin
	Rifapentine[a]	See Rifapentine	See Rifapentine

[a] Rifamycin antibiotics are potent inducers of Phase 1 and Phase 2 drug-metabolizing reactions. Studies have demonstrated that with daily doses of rifampin, enzyme induction increases over a week or more. Based on limited data, larger doses of rifampin (e.g., 1,200 mg) appear to produce the same maximum induction as lower doses, but more rapidly. Single doses of rifampin may not produce significant induction. In general, rifabutin is about 40% as potent a CYP3A4 inducer as rifampin, but this can vary by substrate and enzymatic reaction. In general, daily rifapentine (for active TB disease) is at least as potent an inducer as rifampin. However, the potential of drug interactions with once weekly rifapentine (for latent TB infection, along with isoniazid) is not well studied, and may result in reduced exposure of drugs that are CYP3A4 substrates. When a rifamycin antibiotic is given with a potential interacting drug, close monitoring for clinical efficacy of the coadministered agent is advised.

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

Key: 14-OH = active metabolite of clarithromycin; ARV = antiretroviral; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{24h} = concentration at 24 hours post dose; C_{min} = minimum concentration; C_{ss} = concentration at steady state; CYP3A4 = Cytochrome P450 3A4; des-Rbt = desacetyl rifabutin; DHA = dihydroartemisinin; DRV/r = darunavir/ritonavir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; HCV = hepatitis C virus; LPV/r = lopinavir/ritonavir; OI = opportunistic infection; PK = pharmacokinetic; RPV = rilpivirine; RTV = ritonavir; SOF = sofosbuvir; $T_{1/2}$ = half-life; TAF = tenofovir alafenamide; TB = tuberculosis; TDF = tenofovir disoproxil fumarate; TDM = therapeutic drug monitoring; TFV= tenofovir; TFV-DP = tenofovir diphosphate; VEL = velpastavir; VOX = voxilaprevir