Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections

Updated: June 05, 2025
Reviewed: June 05, 2025

The potential exists for significant drug interactions and overlapping toxicities in children receiving medications for treatment or prevention of opportunistic infections (OIs). These children often receive other medications, including antiretrovirals, that interfere with the metabolism or elimination of OI medications. In particular, protease inhibitors and non-nucleoside reverse transcriptase inhibitors affect the cytochrome P450 or other transporter systems and may be associated with clinically significant drug interactions. The integrase strand transfer inhibitors cabotegravir and raltegravir are primarily metabolized by uridine diphosphate glucuronosyltransferase 1A1 and may be a suitable option when trying to minimize interactions with other drug classes.

Table 5 provides clinicians with information regarding known or suspected drug interactions between drugs commonly used for the treatment or prevention of HIV-associated OIs and treatment of HIV infection. Drug interaction information is generally obtained from studies involving healthy adult volunteers. Some pharmacokinetic data are available from studies involving adults with HIV, whereas data in children are extremely limited. New information continues to become available, and carefully reviewing each child's current medications, including prescription and over-the-counter medications, is important. Predicting the interaction potential is difficult when three or more drugs with similar metabolic pathways are coadministered, and significant interpatient variability amplifies these challenges. When possible, alternative agents with less drug interaction potential or use of therapeutic drug monitoring should be considered.

Drug Name	Toxicities	Recommendation
* The drug interactions included in this table were selected based on their potential clinical significance and are not inclusive of all potential drug interactions (see FDA Online Label Repository for complete information on drug interactions).		
Acyclovir	Overlapping Toxicities • Nephrotoxic drugs	Avoid other nephrotoxic drugs.
	Increased Concentrations (Both Drugs) and Overlapping Toxicities • *Antivirals*: valacyclovir, valganciclovir, ganciclovir, cidofovir • *ARVs:* tenofovir • *Immunosuppressive agents*: mycophenolate	Monitor for toxicities of these drugs.
Albendazole	Increased Albendazole Concentrations • *Anthelmintics*: praziquantel Decreased Albendazole Concentrations • *Anticonvulsants*: carbamazepine, phenobarbital, phenytoin • *Antivirals*: nirmatrelvir and ritonavir	Caution advised.
Amikacin	Overlapping Toxicities • *Antituberculars* (injectable): kanamycin, streptomycin • *Nephrotoxic or ototoxic drugs* • *Antimycobacterials*: capreomycin • ARVs: tenofovir • *Antivirals*: cidofovir	Caution advised. Avoid combining with cidofovir.
Amphotericin B Amphotericin B Lipid Complex Amphotericin B Liposome	Overlapping Toxicities • *Bone marrow suppressants*: corticosteroids • *Nephrotoxic drugs* • *Neuromuscular blockers*	Caution advised.

Drug Name	Toxicities	Recommendation
Artemether-Lumefantrine	Increased Drug Concentrations • *ARVs*: nevirapine	Monitor therapy when combined.
	Overlapping Toxicities • *ARVs*: PIs • *Antibacterials*: fluoroquinolones, macrolides • *Antifungals*: fluconazole, voriconazole • *Antimalarials*: quinidine, quinine • *Psychotropics*: quetiapine, tricyclic antidepressants	Coadministration with fluconazole or voriconazole should be avoided. For all other drugs, coadministration should be avoided, if possible; monitor for toxicities (QT prolongation).
Atovaquone	Decreased Atovaquone Concentrations • *Antimycobacterials*: rifampin, rifabutin • *ARVs*: lopinavir/ritonavir, atazanavir/ritonavir • *Antibiotics*: doxycycline	Coadministration of atovaquone and rifampin or atovaquone and rifabutin should be avoided.
Azithromycin	Overlapping Toxicities • *Antimalarials*: artemether/lumefantrine, chloroquine, quinine	Caution advised. Increased risk of QT prolongation.
Bedaquiline	Overlapping Toxicities • QT-prolonging agents	Bedaquiline may enhance the QTc-prolonging effects. Avoid concomitant use.
	• *Fecal microbiota (live)* (oral and rectal)	Avoid concomitant use.
Caspofungin	Decreased Caspofungin Concentrations • *Anticonvulsants*: phenytoin • *Antimycobacterials*: rifampin • A*RVs*: efavirenz, nevirapine	Increase in dose of caspofungin is recommended when coadministered with CYP450 inducers.
Cidofovir	Overlapping Toxicities • *Antibacterials*: aminoglycosides • *Antivirals*: foscarnet • *ARVs*: tenofovir • *Nephrotoxic drugs*	Monitor for toxicities of these drugs. Prehydrate with IV normal saline and probenecid to avoid nephrotoxicity.

Drug Name	Toxicities	Recommendation
Ciprofloxacin	Decreased Ciprofloxacin Absorption • *ARVs*: didanosine • *Minerals*: ferrous sulfate, zinc • *Gastrointestinal drugs*: antacids, sucralfate, magnesium-containing laxatives	Give oral ciprofloxacin 2 hours before or 6 hours after drugs that may interfere with absorption.
	Overlapping Toxicities • *Antimalarials*: artemether/lumefantrine, quinine • *Antibacterials:* clarithromycin	Caution advised.
	• *Fecal microbiota (live)* (oral and rectal)	Avoid concomitant use.
Clarithromycin	Increased Clarithromycin Concentrations • *ARVs:* atazanavir/ritonavir, lopinavir/ritonavir • *Antifungals*: itraconazole (itraconazole concentrations also increased)	Caution advised. Concern for QTc prolongation. Decrease clarithromycin dose or consider switching to azithromycin, which has less potential for drug interactions.
	Increased Concomitant Drug Concentrations • *ARVs*: etravirine	Consider alternative ARV.
	Decreased Clarithromycin Concentrations • *ARVs*: efavirenz, etravirine, nevirapine • *Antimycobacterials*: rifampin, rifabutin (rifabutin concentrations also increased)	Consider switching to azithromycin, which has less potential for drug interaction. For concomitant use of rifabutin and clarithromycin, consider decreasing dose of rifabutin or switching to azithromycin.
	Overlapping Toxicities • *Fecal microbiota (live)* (oral/rectal)	Clarithromycin may reduce fecal microbiota (live) (rectal) effectiveness.
Clindamycin	Decreased Clindamycin Antibacterial Efficacy • *Antibacterials*: chloramphenicol, erythromycin Overlapping Toxicities • *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.

Drug Name	Toxicities	Recommendation
Cycloserine	Overlapping Toxicities • *Antimycobacterials*: ethionamide, isoniazid	Caution advised.
	• *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.
Dapsone	Decreased Dapsone Concentrations • *Antimycobacterials*: rifampin	Coadministration should be avoided if possible. Consider alternatives for dapsone or use rifabutin.
	Decreased Dapsone Absorption • *ARVs*: atazanavir, didanosine suspension • *Gastrointestinal drugs*: antacids	For coadministration with antacids or didanosine suspension, give dapsone 1 hour before or 4 hours after the other medication.
	Overlapping Toxicities • *Bone marrow suppressants* or drugs associated with hemolysis	Caution advised.
	• *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.
Doxycycline	Decreased Doxycycline Concentrations • *Anticonvulsants*: carbamazepine, phenytoin • *Antimycobacterials*: rifampin	Potential for decreased doxycycline efficacy. Monitor for therapeutic failure.
	Overlapping Toxicities • *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.
Erythromycin	Increased Concentrations of Erythromycin • *Antifungals*: itraconazole (itraconazole concentrations also increased) Increased Concomitant Drug Concentrations • *ARVs*: tenofovir	Monitor for toxicities of both drugs, potential for QT prolongation.
	Overlapping Toxicities • *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.

Drug Name	Toxicities	Recommendation
Ethambutol	Overlapping Toxicities • *Neurotoxic drugs*	Caution advised.
	• *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.
Ethionamide	Potential for Increased Toxicity Due to Overlapping Toxicity • *Neurotoxic drugs* • *Antimycobacterials*: cycloserine, isoniazid	Caution advised.
	• *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.
Fluconazole	Decreased Fluconazole Levels • *Anticonvulsants*: phenytoin • *Antimycobacterials:* rifampin • *ARVs*: rilpivirine	Monitor for efficacy. May need to increase fluconazole dose.
	Increases Concomitant Drug Concentrations • *ARVs*: etravirine, nevirapine, saquinavir, tipranavir	May need to decrease dose of saquinavir. Avoid tipranavir with high doses of fluconazole (maximum fluconazole dose in adults: 200 mg). Caution advised with etravirine.
	• *Antineoplastics*: venetoclax	Decrease venetoclax dose by at least 50% in children requiring concomitant treatment.
	• *Antimycobacterials*: rifabutin	May need to decrease dose of rifabutin.
	• *Statins*: atorvastatin, lovastatin, simvastatin	Do not coadminister with simvastatin or lovastatin. Avoid use of atorvastatin if possible. Alternative statins, such as fluvastatin, rosuvastatin, and pravastatin, are preferred, or discontinue statin during antifungal therapy.
Flucytosine	Increased Flucytosine Concentrations • *Nephrotoxic drugs* Overlapping Toxicities • *QT-prolonging drugs*	Caution advised. Dose adjustments with therapeutic drug monitoring recommended with impaired renal function.

Drug Name	Toxicities	Recommendation
Foscarnet	Overlapping Toxicities • *Antivirals*: cidofovir • *Anti-pneumocystis drugs*: pentamidine • *Nephrotoxic drugs*	Monitor for toxicities of these drugs.
Ganciclovir	Increased Ganciclovir Concentrations • *ARVs*: tenofovir (concentrations also increased)	Monitor for toxicities of these drugs.
	Increased Concomitant Drug Concentrations • *ARVs*: didanosine	Caution advised.
	Overlapping Toxicities • *Antibacterials*: imipenem-cilastatin • *ARVs*: zidovudine • *Bone marrow suppressants* • *Nephrotoxic drugs*	Caution advised. Increased risk of seizures with imipenem-cilastatin.
Isavuconazole	Increased Concomitant Drug Concentrations • *Antineoplastics*: venetoclax	Reduce venetoclax dose by at least 50% in children requiring concomitant treatment. Resume previous venetoclax dose two to three days after discontinuation of isavuconazole.
Isoniazid	Decreased Isoniazid Concentrations • *Corticosteroids*: glucocorticoids (e.g., prednisolone)	Use with caution.
	Decreased Isoniazid Absorption • *Gastrointestinal drugs*: antacids	Caution advised. Take ≥1 hour before aluminum-containing antacids.
	Increased Concomitant Drug Concentrations • *Sedatives/hypnotics*: diazepam	Caution advised.
	Decreased Concomitant Drug Concentrations • *Antifungals*: itraconazole, ketoconazole	Coadministration should be avoided, if possible.

Drug Name	Toxicities	Recommendation
	Overlapping Toxicities • *Antimycobacterials*: cycloserine, ethionamide, itraconazole • *Hepatotoxic drugs* • *Neurotoxic drugs*	Caution advised.
Itraconazole and Ketoconazole	Increased Azole Concentrations • *Antibacterials*: clarithromycin, ciprofloxacin, erythromycin • *ARVs*: PIs	Monitor for toxicities and monitor concentrations. Consider azithromycin instead of other macrolides. High doses of itraconazole are not recommended with PIs.
	Increased Concomitant Drug Concentrations • *ARVs*: etravirine, maraviroc, PIs	Caution advised. Monitor for toxicities. Decrease adult maraviroc dose to 150 mg twice daily.
	• *Statins*: atorvastatin, lovastatin, simvastatin	Do not coadminister with simvastatin or lovastatin. Avoid use of atorvastatin if possible. Alternative statins such as fluvastatin, rosuvastatin, and pravastatin are preferred; alternatively, discontinue statin during antifungal therapy.
	• *Antibacterials:* clarithromycin, erythromycin	Consider switching to azithromycin, which has less potential for drug interaction.
	• *Sedatives/hypnotics*: alprazolam, diazepam, midazolam	Coadministration of midazolam and alprazolam should be avoided. Coadministration of diazepam should be avoided, if possible.
	• *Antimalarial:* quinidine	Coadministration of quinidine should be avoided. QT prolongation may occur.
	Decreased Azole Concentrations • *ARVs*: efavirenz, etravirine, nevirapine, rilpivirine	Monitor concentrations. Coadministration of efavirenz should be avoided if possible.
	• *Anticonvulsants*: carbamazepine, fosphenytoin	Monitor concentrations.
	• *Antimycobacterials*: isoniazid, rifabutin, rifampin, rifapentine	Coadministration with rifampin should be avoided. Coadministration with rifabutin should be avoided, if possible. Monitor for toxicities and monitor concentrations.

Drug Name	Toxicities	Recommendation
	Decreased Azole Absorption • *ARVs*: didanosine • *Gastrointestinal drugs*: antacids, anticholinergics/antispasmodics, histamine H2-receptor antagonists, omeprazole, sucralfate	Monitor concentrations.
Mefloquine	Decreased Mefloquine Concentrations • *Antimalarials*: quinine • *Antimycobacterials:* rifampin	Monitor for decreased mefloquine efficacy. Coadministration of rifampin should be avoided, if possible; use rifabutin instead.
	Decreased Concomitant Drug Concentrations • *ARVs*: ritonavir, possibly other PIs	Monitor for virologic failure of PI-containing ART regimen.
	Overlapping Toxicities • *Antimalarials*: quinine • *QT-prolonging drugs*	Avoid coadministration, if possible. Monitor for toxicities (EKG changes, cardiac arrest, and seizures with quinine). If coadministered with quinine, give mefloquine at least 12 hours after last dose of quinine.
Nitazoxanide	Increased Concomitant Drug Concentrations • *Anticonvulsants*: phenytoin	Potential for interaction with other medications that are highly protein-bound. Use with caution as interaction will increase concentrations of concomitant medication.
Pentamidine	Overlapping Toxicities • *Antivirals*: foscarnet	Coadministration should be avoided, if possible. Monitor for toxicities (hypocalcemia, QT prolongation).
	• *ARVs*: didanosine, PIs	Coadministration should be avoided, if possible. Monitor for toxicities (QT prolongation with PIs; pancreatitis for didanosine).
	• *Bone marrow suppressants*	Monitor for toxicities.
	• *Nephrotoxic drugs*	Monitor for toxicities.
	• *QT-prolonging drugs*	Monitor for toxicities. Avoid coadministration, if possible.
	• *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.

Drug Name	Toxicities	Recommendation
Posaconazole	Decreased Posaconazole Drug Concentrations • *ARVs*: efavirenz, fosamprenavir, rilpivirine	Coadministration of fosamprenavir should be avoided. Coadministration of efavirenz should be avoided, if possible. If coadministered, monitor posaconazole concentrations and adjust dose accordingly.
	• *Anticonvulsants*: phenytoin	Coadministration should be avoided, if possible. If coadministered, monitor posaconazole concentrations and adjust dose accordingly.
	• *Antimycobacterials*: rifabutin, rifampin	Coadministration should be avoided, if possible. If coadministered, monitor posaconazole concentrations and adjust dose accordingly.
	Increased Concomitant Drug Concentrations • *ARVs*: atazanavir, etravirine, lopinavir, ritonavir, saquinavir	Coadministration should be avoided, if possible. Monitor for toxicities. Consider monitoring concentrations and adjust dose as necessary.
	• *Antibacterials*: clarithromycin, erythromycin	Coadministration should be avoided.
	• *Anticonvulsants*: phenytoin	Coadministration should be avoided.
	• *Sedatives/hypnotics*: alprazolam, diazepam, midazolam	Coadministration should be avoided, if possible. Monitor for toxicities.
	• *Antimycobacterials*: rifabutin	Coadministration should be avoided.
	• *Statins*: atorvastatin, lovastatin, simvastatin • *Antineoplastics*: venetoclax • *Immunosuppressives*: sirolimus, tacrolimus	Do not coadminister with simvastatin or lovastatin. Avoid use of atorvastatin if possible. Alternative statins such as fluvastatin, rosuvastatin, and pravastatin are preferred; alternatively, discontinue statin during antifungal therapy.
	• *Antimalarials*: halofantrine, lumefantrine, mefloquine, quinidine, quinine	Coadministration should be avoided.
	Decreased Concomitant Drug Concentrations • *ARVs*: fosamprenavir	Coadministration should be avoided.
	• *QT-prolonging drugs*	Use with caution. Monitor for toxicities.

Drug Name	Toxicities	Recommendation
Proguanil	Decreased Proguanil Concentrations • *ARVs*: Atazanavir/ritonavir, efavirenz, lopinavir/ritonavir	Use with caution.
Pyrazinamide	Overlapping Toxicities • *Antimycobacterials*: ethionamide, rifampin • *Hepatotoxic drugs*	Use with caution. Monitor for hepatotoxicity.
	• *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.
Quinidine	Increased Quinidine Concentrations • *ARVs*: PIs	Coadministration of PIs should be avoided. Increased risk of arrhythmia. Coadministration may be necessary in the presence of life-threatening, severe malaria and in the absence of other therapy, while artesunate is obtained from the CDC.
	• *Antifungals*: itraconazole, posaconazole, voriconazole	Coadministration should be avoided. Increased risk of arrhythmia.
	Decreased Quinidine Concentrations • *ARVs*: etravirine	Use with caution. Monitor quinidine levels.
	Increased Concomitant Drug Concentrations • *Tricyclic antidepressants*	Coadministration should be avoided, if possible. Monitor for toxicities.
	Overlapping Toxicities • *QT-prolonging drugs*	Coadministration should be avoided, if possible. Monitor for toxicities (QT prolongation).
Ribavirin	Increased Concomitant Drug Concentrations • *ARVs*: didanosine	Coadministration should be avoided. Potential for increased risk of pancreatitis and mitochondrial toxicity.
	Decreased Concomitant Drug Concentrations • *ARVs*: stavudine, zidovudine	Coadministration should be avoided, if possible.
	Overlapping Toxicities • *ARVs*: zidovudine, all NRTIs	Coadministration should be avoided, if possible. Monitor for toxicities (anemia for zidovudine, lactic acidosis for all NRTIs).

Drug Name	Toxicities	Recommendation
Rifabutin	Increased Rifabutin Concentrations • *ARVs*: cobicistat, PIs	Use with caution. Monitor for rifabutin toxicity. Reduce rifabutin dose if coadministered with PIs.
	• Fluconazole	Use with caution. Monitor for rifabutin toxicity. Consider rifabutin dose reduction.
	• Voriconazole, itraconazole, posaconazole	Coadministration should be avoided, if possible. If coadministered, consider TDM and monitor for rifabutin toxicities (and azole clinical efficacy).
	• *Antibacterials*: clarithromycin	Coadministration should be avoided, if possible. Monitor for rifabutin toxicity. Consider rifabutin dose reduction or using azithromycin instead.
	Increased Concomitant Drug Concentrations • *ARVs*: didanosine	Use with caution. Monitor for didanosine toxicity.
	Decreased Rifabutin Concentrations • *ARVs*: efavirenz, etravirine	Use with caution. Higher rifabutin dose required with efavirenz. Consider TDM.
	Decreased Concomitant Drug Concentrations • *ARVs*: rilpivirine, bictegravir, cabotegravir, dolutegravir, raltegravir, lenacapavir	Coadministration should be avoided.
	• *ARVs*: etravirine, maraviroc, saquinavir	Coadministration should be avoided, if possible.
	• *Antibacterials*: atovaquone, dapsone	Use with caution. Monitor for dapsone treatment failure.
	• *Antifungals*: azoles (except for fluconazole)	Coadministration should be avoided, if possible. If coadministered, consider TDM and monitor for rifabutin toxicities (and azole clinical efficacy).
	• *Contraceptives*: oral	Oral contraceptives less effective. Additional non-hormonal contraceptive or alternative recommended.

Drug Name	Toxicities	Recommendation
Rifampin	Decreased Concomitant Drug Concentrations • *Contraceptives*: oral	Oral contraceptives less effective. Additional non-hormonal contraceptive or alternative recommended.
	• *ARVs*: PIs ± ritonavir, nevirapine, bictegravir, cabotegravir, dolutegravir, raltegravir, rilpivirine, maraviroc, cobicistat, zidovudine, lenacapavir	Significantly decreases exposure of ARVs; coadministration should be avoided if possible. Nevirapine: use only if other options are not available and close virologic and immunologic monitoring can be done; consider efavirenz instead. Raltegravir and dolutegravir dose increases may be required.
	• *Antimicrobials*: atovaquone, clarithromycin, dapsone, doxycycline	Coadministration of atovaquone and rifampin should be avoided. Consider switching clarithromycin to azithromycin, which has less potential for drug interaction. Dapsone and doxycycline efficacy may be reduced.
	• *Antifungals*: azoles, caspofungin	Increase in dose of caspofungin is recommended when coadministered with CYP450 inducers. Monitor azoles for efficacy. May need to increase azole dose.
	• *Other*: corticosteroids, methadone	Caution advised with corticosteroids (decreased efficacy). Monitor for efficacy and/or opiate withdrawal symptoms with methadone.
	Overlapping Toxicities • *Bone marrow suppressants* • *Hepatotoxic drugs*	Monitor for toxicities of these drugs.
Streptomycin	Overlapping Toxicities • *Nephrotoxic drugs* • *Neuromuscular blockers*	Monitor for toxicities of these drugs.
	• *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.

Drug Name	Toxicities	Recommendation
Trimethoprim-Sulfamethoxazole (TMP-SMX)	Overlapping Toxicities • *Folate antagonists* • *Bone marrow suppressants*	Monitor for toxicities of these drugs.
	• *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.
Valacyclovir	Potential for Increased Concentrations (of Both Drugs) and Overlapping Toxicities • *Antivirals*: acyclovir, cidofovir, ganciclovir, valganciclovir • *ARVs*: tenofovir, zidovudine	Monitor for toxicities of these drugs. Avoid other nephrotoxic drugs.
Valganciclovir	Potential for Increased Concentrations (of Both Drugs) and Overlapping Toxicities • *Antivirals*: acyclovir, cidofovir, ganciclovir, valacyclovir • *ARVs*: tenofovir, zidovudine	Monitor for toxicities of these drugs. Avoid other nephrotoxic drugs.
Voriconazole	Decreased Voriconazole Concentrations • *Anticonvulsants*: carbamazepine, long-acting barbiturates	Caution advised.
	• *Antimycobacterials*: rifabutin, rifampin	Rifabutin and rifampin coadministration should be avoided.
	• *ARVs*: efavirenz, nevirapine, ritonavir-boosted PIs	Standard doses of efavirenz and voriconazole should not be used; voriconazole dose may need to be increased and efavirenz dose decreased, or use alternative antifungal agent. Potential for increased PI concentrations and decreased voriconazole concentrations; consider monitoring voriconazole concentrations and adjust dose accordingly; monitor for PI-associated toxicities or consider using an alternative antifungal agent.
	Increased Voriconazole Concentrations • *ARVs*: etravirine (etravirine concentrations also increased)	Monitor voriconazole concentrations to reduce toxicity.

Drug Name	Toxicities	Recommendation
	Increased Concomitant Drug Concentrations • *Antimycobacterials*: rifabutin	Caution advised.
	• *ARVs*: ritonavir-boosted PIs, efavirenz	Caution advised.
	• *Statins*: atorvastatin, lovastatin, simvastatin	Do not coadminister with simvastatin or lovastatin. Avoid use of atorvastatin if possible. Alternative statins such as fluvastatin, rosuvastatin, and pravastatin are preferred; alternatively, discontinue statin during antifungal therapy.
	• *Sedatives/hypnotics*: alprazolam, midazolam, triazolam	Coadministration should be avoided if possible. Monitor for toxicities.

Key: ART = antiretroviral therapy; ARV = antiretroviral; CDC = Centers for Disease Control and Prevention; CYP450 = cytochrome P450; EKG = electrocardiogram; FDA = U.S. Food and Drug Administration; IV = intravenous; NRTI = nucleoside reverse transcriptase inhibitors; PI = protease inhibitors; QT = interval between Q and T waves; QTc = QT interval corrected for heart rate; TDM = therapeutic drug monitoring