



## **Guidelines for the Prevention and Treatment of Opportunistic Infections Among HIV-Exposed and HIV-Infected Children**

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## Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (Last updated November 6, 2013; last reviewed November 6, 2013)

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There is the potential for significant drug interactions and overlapping toxicities in patients receiving medications for treatment or prevention of opportunistic infections (OIs). These patients often are receiving other medications, including antiretrovirals that interfere with metabolism or elimination of OI medications. In particular, protease inhibitors and non-nucleoside reverse transcriptase inhibitors affect the CYP450 or other transporter systems and may be associated with clinically significant drug interactions. The integrase inhibitor raltegravir is metabolized by UGT1A1 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 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 (PK) data are available from studies involving HIV-infected adults, whereas data in children are extremely limited. New information continues to become available and it is important to carefully review a patient's current medications, including prescription and over-the-counter medications. It is difficult to predict the interaction potential when three or more drugs with similar metabolic pathways are co-administered and there is substantial inter-patient variability in the magnitude of these interactions. When possible, alternative agents with less drug interaction potential or use of therapeutic drug monitoring should be considered.

**Table 5 contains only a partial listing of drug interactions for drugs used to treat or prevent OIs.** The links below are excellent resources for investigating the potential for drug interactions. These tools include more comprehensive information and provide up-to-date information as new PK data become available.

<http://www.hiv-druginteractions.org/>

[http://tdm.pharm.buffalo.edu/home/di\\_search/](http://tdm.pharm.buffalo.edu/home/di_search/)

<http://www.aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/32/drug-interactions/>

[http://www.drugs.com/drug\\_interactions.html](http://www.drugs.com/drug_interactions.html)

<http://hivinsite.ucsf.edu/InSite?page=ar-00-02>

[http://www.nynjaetc.org/clinical\\_support.html](http://www.nynjaetc.org/clinical_support.html)

<http://www.clinicaloptions.com/inPractice.aspx>

<http://epocrates.com>

**Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections**  
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Drug Name	Overlapping Toxicities	Recommendation
<p><b>* The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).</b></p>		
<p><b>Acyclovir</b> (Zovirax)</p>	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Nephrotoxic drugs</li> </ul>	<p>Monitor for toxicities of these drugs.</p>
	<p><u>Increased Concentrations (Both Drugs) and Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Antivirals: valacyclovir, valganciclovir, ganciclovir, cidofovir</li> <li>• ARVs: tenofovir</li> </ul>	<p>Monitor for toxicities of these drugs.</p>
<p><b>Albendazole</b></p>	<p><u>Increases Albendazole Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Anthelmintic drugs: praziquantel</li> </ul>	<p>Caution advised.</p>
<p><b>Amikacin</b></p>	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Anti-tuberculosis drugs (injectable): streptomycin, kanamycin</li> <li>• Nephrotoxic or ototoxic drugs</li> <li>• Antimycobacterial drugs: capreomycin</li> <li>• Antivirals: cidofovir</li> </ul>	<p>Caution advised. Avoid combination of amikacin and cidofovir.</p>
<p><b>Amphotericin B</b> Amphotericin B Lipid Complex (Abelcet)  Amphotericin B Liposome (Ambisome)</p>	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Bone marrow suppressant drugs: corticosteroids</li> <li>• Nephrotoxic drugs</li> <li>• Neuromuscular blocking drugs</li> </ul>	<p>Caution advised.</p>
<p><b>Atovaquone</b></p>	<p><u>Decreases Atovaquone Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Antimycobacterial drugs: rifampin, rifabutin</li> <li>• ARVs: lopinavir/ritonavir, atazanavir/ritonavir</li> <li>• Antibiotics: doxycycline</li> </ul>	<p>Co-administration of atovaquone and rifampin should be avoided.</p>
<p><b>Azithromycin</b></p>	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Artemether/lumefantrine, chloroquine, quinine</li> </ul>	<p>Caution advised. Increased risk of QT prolongation.</p>
<p><b>Boceprevir</b></p>	<p>Please see <a href="#">Adult OI guidelines</a> for information about drug interactions, including warnings about interactions between boceprevir and HIV protease inhibitors.</p>	
<p><b>Capreomycin</b></p>	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Nephrotoxic or ototoxic drugs</li> <li>• Neuromuscular blocking drugs</li> <li>• Antibacterial drugs: aminoglycosides (parenteral)</li> </ul>	<p>Caution advised.</p>
<p><b>Caspofungin</b></p>	<p><u>Decreases Caspofungin Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Anticonvulsant drugs: phenytoin</li> <li>• Antimycobacterial drugs: rifampin</li> <li>• ARV drugs: efavirenz, nevirapine</li> </ul>	<p>Increase in dose of caspofungin is recommended when co-administered with CYP450 inducers.</p>

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Drug Name	Overlapping Toxicities	Recommendation
<p><b>* The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).</b></p>		
Cidofovir	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Antibacterial drugs: aminoglycosides</li> <li>• Antiviral drugs: foscarnet</li> <li>• Nephrotoxic drugs</li> </ul>	Monitor for toxicities of these drugs.
Ciprofloxacin	<p><u>Decreases Ciprofloxacin Absorption:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: didanosine</li> <li>• Minerals: ferrous sulfate, zinc</li> <li>• Gastrointestinal drugs: antacids, sucralfate, magnesium-containing laxatives</li> </ul>	Give oral ciprofloxacin 2 hours before or 6 hours after drugs that may interfere with absorption.
	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Artemether/lumefantrine, clarithromycin, quinine</li> </ul>	Caution advised.
Clarithromycin	<p><u>Increases Clarithromycin Concentrations:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: atazanavir/ritonavir, lopinavir/ritonavir</li> <li>• Antifungals: itraconazole (itraconazole concentrations also increased)</li> </ul>	Caution advised. Concern for QTc prolongation. Decrease clarithromycin dose or consider switching to azithromycin, which has less potential for drug interactions.
	<p><u>Increases Concentration of Other Medications:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: etravirine</li> </ul>	Consider alternative agent.
	<p><u>Decreases Clarithromycin Concentrations:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: efavirenz, etravirine, nevirapine</li> <li>• Antimycobacterial drugs: rifampin, rifabutin (rifabutin concentrations also increased)</li> </ul>	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.
Clindamycin	<p><u>Decreases Clindamycin Antibacterial Efficacy:</u></p> <ul style="list-style-type: none"> <li>• Antibacterial drugs: chloramphenicol, erythromycins</li> </ul>	Avoid concomitant use.
Cycloserine	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Antimycobacterial drugs: ethionamide, isoniazid</li> </ul>	Caution advised.
Dapsone	<p><u>Decreases Dapsone Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Antimycobacterial drugs: rifampin</li> </ul>	Co-administration should be avoided if possible. Consider alternatives for dapsone or use rifabutin.
	<p><u>Decreases Dapsone Absorption:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: didanosine suspension</li> <li>• Gastrointestinal drugs: antacids</li> </ul>	For co-administration with antacids or didanosine suspension, give dapsone 1 hour before or 4 hours after the other medication.
	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Bone marrow suppressant drugs or drugs associated with hemolysis</li> </ul>	Caution advised.
Doxycycline	<p><u>Decreases Doxycycline Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Anticonvulsant drugs: phenytoin, carbamazepine</li> <li>• Antimycobacterial drugs: rifampin</li> </ul>	Potential for decreased doxycycline efficacy. Monitor for therapeutic failure.

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Drug Name	Overlapping Toxicities	Recommendation
<p><b>* The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).</b></p>		
<p><b>Erythromycin</b></p>	<p><u>Increases Concentrations of Erythromycin and Co-Administered Medication:</u></p> <ul style="list-style-type: none"> <li>• Antifungals: itraconazole</li> </ul>	<p>Monitor for toxicities of both drugs, potential for QT prolongation.</p>
<p><b>Ethambutol</b></p>	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Neurotoxic drugs</li> </ul>	<p>Caution advised.</p>
<p><b>Ethionamide</b></p>	<p><u>Potential for Increased Toxicity Due to Overlapping Toxicity:</u></p> <ul style="list-style-type: none"> <li>• Neurotoxic drugs</li> <li>• Antimycobacterial drugs: cycloserine, isoniazid</li> </ul>	<p>Caution advised.</p>
<p><b>Fluconazole</b></p>	<p><u>Decreases Fluconazole Levels:</u></p> <ul style="list-style-type: none"> <li>• Anticonvulsant drugs: phenytoin</li> <li>• Antimycobacterial drugs: rifampin</li> <li>• ARV drugs: rilpivirine</li> </ul>	<p>Monitor for efficacy. May need to increase fluconazole dose.</p>
	<p><u>Increases Concomitant Drug Concentrations:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: saquinavir, tipranavir, nevirapine, and etravirine</li> </ul>	<p>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.</p>
	<ul style="list-style-type: none"> <li>• Antimycobacterial drugs: rifabutin</li> </ul>	<p>May need to decrease dose of rifabutin.</p>
	<ul style="list-style-type: none"> <li>• Statins: simvastatin, lovastatin, atorvastatin</li> </ul>	<p>Do not co-administer with simvastatin or lovastatin. Avoid use of atorvastatin if possible. Alternative statins such as fluvastatin, rosuvastatin, pravastatin are preferred or discontinue statin during antifungal therapy.</p>
<p><b>Flucytosine</b></p>	<p><u>Increases Flucytosine Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Nephrotoxic drugs</li> </ul>	<p>Caution advised.</p>
<p><b>Foscarnet</b></p>	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Antiviral drugs: cidofovir</li> <li>• Anti-pneumocystis drugs: pentamidine</li> <li>• Nephrotoxic drugs</li> </ul>	<p>Monitor for toxicities of these drugs.</p>
<p><b>Ganciclovir</b></p>	<p><u>Increases Ganciclovir Concentrations :</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: tenofovir (concentrations also increased)</li> </ul>	<p>Monitor for toxicities of these drugs.</p>
	<p><u>Increases Concomitant Drug Concentrations:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: didanosine, tenofovir</li> </ul>	<p>Caution advised.</p>
	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Antibacterial drugs: imipenem-cilastatin</li> <li>• ARV drugs: zidovudine</li> <li>• Bone marrow suppressant drugs</li> <li>• Nephrotoxic drugs</li> </ul>	<p>Caution advised. Increased risk of seizures with imipenem-cilastatin.</p>

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Drug Name	Overlapping Toxicities	Recommendation
<p><b>* The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).</b></p>		
<p><b>Interferon-Alfa</b></p>	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: zidovudine, lamivudine</li> <li>• Bone marrow suppressant drugs</li> </ul>	<p>Co-administration of zidovudine and lamivudine should be avoided if possible. Caution advised with other bone marrow suppressant drugs.</p>
<p><b>Isoniazid</b></p>	<p><u>Decreases Isoniazid Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Corticosteroids: glucocorticoids (e.g., prednisolone)</li> </ul>	<p>Use with caution.</p>
	<p><u>Decreases Isoniazid Absorption:</u></p> <ul style="list-style-type: none"> <li>• Gastrointestinal drugs: antacids</li> </ul>	<p>Caution advised.</p>
	<p><u>Increases Concomitant Drug Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Diazepam</li> </ul>	<p>Caution advised.</p>
	<p><u>Decreases Concomitant Drug Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Antifungal drugs: ketoconazole, itraconazole</li> </ul>	<p>Co-administration should be avoided, if possible.</p>
	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Antimycobacterial drugs: rifampin, cycloserine, ethionamide</li> <li>• Hepatotoxic drugs</li> <li>• Neurotoxic drugs</li> </ul>	<p>Caution advised.</p>
<p><b>Itraconazole</b></p>	<p><u>Increases Itraconazole Concentration:</u></p> <ul style="list-style-type: none"> <li>• Antibacterial: clarithromycin, erythromycin, ciprofloxacin</li> <li>• ARVs: protease inhibitors</li> </ul>	<p>Monitor for toxicities. Monitor itraconazole concentration. Consider azithromycin instead of other macrolides. High doses of itraconazole are not recommended with PIs.</p>
	<p><u>Increases Concomitant Drug Concentrations:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: etravirine, maraviroc, protease inhibitors</li> </ul>	<p>Caution advised. Monitor for toxicities. Decrease adult maraviroc dose to 150 mg twice daily.</p>
	<ul style="list-style-type: none"> <li>• Statins: lovastatin, simvastatin, atorvastatin</li> </ul>	<p>Do not co-administer with simvastatin or lovastatin. Avoid use of atorvastatin if possible. Alternative statins such as fluvastatin, rosuvastatin, pravastatin are preferred or discontinue statin during antifungal therapy.</p>
	<ul style="list-style-type: none"> <li>• Antibacterial: clarithromycin, erythromycin</li> </ul>	<p>Consider switching to azithromycin, which has less potential for drug interaction.</p>
	<ul style="list-style-type: none"> <li>• Sedatives/hypnotics: midazolam, alprazolam, diazepam</li> </ul>	<p>Co-administration of midazolam and alprazolam should be avoided. Co-administration of diazepam should be avoided, if possible.</p>
	<ul style="list-style-type: none"> <li>• Cardiac: quinidine</li> </ul>	<p>Co-administration of quinidine should be avoided. QT prolongation.</p>
	<p><u>Decreases Itraconazole Concentrations:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: efavirenz, etravirine, nevirapine, rilpivirine</li> </ul>	<p>Monitor itraconazole concentration. Co-administration of efavirenz should be avoided if possible.</p>
	<ul style="list-style-type: none"> <li>• Anticonvulsant drugs: carbamazepine, (fos)phenytoin</li> </ul>	<p>Monitor itraconazole concentration.</p>

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<p><b>* The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).</b></p>		
<p><b>Itraconazole, continued</b></p>	<ul style="list-style-type: none"> <li>• Antimycobacterial drugs: rifampin, rifabutin, rifapentine, isoniazid</li> </ul>	<p>Co-administration with rifampin should be avoided. Co-administration with rifabutin should be avoided, if possible. Monitor for toxicities. Monitor itraconazole concentration.</p>
	<p><u>Decreases Itraconazole Absorption:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: didanosine</li> <li>• Gastrointestinal drugs: antacids, anticholinergics/antispasmodics, histamine H<sub>2</sub>-receptor antagonists, omeprazole, sucralfate</li> </ul>	<p>Monitor itraconazole concentration.</p>
<p><b>Lumefantrine</b></p>	<p><u>Increases Concomitant Drug Levels:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: nevirapine</li> </ul>	<p>Monitor for nevirapine toxicity.</p>
	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: protease inhibitors</li> <li>• Antibacterial drugs: macrolides, fluoroquinolones</li> <li>• Antifungal drugs: fluconazole, voriconazole</li> <li>• Antimalarial drugs: quinine, quinidine</li> <li>• Psychotropic drugs: quetiapine, tricyclic antidepressants</li> </ul>	<p>Co-administration with fluconazole or voriconazole should be avoided. For all other drugs, co-administration should be avoided, if possible; monitor for toxicities (QT prolongation).</p>
<p><b>Mefloquine</b></p>	<p><u>Decreases Mefloquine Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Antimalarial drugs: quinine</li> <li>• Antimycobacterial: rifampin</li> </ul>	<p>Monitor for decreased mefloquine efficacy.</p> <p>Co-administration of rifampin should be avoided, if possible; use rifabutin instead.</p>
	<p><u>Decreases Concomitant Drug Concentrations:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: ritonavir, possibly other protease inhibitors</li> </ul>	<p>Monitor for virologic failure of protease inhibitor-containing ART regimen.</p>
	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Anti-malarial drugs: quinine</li> <li>• Other drugs that can cause prolonged QT</li> </ul>	<p>Avoid co-administration, if possible. Monitor for toxicities (EKG changes, cardiac arrest; also seizures with quinine). If co-administered with quinine, give mefloquine at least 12 hours after last dose of quinine.</p>
<p><b>Nitazoxanide</b></p>	<p><u>Increases Concomitant Drug Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Phenytoin</li> </ul>	<p>Potential for interaction with other medications that are highly protein bound. Use with caution as interaction will increase concentrations of concomitant medication.</p>
<p><b>Paromomycin</b></p>	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Neuromuscular blocking drugs</li> </ul>	<p>Use with caution.</p>

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<p><b>* The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).</b></p>		
<p><b>Pentamidine</b></p>	<p><u>Overlapping Toxicities:</u> • Antiviral drugs: foscarnet</p>	<p>Co-administration should be avoided, if possible. Monitor for toxicities (hypocalcaemia, QT prolongation).</p>
	<p>• ARV drugs: protease inhibitors, didanosine</p>	<p>Co-administration should be avoided, if possible. Monitor for toxicities (QT prolongation with protease inhibitors; pancreatitis for didanosine).</p>
	<p>• Bone marrow suppressant drugs</p>	<p>Monitor for toxicities.</p>
	<p>• Nephrotoxic drugs</p>	<p>Monitor for toxicities.</p>
	<p>• Other drugs that can cause prolonged QT</p>	<p>Monitor for toxicities. Avoid co-administration, if possible.</p>
<p><b>Posaconazole</b></p>	<p><u>Decreases Posaconazole Drug Concentrations:</u> • ARV drugs: efavirenz, fosamprenavir, rilpivirine</p>	<p>Co-administration of fosamprenavir should be avoided. Co-administration of efavirenz should be avoided, if possible. If co-administered, monitor posaconazole concentrations and adjust dose accordingly.</p>
	<p>• Anticonvulsant drugs: phenytoin</p>	<p>Co-administration should be avoided, if possible. If co-administered, monitor posaconazole concentrations and adjust dose accordingly.</p>
	<p>• Antimycobacterial drugs: rifabutin, rifampin</p>	<p>Co-administration should be avoided, if possible. If co-administered, monitor posaconazole concentrations and adjust dose accordingly.</p>
	<p><u>Increases Concomitant Drug Concentrations:</u> • ARV drugs: atazanavir, saquinavir, lopinavir, etravirine, and ritonavir</p>	<p>Co-administration should be avoided, if possible. Monitor for toxicities. Consider monitoring concentrations and adjust dose as necessary.</p>
	<p>• Antibacterial drugs: erythromycin, clarithromycin</p>	<p>Co-administration should be avoided.</p>
	<p>• Anticonvulsant drugs: phenytoin</p>	<p>Co-administration should be avoided.</p>
	<p>• Sedatives/hypnotics: midazolam, alprazolam, diazepam</p>	<p>Co-administration should be avoided, if possible. Monitor for toxicities.</p>
	<p>• Antimycobacterial drugs: rifabutin</p>	<p>Co-administration should be avoided.</p>
	<p>• Statins: simvastatin, lovastatin, atorvastatin</p>	<p>Do not co-administer with simvastatin or lovastatin. Avoid use of atorvastatin if possible. Alternative statins such as fluvastatin, rosuvastatin, pravastatin are preferred or discontinue statin during antifungal therapy.</p>
	<p>• Antimalarials: Quinidine, quinine, mefloquine, lumefantrine, halofantrine</p>	<p>Co-administration should be avoided.</p>
	<p><u>Decreases Concomitant Drug Concentrations:</u> • ARV drugs: fosamprenavir • Other drugs that can cause prolonged QT</p>	<p>Co-administration should be avoided. Use with caution. Monitor for toxicities.</p>



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<p><b>* The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).</b></p>		
<p><b>Proguanil</b></p>	<p><u>Decreases Proguanil Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Atazanavir/ritonavir, lopinavir/ritonavir, efavirenz</li> </ul>	<p>Use with caution.</p>
<p><b>Pyrazinamide</b></p>	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Antimycobacterial drugs: rifampin, ethionamide</li> <li>• Hepatotoxic drugs</li> </ul>	<p>Use with caution. Monitor for hepatotoxicity.</p>
<p><b>Quinidine</b></p>	<p><u>Increases Quinidine Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Protease inhibitors</li> </ul>	<p>Co-administration of PIs should be avoided. Increased risk of arrhythmia. Co-administration may be necessary in presence of life-threatening, severe malaria and in the absence of other therapy, while artesunate is obtained from the CDC.</p>
	<ul style="list-style-type: none"> <li>• Itraconazole, posaconazole, voriconazole</li> </ul>	<p>Co-administration should be avoided. Increased risk of arrhythmia.</p>
	<p><u>Decreases Quinidine Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Etravirine</li> </ul>	<p>Use with caution. Monitor quinidine levels.</p>
	<p><u>Increases Concomitant Drug Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Tricyclic antidepressants</li> </ul>	<p>Co-administration should be avoided, if possible. Monitor for toxicities.</p>
	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Other drugs that can prolong QT interval</li> </ul>	<p>Co-administration should be avoided, if possible. Monitor for toxicities (QT prolongation).</p>
<p><b>Ribavirin</b></p>	<p><u>Increases Concentrations Of Concomitant Drug:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: didanosine</li> </ul>	<p>Co-administration should be avoided. Potential for increased risk of pancreatitis and mitochondrial toxicity.</p>
	<p><u>Decreases Concentrations of Concomitant Drug:</u></p> <ul style="list-style-type: none"> <li>• Zidovudine, stavudine</li> </ul>	<p>Co-administration should be avoided, if possible.</p>
	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Zidovudine, all NRTIs</li> </ul>	<p>Co-administration should be avoided, if possible. Monitor for toxicities (anemia for zidovudine; lactic acidosis for all NRTIs).</p>
<p><b>Rifabutin</b></p>	<p><u>Increases Rifabutin Concentrations:</u></p> <ul style="list-style-type: none"> <li>• HIV protease inhibitors</li> </ul>	<p>Use with caution. Monitor for rifabutin toxicity. Reduce rifabutin dose if co-administered with PIs.</p>
	<ul style="list-style-type: none"> <li>• Fluconazole</li> </ul>	<p>Use with caution. Monitor for rifabutin toxicity. Consider rifabutin dose reduction.</p>
	<ul style="list-style-type: none"> <li>• Voriconazole, itraconazole, posaconazole</li> </ul>	<p>Co-administration should be avoided, if possible. If co-administered, consider TDM and monitor for rifabutin toxicities (and azole clinical efficacy).</p>
	<ul style="list-style-type: none"> <li>• Clarithromycin</li> </ul>	<p>Co-administration should be avoided, if possible. Monitor for rifabutin toxicity. Consider rifabutin dose reduction or using azithromycin instead.</p>
	<p><u>Increases Concomitant Drug Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Didanosine</li> </ul>	<p>Use with caution. Monitor for didanosine toxicity.</p>

**Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections**  
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Drug Name	Overlapping Toxicities	Recommendation
<p><b>* The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).</b></p>		
<p><b>Rifabutin,</b> continued</p>	<p><u>Decreases Rifabutin Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Efavirenz, etravirine</li> </ul>	<p>Use with caution. Higher rifabutin dose required when efavirenz co-administered. Consider TDM.</p>
	<p><u>Decreases Concomitant Drug Concentrations:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: rilpivirine</li> </ul>	<p>Co-administration should be avoided.</p>
	<ul style="list-style-type: none"> <li>• ARV drugs: saquinavir, etravirine, maraviroc</li> </ul>	<p>Co-administration should be avoided, if possible.</p>
	<ul style="list-style-type: none"> <li>• Antibacterial drugs: dapsone, atovaquone</li> </ul>	<p>Use with caution. Monitor for dapsone treatment failure.</p>
	<ul style="list-style-type: none"> <li>• Antifungal drugs: azoles (except for fluconazole)</li> </ul>	<p>Co-administration should be avoided, if possible. If co-administered, consider TDM and monitor for rifabutin toxicities (and azole clinical efficacy).</p>
	<ul style="list-style-type: none"> <li>• Contraceptives: oral</li> </ul>	<p>Oral contraceptives less effective. Additional non-hormonal contraceptive or alternative recommended.</p>
<p><b>Rifampin</b></p>	<p><u>Decreases Concomitant Drug Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Contraceptives: oral</li> </ul>	<p>Oral contraceptives less effective. Additional non-hormonal contraceptive or alternative recommended.</p>
	<ul style="list-style-type: none"> <li>• ARV drugs: PIs ± ritonavir, nevirapine, raltegravir, rilpivirine</li> </ul>	<p>Significantly decreases PI exposure; co-administration should be avoided. Nevirapine: use only if other options not available and close virologic and immunologic monitoring can be done; consider efavirenz instead. Raltegravir dose increase may be required. Rilpivirine co-administration should be avoided.</p>
	<ul style="list-style-type: none"> <li>• Antimicrobial: atovaquone, dapsone, clarithromycin, doxycycline</li> </ul>	<p>Co-administration 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.</p>
	<ul style="list-style-type: none"> <li>• Antifungal drugs: azoles, caspofungin</li> </ul>	<p>Increase in dose of caspofungin is recommended when co-administered with CYP450 inducers.</p> <p><u>Azoles:</u> Monitor for efficacy. May need to increase antifungal dose</p>
	<ul style="list-style-type: none"> <li>• Other: corticosteroids, methadone</li> </ul>	<p>Caution advised with corticosteroids (decreased efficacy).</p> <p><u>Methadone:</u> Monitor for efficacy and/or opiate withdrawal symptoms with methadone.</p>
	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Bone marrow suppressant drugs</li> <li>• Hepatotoxic drugs</li> </ul>	<p>Monitor for toxicities of these drugs.</p>
<p><b>Streptomycin</b></p>	<p><u>Potential for Increased Toxicity Due to Overlapping Toxicity:</u></p> <ul style="list-style-type: none"> <li>• Nephrotoxic drugs</li> <li>• Neuromuscular blocking drugs</li> </ul>	<p>Monitor for toxicities of these drugs.</p>

**Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections**  
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Drug Name	Overlapping Toxicities	Recommendation
<p><b>* The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).</b></p>		
Telaprevir	Please see <a href="#">Adult OI guidelines</a> for information about drug interactions, including warnings about interactions between telaprevir and HIV protease inhibitors. Caution advised.	
Trimethoprim-Sulfamethoxazole	<p><u>Overlapping Toxicities:</u></p> <ul style="list-style-type: none"> <li>• Folate antagonists</li> <li>• Bone marrow suppressant drugs</li> </ul>	Monitor for toxicities of these drugs.
Valacyclovir	<p><u>Potential For Increased Concentrations (of Both Drugs) and Overlapping Toxicity:</u></p> <ul style="list-style-type: none"> <li>• Antivirals: acyclovir, valganciclovir, ganciclovir, cidofovir</li> <li>• ARVs: tenofovir</li> </ul>	Monitor for toxicities of these drugs.
Valganciclovir	<p><u>Potential for Increased Concentrations (of Both Drugs) and Overlapping Toxicity:</u></p> <ul style="list-style-type: none"> <li>• Antivirals: valacyclovir, acyclovir, ganciclovir, cidofovir</li> <li>• ARVs: tenofovir</li> </ul>	Monitor for toxicities of these drugs.
Voriconazole	<p><u>Decreases Voriconazole Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Anticonvulsant drugs: carbamazepine, long-acting barbiturates</li> </ul>	Caution advised.
	<ul style="list-style-type: none"> <li>• Antimycobacterial drugs: rifabutin, rifampin</li> </ul>	Rifabutin and Rifampin co-administration should be avoided.
	<ul style="list-style-type: none"> <li>• ARV drugs: efavirenz, nevirapine, PIs boosted with ritonavir</li> </ul>	<p>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.</p> <p>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.</p>
	<p><u>Increases Voriconazole Concentrations:</u></p> <ul style="list-style-type: none"> <li>• ARV drugs: etravirine</li> </ul>	Monitor voriconazole concentrations to reduce toxicity.
	<p><u>Increases Concomitant Drug Concentrations:</u></p> <ul style="list-style-type: none"> <li>• Antimycobacterial drugs: rifabutin</li> </ul>	Caution advised.
	<ul style="list-style-type: none"> <li>• ARV drugs: protease inhibitors boosted with ritonavir, efavirenz, etravirine</li> </ul>	Caution advised.
	<ul style="list-style-type: none"> <li>• Statins: simvastatin, lovastatin, atorvastatin</li> </ul>	<p>Statins: Do not co-administer with simvastatin or lovastatin. Avoid use of atorvastatin if possible. Alternative statins such as fluvastatin, rosuvastatin, pravastatin are preferred or discontinue statin during antifungal therapy.</p>
<ul style="list-style-type: none"> <li>• Sedatives/hypnotics: midazolam, alprazolam, triazolam</li> </ul>	Co-administration should be avoided if possible. Monitor for toxicities.	

**Key to Acronyms:** ART = antiretroviral therapy; ARV = antiretroviral; CDC = Centers for Disease Control and Prevention; EKG = electrocardiogram; NNRTI = non-nucleoside reverse transcriptase inhibitors; NRTI = nucleoside reverse transcriptase inhibitors; OI = opportunistic infection; PI = protease inhibitors; PK = pharmacokinetic; TDM = therapeutic drug monitoring