Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents

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Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 1 of 15) (Last updated September 22, 2017; last reviewed September 22, 2017)

This table lists the known or suspected/predicted pharmacokinetic interactions between drugs used for the treatment or prevention of HIV-associated opportunistic infections (OIs). Many of the drugs listed in this table may also interact with antiretroviral drugs. Clinicians should refer to the drug interaction tables in the most current Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents to assess interaction potentials between OI drugs and antiretroviral therapy (ART).

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 co-administer"

Indicates 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/may result in either:

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

"Co-administration should be avoided, if possible"

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

"Use with caution"

Drug combinations are recommended to be used with caution when:

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

Rifamycin-Related Interactions

Rifamycins are potent inducers of Phase I and Phase II drug metabolizing reactions. Daily doses of rifampin are well studied, and induction increases over a week or more. Based on limited data, larger doses of rifampin (e.g., 1200 mg) appear to produce the same maximum induction, 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 tuberculosis [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, but may result in reduction of exposure of drugs that are CYP3A4 substrates. When a rifamycin is used with a potential interacting drug, close monitoring for clinical efficacy of the other agent is advised.

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Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Artemether/ Lumefantrine	Clarithromycin	↑ Lumefantrine expected	Co-administration 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-associated toxicities.
	Erythromycin	↑ Lumefantrine possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Fluconazole	↑ Lumefantrine possible	Co-administration should be avoided, if possible. If co-administered, monitor for lumefantrine toxicities (e.g., QT prolongation).
	Itraconazole	↑ Lumefantrine expected	Co-administration should be avoided, if possible. If co-administered, monitor for lumefantrine toxicities (e.g., QT prolongation).
	Posaconazole	↑ Lumefantrine expected	Co-administration should be avoided, if possible. If co-administered, monitor for lumefantrine toxicities (e.g., QT prolongation).
	Rifabutin[a]	↓ Artemether, DHA, and lumefantrine expected	Use with caution. Monitor for antimalarial efficacy.
	Rifampin[a]	↓ Artemether, DHA, and lumefantrine AUC by 89%, 85%, and 68%, respectively	Do not co-administer.
	Rifapentine[a]	↓ Artemether, DHA, and lumefantrine expected	Do not co-administer.
	Voriconazole	↑ Lumefantrine expected	Co-administration should be avoided, if possible. If co-administered, monitor for lumefantrine toxicities (e.g., QT prolongation).
Atovaquone	Dasabuvir Ombitasvir Paritaprevir Ritonavir	↔ Atovaquone (based on data from atovaquone and atazanavir/ritonavir interaction)	No dosage adjustment necessary.
	Doxycycline	Atovaquone conc. ↓ by approximately 40% with tetracycline. No interaction study with doxycycline.	Dose adjustment not established; if co-administered, 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 co-administered, take atovaquone with fatty meal and monitor for decreased atovaquone efficacy.
	Rifampin[a]	Atovaquone C_{SS} ↓ 52%; rifampin C_{SS}↑ 37%	Do not co-administer.
	Rifapentine[a]	↓ Atovaquone expected	Do not co-administer.
Bedaquiline	Clarithromycin	↑ Bedaquiline expected	Co-administration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
	Dasabuvir Ombitasvir Paritaprevir Ritonavir	↑ Bedaquiline expected	Co-administration should be avoided, if possible. Consider alternative HCV regimen.

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

Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	Erythromycin	↑ Bedaquiline possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Fluconazole	↑ Bedaquiline possible	Co-administration should be avoided, if possible. If co-administered, monitor for bedaquiline toxicities (e.g., QT prolongation).
	Itraconazole	↑ Bedaquiline expected	Co-administration should be avoided, if possible. If co-administered, monitor for bedaquiline toxicities (e.g., QT prolongation).
	Posaconazole	↑ Bedaquiline expected	Co-administration should be avoided, if possible. If co-administered, monitor for bedaquiline toxicities (e.g., QT prolongation).
	Rifabutin[a]	↓ Bedaquiline possible	If co-administered, monitor for bedaquiline efficacy.
	Rifampin[a]	Bedaquiline AUC ↓ 53%	Do not co-administer.
	Rifapentine[a]	Bedaquiline AUC ↓ 55% (with daily rifapentine)	Do not co-administer.
	Voriconazole	↑ Bedaquiline expected	Co-administration should be avoided, if possible. If co-administered, monitor for bedaquiline toxicities (e.g., QT prolongation).
Caspofungin	Rifabutin[a]	No data. ↓ Caspofungin possible.	Monitor for antifungal efficacy. Dose not established. Consider increasing caspofungin dose to 70 mg/day.
	Rifampin[a]	Caspofungin C_{min} ↓ 30%	Caspofungin dose should be increased to 70 mg/day.
	Rifapentine[a]	No data. ↓ Caspofungin possible.	Monitor for antifungal efficacy. Dose not established. Consider increasing caspofungin dose to 70 mg/day.
Chloroquine	Clarithromycin	↑ Chloroquine expected	Co-administration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
	Erythromycin	↑ Chloroquine possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Fluconazole	↑ Chloroquine possible	Co-administration should be avoided, if possible. If co-administered, monitor for chloroquine toxicities (e.g., QT prolongation).
	Itraconazole	↑ Chloroquine expected	Co-administration should be avoided, if possible. If co-administered, monitor for chloroquine toxicities (e.g., QT prolongation).
	Posaconazole	↑ Chloroquine expected	Co-administration should be avoided, if possible. If co-administered, monitor for chloroquine toxicities (e.g., QT prolongation).
	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	Co-administration should be avoided, if possible. If co-administered, monitor for chloroquine toxicities (e.g., QT prolongation).
Clarithromycin	Artemether/ Lumefantrine	↑ Lumefantrine expected	Co-administration should be avoided if possible. Consider azithromycin in place of clarithromycin.
	Bedaquiline	↑ Bedaquiline expected	Co-administration should be avoided, if possible. Consider azithromycin in place of clarithromycin.

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

Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	Chloroquine	↑ Chloroquine expected	Co-administration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
	Daclatasvir	↑ Daclatasvir expected	↓ Daclatasvir dose to 30 mg once daily.
	Dasabuvir Ombitasvir Paritaprevir Ritonavir	↑ Clarithromycin and paritaprevir expected; ↑ ombitasvir and dasabuvir possible	Co-administration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
	Elbasvir/ Grazoprevir	↑ Elbasvir and grazoprevir expected	Co-administration should be avoided, if possible. If co-administered, monitor closely for hepatotoxicity. Consider azithromycin in place of clarithromycin.
	Fluconazole	Clarithromycin AUC ↑ 18%, C_{min} ↑ 33%	No dose adjustment necessary in patients with normal renal function. Monitor for clarithromycin toxicity.
	Itraconazole	↑ Itraconazole and clarithromycin expected	Co-administration should be avoided, if possible. Consider azithromycin in place of clarithromycin. If co-administered, monitor for toxicities of both itraconazole and clarithromycin (e.g., QT prolongation), consider monitoring itraconazole conc. and adjust dose accordingly.
	Mefloquine	↑ Mefloquine expected	Use with caution. Consider azithromycin in place of clarithromycin. If co-administered, monitor for mefloquine toxicity (e.g., QT prolongation).
	Posaconazole	↑ Clarithromycin expected	Co-administration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
	Quinine	↑ Quinine expected; ↑ clarithromycin possible	Do not co-administer. Consider azithromycin in place of clarithromycin.
	Rifabutin[a]	Clarithromycin AUC ↓ by 44%; 14-OH AUC ↑ 57%; rifabutin AUC ↑ 76% to 99%; des-Rbt AUC ↑ 375%	Use with caution. Consider azithromycin in place of clarithromycin. If co-administered, consider reducing rifabutin dose, monitoring clarithromycin and rifabutin concentrations, and monitoring for rifabutin-associated toxicities (e.g., uveitis).
	Rifampin[a]	Mean clarithromycin conc. ↓ 87%; rifampin AUC ↑ 60%	Do not co-administer. 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 co-administered, monitor for rifapentine-associated toxicities, consider monitoring clarithromycin and rifapentine concentrations and adjusting doses accordingly.
	Simeprevir	↑ Simeprevir expected	Do not co-administer. Consider azithromycin in place of clarithromycin.
	Voriconazole	↑ Clarithromycin expected	Co-administration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
Daclatasvir	Clarithromycin	↑ Daclatasvir expected	Reduce daclatasvir dose to 30 mg once daily.
	Erythromycin	↑ Daclatasvir possible	No dosage adjustment. Monitor for daclatasvir-associated toxicities.
	Fluconazole	↑ Daclatasvir possible	No dosage adjustment. Monitor for daclatasvir-associated toxicities.
	Itraconazole	↑ Daclatasvir expected	Reduce daclatasvir dose to 30 mg once daily.
	Posaconazole	↑ Daclatasvir expected	Reduce daclatasvir dose to 30 mg once daily.

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Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	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 co-administer.
	Rifapentine[a]	↓ Daclatasvir expected	Dose not established. Consider increasing daclatasvir dose to 90 mg once daily and monitor for therapeutic efficacy.
	Simeprevir	Simeprevir AUC ↑ 44%; daclatasvir AUC ↑ 96%	No dosage adjustment. Monitor for simeprevir and daclatasvir-associated toxicities.
	Voriconazole	↑ Daclatasvir expected	Reduce daclatasvir dose to 30 mg once daily.
Dapsone	Rifabutin[a]	Dapsone AUC ↓ 27% to 40%	Co-administration should be avoided if possible. Consider alternatives for dapsone.
	Rifampin[a]	Dapsone conc. ↓ 7- to 10-fold and $t_{1/2}$ ↓ from 24 to 11 hours	Co-administration should be avoided, if possible. Consider alternatives for dapsone.
	Rifapentine[a]	↓ Dapsone expected	Co-administration should be avoided, if possible. Consider alternatives for dapsone.
Dasabuvir Ombitasvir Paritaprevir Ritonavir	Artemether/ Lumefantrine	↑ Artemether and lumefantrine possible	Use with caution. Monitor for artemether- and lumefantrine-associated toxicities.
	Atovaquone	↔ Atovaquone (based on data from atovaquone and ritonavir/ atazanavir interaction)	No dosage adjustment necessary.
	Bedaquiline	↑ Bedaquiline expected	Co-administration should be avoided, if possible. Consider alternative HCV regimen.
	Clarithromycin	↑ Clarithromycin and paritaprevir expected; ↑ ombitasvir and dasabuvir possible	Co-administration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
	Erythromycin	↑ Erythromycin expected and paritaprevir expected; ↑ ombitasvir and dasabuvir possible	Co-administration should be avoided, if possible. Consider azithromycin in place of erythromycin.
	Itraconazole	↑ Itraconazole and paritaprevir expected; ↑ ombitasvir and dasabuvir possible	Itraconazole doses >200 mg/day are not recommended unless dosing is guided by itraconazole levels. Monitor for itraconazole and HCV regimen-associated toxicities.
	Posaconazole	↑ Posaconazole and paritaprevir expected; ↑ ombitasvir and dasabuvir possible	Monitor for posaconazole and HCV regimen-associated toxicities. Monitor posaconazole conc. and adjust dose if necessary.
	Rifabutin[a]	↑ Rifabutin expected; ↓ paritaprevir possible	Co-administration should be avoided if possible. With co-administration, decrease rifabutin dose to 150 mg/ day and monitor rifabutin conc. Monitor HCV regimen for efficacy.
	Rifampin[a]	↓ Paritaprevir, ritonavir, ombitasvir, and dasabuvir expected	Do not co-administer.
	Rifapentine[a]	↓ Paritaprevir, ritonavir, ombitasvir, and dasabuvir expected	Do not co-administer.
	Voriconazole	Voriconazole AUC ↓ 39% (with ritonavir); ↑ paritaprevir expected	Co-administer only if the benefits outweigh the risk. Monitor voriconazole conc. to guide dosage adjustments.

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Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Doxycycline	Atovaquone	Atovaquone concentration ↓ by approximately 40% with tetracycline. No interaction study with doxycycline.	Dose adjustment not established; if co-administered, take atovaquone with fatty meal and monitor for decreased atovaquone efficacy.
	Rifabutin[a]	No data. ↓ Doxycycline possible.	Monitor closely for doxycycline efficacy or consider alternative therapy.
	Rifampin[a]	Doxycycline AUC ↓ by 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	↑ Elbasvir and grazoprevir expected	Co-administration should be avoided, if possible. If co-administered, monitor closely for hepatotoxicity. Consider azithromycin in place of clarithromycin.
	Itraconazole	↑ Elbasvir and grazoprevir expected	Co-administration should be avoided, if possible. If co-administered, monitor closely for hepatotoxicity.
	Posaconazole	↑ Elbasvir and grazoprevir expected	Co-administration should be avoided, if possible. If co-administered, monitor closely for hepatotoxicity.
	Rifabutin[a]	↓ Elbasvir and grazoprevir possible	Co-administration should be avoided if possible. Consider alternative HCV regimen.
	Rifampin[a]	Grazoprevir AUC ↓ 7%, C_{24} ↓ 90%; ↓ elbasvir expected	Do not co-administer.
	Rifapentine[a]	↓ Elbasvir and grazoprevir possible	Do not co-administer.
	Voriconazole	↑ Elbasvir and grazoprevir expected	Co-administration should be avoided if possible. If co-administered, monitor closely for hepatotoxicity.
Erythromycin	Artemether/ Lumefantrine	↑ Lumefantrine possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Bedaquiline	↑ Bedaquiline possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Chloroquine	↑ Chloroquine possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Daclatasvir	↑ Daclatasvir possible	No dosage adjustment. Monitor for daclatasvir-associated toxicities.
	Dasabuvir Ombitasvir Paritaprevir Ritonavir	↑ Erythromycin and paritaprevir expected; ↑ ombitasvir and dasabuvir possible	Co-administration should be avoided, if possible. Consider azithromycin in place of erythromycin.
	Fluconazole	↑ Erythromycin possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Itraconazole	Itraconazole AUC ↑ 36%; ↑ erythromycin possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Mefloquine	↑ Mefloquine possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Posaconazole	↑ Erythromycin expected	Do not co-administer. Consider azithromycin in place of erythromycin.

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

Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	Quinine	↑ Quinine expected; ↑ erythromycin possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Rifabutin[a]	↓ Erythromycin possible; ↑ rifabutin possible	Use with caution. Consider azithromycin in place of erythromycin. If co-administered, monitor for erythromycin efficacy or rifabutin toxicities (e.g., uveitis).
	Rifampin[a]	↓ Erythromycin expected	Consider azithromycin in place of erythromycin. If co-administered, monitor for erythromycin efficacy.
	Rifapentine[a]	↓ Erythromycin expected	Consider azithromycin in place of erythromycin. If co-administered, monitor for erythromycin efficacy.
	Simeprevir	Simeprevir AUC ↑ 647%, C_{min} ↑ 1,174%; erythromycin AUC ↑ 90%, C_{min} ↑ 208%	Do not co-administer. Consider azithromycin in place of erythromycin.
	Voriconazole	↑ Erythromycin expected	Do not co-administer. Consider azithromycin in place of erythromycin.
Fluconazole	Artemether/ Lumefantrine	↑ Lumefantrine possible	Co-administration should be avoided, if possible. If co-administered, monitor for lumefantrine toxicities (e.g., QT prolongation).
	Bedaquiline	↑ Bedaquiline possible	Co-administration should be avoided, if possible. If co-administered, monitor for bedaquiline toxicities (e.g., QT prolongation).
	Chloroquine	↑ Chloroquine possible	Co-administration should be avoided, if possible. If co-administered, monitor for chloroquine toxicities (e.g., QT prolongation).
	Clarithromycin	Clarithromycin AUC ↑ 18%, C_{min} ↑ 33%	No dose adjustment necessary in patients with normal renal function. Monitor for clarithromycin toxicity.
	Daclatasvir	↑ Daclatasvir possible	No dosage adjustment. Monitor for daclatasvir-associated toxicities.
	Erythromycin	↑ Erythromycin possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Mefloquine	↑ Mefloquine possible	Co-administration should be avoided, if possible. If co-administered, monitor for mefloquine toxicities (e.g., QT prolongation).
	Quinine	↑ Quinine expected; ↑ fluconazole possible	Co-administration should be avoided, if possible. If co-administered, monitor for quinine and fluconazole toxicity (e.g., QT prolongation).
	Rifabutin[a]	Rifabutin AUC ↑ 80%; ↔ fluconazole	Use with caution. Monitor for rifabutin-associated toxicities (e.g., uveitis). Consider monitoring rifabutin conc.; may need to lower rifabutin dose to 150 mg/day.
	Rifampin[a]	Fluconazole AUC ↓ 23% to 56%	Monitor for antifungal efficacy; may need to raise fluconazole dose.
	Rifapentine[a]	↓ Fluconazole expected	Monitor for antifungal efficacy; may need to raise fluconazole dose.
	Simeprevir	↑ Simeprevir possible	Do not co-administer.
Itraconazole	Artemether/ Lumefantrine	↑ Lumefantrine expected	Co-administration should be avoided, if possible. If co-administered, monitor for lumefantrine toxicities (e.g., QT prolongation).

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Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	Bedaquiline	↑ Bedaquiline expected	Co-administration should be avoided, if possible. If co-administered, monitor for bedaquiline toxicities (e.g., QT prolongation).
	Chloroquine	↑ Chloroquine expected	Co-administration should be avoided, if possible. If co-administered, monitor for chloroquine toxicities (e.g., QT prolongation).
	Clarithromycin	↑ Itraconazole and clarithromycin expected	Co-administration should be avoided, if possible. Consider azithromycin in place of clarithromycin. If co-administered, monitor for toxicities of both itraconazole and clarithromycin (e.g., QT prolongation), consider monitoring itraconazole conc. and adjusting dose accordingly.
	Daclatasvir	↑ Daclatasvir expected	Reduce daclatasvir dose to 30 mg once daily.
	Dasabuvir Ombitasvir Paritaprevir Ritonavir	↑ Itraconazole and paritaprevir expected; ↑ ombitasvir and dasabuvir possible	Itraconazole doses >200 mg/day are not recommended unless dosing is guided by itraconazole levels. Monitor for itraconazole and HCV regimen-associated toxicities.
	Elbasvir/ Grazoprevir	↑ Elbasvir and grazoprevir expected	Co-administration should be avoided, if possible. If co-administered, monitor closely for hepatotoxicity.
	Erythromycin	Itraconazole AUC ↑ 36%; ↑ erythromycin possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Mefloquine	↑ Mefloquine expected	Co-administration should be avoided, if possible. If co-administered, monitor for mefloquine toxicities (e.g., QT prolongation).
	Quinine	↑ Quinine expected; ↑ itraconazole possible	Co-administration should be avoided, if possible. If used concomitantly, monitor for quinine and itraconazole toxicity (e.g, QT prolongation), monitor itraconazole conc. and adjust dose accordingly.
	Rifabutin[a]	Itraconazole AUC ↓ 70%; ↑ rifabutin expected	Do not co-administer. Consider alternative antifungal and/or antimycobacterial agent(s).
	Rifampin[a]	Itraconazole AUC ↓ 64% to 88%	Do not co-administer. Consider alternative antifungal and/or antimycobacterial agent(s).
	Rifapentine[a]	↓ Itraconazole expected	Do not co-administer. Consider alternative antifungal and/or antimycobacterial agent(s).
	Simeprevir	↑ Simeprevir expected	Do not co-administer.
Ledipasvir/ Sofosbuvir	Rifabutin[a]	↓ Ledipasvir and sofosbuvir expected	Do not co-administer.
	Rifampin[a]	Ledipasvir AUC ↓ 59%; sofosbuvir AUC ↓ 72%	Do not co-administer.
	Rifapentine[a]	↓ Ledipasvir and sofosbuvir expected	Do not co-administer.
	Simeprevir	Ledipasvir AUC ↑ 92%; simeprevir AUC ↑ 116%	Do not co-administer.
	TAF	Ledipasvir AUC ↑ 79%	No dosage adjustment.
	TDF	TDF AUC ↑ 98% (when given with EFV/FTC) TDF AUC ↑ 40% (when given with RPV/FTC) When used with EVG/c/TDF/FTC, ↑ TDF and ledipasvir expected	Monitor for TDF-associated toxicities when coadministered with PI/r, PI/c, or EFV. Consider an alternative to PI/r plus TDF/FTC or alternative HCV therapy if possible. Do not co-administer with EVG/c/TDF/FTC. Consider TAF in place of TDF.

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 9 of 15)

Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Linezolid	Rifabutin[a]	No data. ↓ Linezolid possible.	Monitor for linezolid efficacy.
	Rifampin[a]	Linezolid AUC ↓ 32%	Monitor for linezolid efficacy.
	Rifapentine[a]	No data. ↓ Linezolid possible.	Monitor for linezolid efficacy.
Mefloquine	Clarithromycin	↑ Mefloquine expected	Use with caution. Consider azithromycin in place of clarithromycin. If co-administered, monitor for mefloquine toxicity (e.g., QT prolongation).
	Erythromycin	↑ Mefloquine possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Fluconazole	↑ Mefloquine possible	Co-administration should be avoided, if possible. If co-administered, monitor for mefloquine toxicities (e.g., QT prolongation).
	Itraconazole	↑ Mefloquine expected	Co-administration should be avoided, if possible. If co-administered, monitor for mefloquine toxicities (e.g., QT prolongation).
	Posaconazole	↑ Mefloquine expected	Co-administration should be avoided, if possible. If co-administered, monitor for mefloquine toxicities (e.g., QT prolongation).
	Rifabutin[a]	↓ Mefloquine possible	Monitor for mefloquine efficacy.
	Rifampin[a]	Mefloquine AUC ↓ 68%	Do not co-administer. Use alternative antimalarial drug or rifabutin.
	Rifapentine[a]	↓ Mefloquine expected	Do not co-administer. Use alternative antimalarial drug or rifabutin.
	Voriconazole	↑ Mefloquine expected	Co-administration should be avoided, if possible. If co-administered, monitor for mefloquine toxicities (e.g., QT prolongation).
Posaconazole	Artemether/ Lumefantrine	↑ Lumefantrine expected	Co-administration should be avoided, if possible. If co-administered, monitor for lumefantrine toxicities (e.g., QT prolongation).
	Bedaquiline	↑ Bedaquiline expected	Co-administration should be avoided, if possible. If co-administered, monitor for bedaquiline toxicities (e.g., QT prolongation).
	Chloroquine	↑ Chloroquine expected	Co-administration should be avoided, if possible. If co-administered, monitor for chloroquine toxicities (e.g., QT prolongation).
	Clarithromycin	↑ Clarithromycin expected	Co-administration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
	Daclatasvir	↑ Daclatasvir expected	Reduce daclatasvir dose to 30 mg once daily.
	Dasabuvir Ombitasvir Paritaprevir Ritonavir	↑ Posaconazole and paritaprevir expected; ↑ ombitasvir and dasabuvir possible	Monitor for posaconazole and HCV regimen-associated toxicities. Monitor posaconazole conc. and adjust dose if necessary.
	Elbasvir/ Grazoprevir	↑ Elbasvir and grazoprevir expected	Co-administration should be avoided, if possible. If co-administered, monitor closely for hepatotoxicity.
	Erythromycin	↑ Erythromycin expected	Do not co-administer. Consider azithromycin in place of erythromycin.

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 10 of 15)

Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	Dasabuvir Ombitasvir Paritaprevir Ritonavir	↑ Posaconazole and paritaprevir expected; ↑ ombitasvir and dasabuvir possible	Monitor for posaconazole and HCV regimen-associated toxicities. Monitor posaconazole conc. and adjust dose if necessary.
	Elbasvir/grazoprevir	↑ Elbasvir and grazoprevir expected	Co-administration should be avoided, if possible. If co-administered, monitor closely for hepatotoxicity.
	Erythromycin	↑ Erythromycin expected	Do not co-administer. Consider azithromycin in place of erythromycin.
	Mefloquine	↑ Mefloquine expected	Co-administration should be avoided, if possible. If co-administered, monitor for mefloquine toxicities (e.g., QT prolongation).
	Quinine	↑ Quinine expected; ↑ posaconazole possible	Co-administration should be avoided, if possible. If co-administered, monitor for quinine toxicities (e.g., QT prolongation).
	Rifabutin[a]	Posaconazole AUC ↓ 49%; rifabutin AUC ↑ 72%	Co-administration should be avoided, if possible. If co-administered, monitor posaconazole and rifabutin conc. and adjust doses accordingly; monitor for clinical response to posaconazole and rifabutin toxicities (e.g., uveitis).
	Rifampin[a]	↓ Posaconazole expected	Co-administration should be avoided, if possible. If co-administered, monitor posaconazole conc. and adjust dose accordingly; monitor for clinical response.
	Rifapentine[a]	↓ Posaconazole expected	Co-administration should be avoided, if possible, or monitor posaconazole conc. and adjust dose accordingly; monitor clinical response.
	Simeprevir	↑ Simeprevir expected	Do not co-administer.
Quinine	Clarithromycin	↑ Quinine expected; ↑ clarithromycin possible	Do not co-administer. Consider azithromycin in place of clarithromycin.
	Erythromycin	↑ Quinine expected; ↑ erythromycin possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Fluconazole	↑ Quinine expected; ↑ fluconazole possible	Co-administration should be avoided, if possible. If co-administered, monitor for quinine and fluconazole toxicity (e.g., QT prolongation).
	Itraconazole	↑ Quinine expected; ↑ itraconazole possible	Co-administration should be avoided, if possible. If used concomitantly, monitor for quinine and itraconazole toxicity (e.g., QT prolongation), monitor itraconazole conc. and adjust dose accordingly.
	Posaconazole	↑ Quinine expected; ↑ posaconazole possible	Co-administration should be avoided, if possible. If co-administered, monitor for quinine toxicities (e.g., QT prolongation).
	Rifabutin[a]	↓ Quinine possible; ↑ rifabutin possible	Monitor for quinine efficacy. Monitor rifabutin conc. and toxicity (e.g., uveitis).
	Rifampin[a]	Quinine AUC ↓ 75% to 85%	Do not co-administer.
	Rifapentine[a]	↓ Quinine expected	Do not co-administer.
	Voriconazole	↑ Quinine expected	Co-administration should be avoided, if possible. If co-administered, monitor for quinine toxicities (e.g., QT prolongation).
Rifabutin[a]	Artemether/ Lumefantrine	↓ Artemether, DHA, and lumefantrine expected	Use with caution. Monitor for antimalarial efficacy.

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

Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	Atovaquone	Atovaquone C_{SS} ↓ 34%; rifabutin C_{SS} ↓ 19%	Dose adjustment not established; if co-administered, take atovaquone with fatty meal and monitor for decreased atovaquone efficacy.
	Bedaquiline	↓ Bedaquiline possible	If co-administered, monitor for bedaquiline efficacy.
	Caspofungin	No data. ↓ Caspofungin possible.	Monitor for antifungal efficacy. Dose not established. Consider increasing caspofungin dose to 70 mg/day.
	Chloroquine	↓ Chloroquine expected	Monitor for chloroquine efficacy.
	Clarithromycin	Clarithromycin AUC ↓ by 44%; 14-OH AUC ↑ 57%; rifabutin AUC ↑ 76% to 99%; des-Rbt AUC ↑ 375%	Use with caution. Consider azithromycin in place of clarithromycin. If co-administered, consider reducing rifabutin dose, monitoring clarithromycin and rifabutin conc., and monitoring for rifabutin-associated toxicities (e.g., uveitis).
	Daclatasvir	↓ Daclatasvir expected	Dose not established. Consider increase daclatasvir dose to 90 mg once daily and monitoring for therapeutic efficacy.
	Dasabuvir Ombitasvir Paritaprevir Ritonavir	↑ Rifabutin expected; ↓ paritaprevir possible	Co-administration should be avoided if possible. With co-administration, decrease rifabutin dose to 150 mg/day and monitor rifabutin conc. Monitor HCV regimen for efficacy.
	Dapsone	Dapsone AUC ↓ 27% to 40%	Co-administration should be avoided, if possible. Consider alternatives for dapsone.
	Doxycycline	No data. ↓ Doxycycline possible.	Monitor closely for doxycycline efficacy or consider alternative therapy.
	Elbasvir/ Grazoprevir	↓ Elbasvir and grazoprevir possible	Co-administration should be avoided, if possible. Consider alternative HCV regimen.
	Erythromycin	↓ Erythromycin possible; ↑ rifabutin possible	Use with caution. Consider azithromycin in place of erythromycin. If co-administered, monitor for erythromycin efficacy or rifabutin toxicities (e.g., uveitis).
	Fluconazole	Rifabutin AUC ↑ 80%; ↔ fluconazole	Use with caution. Monitor for rifabutin-associated toxicities (e.g., uveitis). Consider monitoring rifabutin conc.; may need to lower rifabutin dose to 150 mg/day.
	Itraconazole	Itraconazole AUC ↓ 70%; ↑ rifabutin expected	Do not co-administer. Consider alternative antifungal and/or antimycobacterial agent(s).
	Ledipasvir/ Sofosbuvir	↓ Ledipasvir and sofosbuvir expected	Do not co-administer.
	Linezolid	No data. ↓ Linezolid possible.	Monitor for linezolid efficacy.
	Mefloquine	↓ Mefloquine possible	Monitor for mefloquine efficacy.
	Posaconazole	Posaconazole AUC ↓ 49%; rifabutin AUC ↑ 72%	Co-administration should be avoided, if possible. If co-administered, monitor posaconazole and rifabutin conc. and adjust doses accordingly; monitor for clinical response to posaconazole and rifabutin toxicities (e.g., uveitis).
	Quinine	↓ Quinine possible; ↑ rifabutin possible	Monitor for quinine efficacy. Monitor rifabutin conc. and toxicity (e.g., uveitis).
	Simeprevir	↓ Simeprevir expected	Do not co-administer.
	Sofosbuvir	↓ Sofosbuvir expected	Do not co-administer.
	TAF	↓ TAF expected	Do not co-administer
	Velpatasvir/ Sofosbuvir	↓ Velpatasvir and sofosbuvir expected	Do not co-administer.

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

Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	Voriconazole	Voriconazole AUC ↓ 79%; rifabutin AUC ↑4-fold	Do not co-administer. Consider alternative antifungal and/or antimycobacterial agent(s). If coadministration is absolutely necessary, monitor voriconazole and rifabutin conc. to guide therapy.
Rifampin[a]	Artemether/ Lumefantrine	↓ Artemether, DHA, and lumefantrine AUC by 89%, 85%, and 68%, respectively	Do not co-administer.
	Atovaquone	Atovaquone C_{ss} ↓ 52% and $t_{1/2}$ ↓ 40%; rifampin C_{ss} ↑ 37%	Do not co-administer.
	Bedaquiline	Bedaquiline AUC ↓ 53%	Do not co-administer.
	Caspofungin	Caspofungin C_{min} ↓ 30%	Caspofungin dose should be ↑ to 70 mg/day.
	Chloroquine	↓ Chloroquine expected	Monitor for chloroquine efficacy.
	Clarithromycin	Mean clarithromycin conc. ↓ 87%; rifampin AUC ↑ 60%	Do not co-administer. Use azithromycin in place of clarithromycin.
	Daclatasvir	Daclatasvir AUC ↓ 79%	Do not co-administer.
	Dasabuvir Ombitasvir Paritaprevir Ritonavir	↓ Paritaprevir, ritonavir, ombitasvir, and dasabuvir expected	Do not co-administer.
	Dapsone	Dapsone conc. ↓ 7- to 10-fold and $t_{1/2}$ ↓ from 24 to 11 hours	Co-administration should be avoided, if possible. Consider alternatives for dapsone.
	Doxycycline	Doxycycline AUC ↓ by 59%	Use with caution. Monitor closely for doxycycline efficacy or consider alternative therapy.
	Elbasvir/ Grazoprevir	Grazoprevir AUC ↓ 7%, C_{24} ↓ 90%; ↓ elbasvir expected	Do not co-administer.
	Erythromycin	↓ Erythromycin expected	Consider azithromycin in place of erythromycin. If co-administered, monitor for erythromycin efficacy.
	Fluconazole	Fluconazole AUC ↓ by 23% to 56%	Monitor for antifungal efficacy. May need to increase fluconazole dose.
	Itraconazole	Itraconazole AUC ↓ 64% to 88%	Do not co-administer. Consider alternative antifungal and/or antimycobacterial agent(s).
	Ledipasvir/ Sofosbuvir	Ledipasvir AUC ↓ 59%; sofosbuvir AUC ↓ 72%	Do not co-administer.
	Linezolid	Linezolid AUC ↓ 32%	Monitor for linezolid efficacy.
	Mefloquine	Mefloquine AUC ↓ 68%	Do not co-administer. Use alternative antimalarial drug or rifabutin.
	Posaconazole	↓ Posaconazole expected	Co-administration should be avoided, if possible. If co-administered, monitor posaconazole conc. and adjust dose accordingly; monitor for clinical response.
	Quinine	Quinine AUC ↓ 75% to 85%	Do not co-administer.
	Simeprevir	Simeprevir C_{min} ↓92%, AUC ↓ 48%	Do not co-administer.
	Sofosbuvir	Sofosbuvir AUC ↓ 72%	Do not co-administer.
	TAF	↓ TAF expected	Do not co-administer
	Velpatasvir/ Sofosbuvir	Velpatasvir AUC ↓ 82%; sofosbuvir AUC ↓ 72%	Do not co-administer.
	Voriconazole	Voriconazole AUC ↓ 96%	Do not co-administer. Consider alternative antifungal and/or antimycobacterial agent(s).

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

Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Rifapentine[a]	Artemether/ Lumefantrine	↓ Artemether, DHA, lumefantrine expected	Do not co-administer.
	Atovaquone	↓ Atovaquone expected	Do not co-administer.
	Bedaquiline	Bedaquiline AUC ↓ 55% (with daily rifapentine)	Do not co-administer.
	Caspofungin	No data. ↓ Caspofungin possible.	Monitor for antifungal efficacy. Dose not established. Consider increasing caspofungin dose to 70 mg/day.
	Chloroquine	↓ Chloroquine expected	Monitor for chloroquine efficacy.
	Clarithromycin	↓ Clarithromycin expected; ↑ 14-OH and rifapentine expected	Use with caution. Consider azithromycin in place of clarithromycin. If co-administered, monitor for rifapentine-associated toxicities, consider monitoring clarithromycin and rifapentine conc. and adjusting doses accordingly.
	Daclatasvir	↓ Daclatasvir expected	Dose not established. Consider increasing daclatasvir dose to 90 mg once daily and monitoring for therapeutic efficacy
	Dapsone	↓ Dapsone expected	Co-administration should be avoided, if possible. Consider alternatives for dapsone.
	Dasabuvir Ombitasvir Paritaprevir Ritonavir	↓ Paritaprevir, ritonavir, ombitasvir, and dasabuvir expected.	Do not co-administer.
	Elbasvir/ Grazoprevir	↓ Elbasvir and grazoprevir possible	Do not co-administer.
	Doxycycline	No data. ↓ Doxycycline possible.	Monitor closely for doxycycline efficacy or consider alternative therapy.
	Erythromycin	↓ Erythromycin expected	Consider azithromycin in place of erythromycin. If co-administered, monitor for erythromycin efficacy.
	Fluconazole	↓ Fluconazole expected	Monitor for antifungal efficacy; may need to ↑ fluconazole dose.
	Itraconazole	↓ Itraconazole expected	Do not co-administer. Consider alternative antifungal and/or antimycobacterial agent(s).
	Ledipasvir/ Sofosbuvir	↓ Ledipasvir and sofosbuvir expected	Do not co-administer.
	Linezolid	No data. ↓ Linezolid possible.	Monitor for linezolid efficacy.
	Mefloquine	↓ Mefloquine expected	Do not co-administer. Use alternative antimalarial drug or rifabutin.
	Posaconazole	↓ Posaconazole expected	Co-administration should be avoided, if possible, or monitor posaconazole conc. and adjust dose accordingly; monitor for clinical response.
	Quinine	↓ Quinine expected	Do not co-administer.
	Simprevir	↓ Simeprevir expected	Do not co-administer.
	Sofosbuvir	↓ Sofosbuvir expected	Do not co-administer.
	TAF	↓ TAF expected	Do not co-administer
	Velpatasvir/ Sofosbuvir	↓ Velpatasvir and sofosbuvir expected	Do not co-administer.

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

Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	Voriconazole	↓ Voriconazole expected	Do not co-administer. Consider alternative antifungal and/or antimycobacterial agent(s).
Simeprevir	Clarithromycin	↑ Simeprevir expected	Do not co-administer. Consider azithromycin in place of clarithromycin.
	Daclatasvir	Simeprevir AUC ↑ 44%; daclatasvir AUC ↑ 96%	No dosage adjustment. Monitor for simeprevir- and daclatasvir-associated toxicities.
	Erythromycin	Simeprevir AUC ↑ 647%, C_{min} ↑ 1,174%; erythromycin AUC ↑ 90%, C_{min} ↑ 208%	Do not co-administer. Consider azithromycin in place of clarithromycin.
	Fluconazole	↑ Simeprevir possible	Do not co-administer.
	Itraconazole	↑ Simeprevir expected	Do not co-administer.
	Ledipasvir/Sofosbuvir	Ledipasvir AUC ↑ 92%; simeprevir AUC ↑ 116%	Do not co-administer.
	Posaconazole	↑ Simeprevir expected	Do not co-administer.
	Rifabutin[a]	↓ Simeprevir expected	Do not co-administer.
	Rifampin[a]	Simeprevir C_{min} ↓ 92%, AUC ↓ 48%	Do not co-administer.
	Rifapentine[a]	↓ Simeprevir expected	Do not co-administer.
	Voriconazole	↑ Simeprevir expected	Do not co-administer.
Sofosbuvir	Rifabutin[a]	↓ Sofosbuvir expected	Do not co-administer.
	Rifampin[a]	Sofosbuvir AUC ↓ 72%	Do not co-administer.
	Rifapentine[a]	↓ Sofosbuvir expected	Do not co-administer.
TAF	Ledipasvir/Sofosbuvir	Ledipasvir AUC ↑79%	No dosage adjustment.
	Rifabutin[a]	↓ TAF expected	Do not co-administer
	Rifampin[a]	↓ TAF expected	Do not co-administer
	Rifapentine[a]	↓ TAF expected	Do not co-adminster
	Velpatasvir/Sofosbuvir	TAF AUC ↓ 13%	No dosage adjustment.
TDF	Ledipasvir/ Sofosbuvir	TDF AUC ↑ 98% (when given with EFV/FTC) TDF AUC ↑ 40% (when given with RPV/FTC) When used with EVG/c/TDF/FTC, ↑ TDF and ledipasvir expected	Monitor for TDF-associated toxicities when coadministered with PI/r, PI/c, or EFV. Consider an alternative to PI/r plus TDF/FTC or alternative HCV therapy if possible. Do not co-administer with EVG/c/TDF/FTC. Consider TAF in place of TDF.
	Velpatasvir/ Sofosbuvir	TDF AUC ↑35% to 40% when given with EVG/c/FTC or RPV/FTC TDF AUC ↑ 81% when given with EFV/FTC	Monitor for TDF-associated toxicities with PI/r or EFV co-administration. Consider TAF in place of TDF.
Velpatasvir/ Sofosbuvir	Rifabutin[a]	↓ Velpatasvir and sofosbuvir expected	Do not co-administer.
	Rifampin[a]	Velpatasvir AUC ↓ 82%; sofosbuvir AUC ↓ 72%	Do not co-administer.
	Rifapentine[a]	↓ Velpatasvir and sofosbuvir expected	Do not co-administer.
	TAF	TAF AUC ↓ 13%	No dosage adjustment.
	TDF	TDF AUC ↑35% to 40% when given with EVG/c/FTC or RPV/FTC TDF AUC ↑ 81% when given with EFV/FTC	Monitor for TDF-associated toxicities with PI/r or EFV co-administration. Consider TAF in place of TDF.

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

Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Voriconazole	Artemether/ Lumefantrine	↑ Lumefantrine expected	Co-administration should be avoided, if possible. If co-administered, monitor for lumefantrine toxicities (e.g., QT prolongation).
	Bedaquiline	↑ Bedaquiline expected	Co-administration should be avoided, if possible. If co-administered, monitor for bedaquiline toxicities (e.g., QT prolongation).
	Chloroquine	↑ Chloroquine expected	Co-administration should be avoided, if possible. If co-administered, monitor for chloroquine toxicities (e.g., QT prolongation).
	Clarithromycin	↑ Clarithromycin expected	Co-administration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
	Daclatasvir	↑ Daclatasvir expected	Reduce daclatasvir dose to 30 mg once daily.
	Dasabuvir Ombitasvir Paritaprevir Ritonavir	Voriconazole AUC ↓ 39% (with ritonavir); ↑ paritaprevir expected	Co-administer only if the benefits outweigh the risks. Monitor voriconazole conc. to guide dosage adjustments.
	Elbasvir/Grazoprevir	↑ Elbasvir and grazoprevir expected	Co-administration should be avoided, if possible. If co-administered, monitor closely for hepatotoxicity.
	Erythromycin	↑ Erythromycin expected	Do not co-administer. Consider azithromycin in place of erythromycin.
	Mefloquine	↑ Mefloquine expected	Co-administration should be avoided, if possible. If co-administered, monitor for mefloquine toxicities (e.g., QT prolongation).
	Quinine	↑ Quinine expected	Co-administration should be avoided, if possible. If co-administered, monitor for quinine toxicities (e.g., QT prolongation).
	Rifabutin[a]	Voriconazole AUC ↓ 79%; rifabutin AUC ↑ 4-fold	Do not co-administer. Consider alternative antifungal and/or antimycobacterial agent(s). If coadministration is absolutely necessary, monitor voriconazole and rifabutin conc. to guide therapy.
	Rifampin[a]	Voriconazole AUC ↓ 96%	Do not co-administer. Consider alternative antifungal and/or antimycobacterial agent(s).
	Rifapentine[a]	↓ Voriconazole expected	Do not co-administer. Consider alternative antifungal and/or antimycobacterial agent(s).
	Simeprevir	↑ Simeprevir expected	Do not co-administer.

Key to Acronyms: 14-OH = active metabolite of clarithromycin; AUC = area under the curve; C_{24} = concentration at 24h post dose; C_{min} = minimum concentration; C_{ss} = concentration at steady state; CYP3A4 = Cytochrome P450 3A4; des-Rbt = desacetyl rifabutin; DHA = dihydroartemisinin; EFV = efavirenz; EVG = elvitegravir; FTC = emtricitabine; HCV = hepatitis C virus; PI/c = cobicistat-boosted protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; RPV = rilpivirine; $T_{1/2}$ = half-life; TAF = tenofovir alafenamide; TB = tuberculosis; TDF = tenofovir disoproxil fumarate

[a] Rifamycins are potent inducers of Phase I and Phase II drug-metabolizing reactions. Daily doses of rifampin are well studied, and induction increases over a week or more. Based on limited data, larger doses of rifampin (for example, 1200 mg) appear to produce the same maximum induction, 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, but may result in reduction of exposure of drugs that are CYP3A4 substrates. When a rifamycin is used with a potential interacting drug, close monitoring for clinical efficacy of the other agent is advised.