Table 1. Chemoprophylaxis to Prevent First Episode of Opportunistic Disease

This table provides recommendations for the use of chemoprophylaxis to prevent the first episode of opportunistic disease. For the use of immunizations to prevent hepatitis A virus, hepatitis B virus, human papillomavirus, influenza A and B viruses, *Streptococcus pneumoniae,* and varicella-zoster virus infections, please refer to the Immunizations for Preventable Diseases in Adults and Adolescents Living with HIV section.

(Last updated February 17, 2022; last reviewed February 17, 2022)

Opportunistic Infections	Indication	Preferred	Alternative
Coccidioidomycosis	A new positive IgM or IgG serologic test in patients who live in a disease-endemic area and with CD4 count <250 cells/μL (BIII)	Fluconazole 400 mg PO daily (BIII)	
Histoplasma capsulatum infection	CD4 count ≤150 cells/μL and at high risk because of occupational exposure or living in a community with a hyperendemic rate of histoplasmosis (>10 cases/100 patient-years) (BI)	Itraconazole 200 mg PO daily (BI)	
Malaria	Travel to disease-endemic area	Recommendations are the same for HIV-infected and HIV-uninfected patients. Recommendations are based on the region of travel, malaria risks, and drug susceptibility in the region. Refer to the Centers for Disease Control and Prevention webpage for the most recent recommendations based on region and drug susceptibility: Malaria.	
Mycobacterium avium complex (MAC) disease	CD4 count <50 cells/mm^3 Not recommended for those who immediately initiate ART (AII). Recommended for those who are not on fully suppressive ART, after ruling out active disseminated MAC disease (AI).	Azithromycin 1,200 mg PO once weekly (AI), *or* Clarithromycin 500 mg PO BID (AI), *or* Azithromycin 600 mg PO twice weekly (BIII)	Rifabutin (dose adjusted based on concomitant ART)[a] (BI); rule out active TB before starting rifabutin.

Opportunistic Infections	Indication	Preferred	Alternative
Mycobacterium tuberculosis infection (TB) (i.e., treatment of latent TB infection [LTBI])	Positive screening test for LTBI,[b] with no evidence of active TB, and no prior treatment for active TB or LTBI (AI), *or* Close contact with a person with infectious TB, with no evidence of active TB, regardless of screening test results (AII) LTBI treatment and ART act independently to decrease the risk of TB disease. Thus, ART is recommended for all persons with HIV and LTBI (AI).	(Rifapentine [see dose below] plus INH 900 mg plus pyridoxine 50 mg) PO once weekly for 12 weeks (AII) Note: Rifapentine is recommended only for persons receiving EFV, RAL, or once daily DTG -based ARV regimen. Weight-Based Rifapentine Dose • *Weighing* 32.1–49.9 kg: 750 mg PO once weekly • *Weighing* >50 kg: 900 mg PO once weekly *or* (INH 300 mg plus rifampin 600mg plus pyridoxine 25–50 mg) PO daily for 3 months (AI) See Table 3 in the *Mycobacterium tuberculosis* Infection and Disease section for the list of ARV drugs not recommended to be used with rifampin and those which require dosage adjustment.	(INH 300 mg plus pyridoxine 25–50 mg) PO daily for 9 months (AII), *or* Rifampin 600 mg PO daily for 4 months (BI), *or* (Rifapentine [see dose below] plus INH 300 mg plus pyridoxine 25–50 mg) PO once daily for 4 weeks (AII) Weight-Based Rifapentine Dose • *Weighing* <35 kg: 300 mg PO once daily • *Weighing* 35–45 kg: 450 mg PO once daily • *Weighing* >45 kg: 600 mg PO once daily See Table 3 in the *Mycobacterium tuberculosis* Infection and Disease section for the list of ARV drugs not recommended to be used with rifampin and those which require dosage adjustment. For persons exposed to drug-resistant TB, select anti-TB drugs after consultation with experts or public health authorities (AII).
Pneumocystis Pneumonia (PCP)	CD4 count <200 cells/mm^3 (AI), *or* CD4 <14% (BII), *or* If ART initiation must be delayed, CD4 count ≥200 cells/mm^3 but <250 cells/mm^3 and if monitoring of CD4 cell count every 3 months is not possible (BII) Note: Patients who are receiving pyrimethamine/ sulfadiazine for treatment or suppression of toxoplasmosis do not require additional PCP prophylaxis (AII).	TMP-SMX[c] 1 DS tablet PO daily (AI), *or* TMP-SMX[c] 1 SS tablet daily (AI)	• TMP-SMX[c] 1 DS PO three times weekly (BI), *or* • Dapsone[d] 100 mg PO daily or 50 mg PO BID (BI), *or* • Dapsone[d] 50 mg PO daily with (pyrimethamine[e] 50 mg plus leucovorin 25 mg) PO weekly (BI), *or* • (Dapsone[d] 200 mg plus pyrimethamine[e] 75 mg plus leucovorin 25 mg) PO weekly (BI); *or* • Aerosolized pentamidine 300 mg via Respigard II™ nebulizer every month (BI), *or* • Atovaquone 1,500 mg PO daily (BI), *or* • (Atovaquone 1,500 mg plus pyrimethamine[e] 25 mg plus leucovorin 10 mg) PO daily (CIII)

Opportunistic Infections	Indication	Preferred	Alternative
Syphilis	For individuals exposed to a sex partner with a diagnosis of primary, secondary, or early latent syphilis within the past 90 days (AII), *or* For individuals exposed to a sex partner >90 days before syphilis diagnosis in the partner, if serologic test results are not available immediately and the opportunity for follow-up is uncertain (AIII)	Benzathine penicillin G 2.4 million units IM for 1 dose (AII)	For penicillin-allergic patients: • Doxycycline 100 mg PO BID for 14 days (BII), *or* • Ceftriaxone 1 g IM or IV daily for 8–10 days (BII), *or* • Azithromycin 2 g PO for 1 dose (BII)—**not recommended** for men who have sex with men or pregnant people (AII)
Talaromycosis (Penicilliosis)	Persons with HIV and CD4 cell counts <100 cells/mm^3, who are unable to have ART, or have treatment failure without access to effective ART options, and— • Who reside in the highly endemic regions* in northern Thailand, northern or southern Vietnam, or southern China (BI), *or* • Who are from countries outside of the endemic region, and must travel to the region (BIII) * Particularly in highland regions during the rainy and humid months	For persons who reside in endemic areas, itraconazole 200 mg PO once daily (BI) For those traveling to the highly endemic regions, begin itraconazole 200 mg PO once daily 3 days before travel, and continue for 1 week after leaving the endemic area (BIII).	For persons who reside in endemic areas, fluconazole 400 mg PO once weekly (BII) For those traveling to the highly endemic regions, take the first dose of fluconazole 400 mg 3 days before travel, continue 400 mg once weekly, and take the final dose after leaving the endemic area (BIII).
Toxoplasma gondii encephalitis	Toxoplasma IgG-positive patients with CD4 count <100 cells/μL (AII) Note: All regimens recommended for primary prophylaxis against toxoplasmosis also are effective as PCP prophylaxis.	TMP-SMX[a] 1 DS PO daily (AII)	• TMP-SMX[c] 1 DS PO three times weekly (BIII), *or* • TMP-SMX[c] 1 SS PO daily (BIII), *or* • Dapsone[d] 50 mg PO daily plus (pyrimethamine[e] 50 mg plus leucovorin 25 mg) PO weekly (BI), *or* • (Dapsone[d] 200 mg plus pyrimethamine[e] 75 mg plus leucovorin 25 mg) PO weekly (BI), *or* • Atovaquone 1500 mg PO daily (CIII), *or* • (Atovaquone 1500 mg plus pyrimethamine[e] 25 mg plus leucovorin 10 mg) PO daily (CIII)

[a] Refer to the Drug–Drug Interactions section of the Adult and Adolescent Antiretroviral Guidelines for dosing recommendations.

[b] Screening tests for LTBI include tuberculin skin test or interferon-gamma release assays.

[c] TMP-SMX DS once daily also confers protection against toxoplasmosis and many respiratory bacterial infections; lower dose also likely confers protection.

[d] Patients should be tested for glucose-6-phosphate dehydrogenase (G6PD) before administration of dapsone or primaquine. An alternative agent should be used in patients found to have G6PD deficiency.

[e] Refer to Daraprim Direct for information regarding how to access pyrimethamine.

For information regarding the evidence ratings, refer to the Rating System for Prevention and Treatment Recommendations in the Introduction section of the Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV.

Key: ART = antiretroviral therapy; ARV = antiretroviral; BID = twice daily; CD4 = CD4 T lymphocyte cell; DS = double strength; DTG = dolutegravir; EFV = efavirenz; IgG = immunoglobulin G; IgM = immunoglobulin M; IM = intramuscular; INH = isoniazid; IV = intravenously; LTBI = latent tuberculosis infection; MAC = *Mycobacterium avium* complex; PCP = *Pneumocystis* pneumonia; PO = orally; RAL= raltegravir; SS = single strength; TB = tuberculosis; TMP-SMX = trimethoprim-sulfamethoxazole

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy)

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Opportunistic Infection		Preferred Therapy	Alternative Therapy	Other Comments
Bacterial Enteric Infections	Empiric therapy pending definitive diagnosis	Diagnostic fecal specimens should be obtained before the initiation of empiric antimicrobial therapy. If a pathogen is identified, antibiotic susceptibilities should be performed to confirm and inform antibiotic choices given increased reports of antibiotic resistance. Reflex culture for antibiotic susceptibilities should also be done if diagnosis is made using PCR-based methods. Empiric antibiotic therapy may be indicated for patients with CD4 count 200–500 cells/mm^3 where diarrhea is severe enough to compromise quality of life or the ability to work (CIII) and is indicated in patients with CD4 count <200 cells/mm^3 or concomitant AIDS-defining illness and with clinically severe diarrhea (≥6 stools per day or bloody stool) and/or accompanying fever or chills (AIII). Empiric Therapy • Ciprofloxacin 500–750 mg PO (or 400 mg IV) every 12 hours for 5 days (AIII) (particularly if diarrhea is not associated with international travel) Therapy should be adjusted based on the results of a diagnostic work-up. For patients with chronic diarrhea (>14 days) without severe clinical signs, empiric antibiotics therapy is not necessary. Treatment can be withheld until a diagnosis is made.	Empiric Therapy *In Patients with Marked Nausea, Vomiting, Diarrhea, Electrolyte Abnormalities, Acidosis, Blood Pressure Instability, and/or When Hospitalization Is Needed* • Ceftriaxone 1 g IV every 24 hours (BIII), *or* • Cefotaxime 1 g IV every 8 hours (BIII)	Oral or IV rehydration (if indicated) should be given to patients with diarrhea (AIII). Anti-motility agents should be avoided if there is concern about inflammatory diarrhea, including CDI (BIII). If no clinical response is observed after 3–4 days, consider a follow-up stool culture with antibiotic susceptibility testing or alternative diagnostic tests (e.g., toxin assays, molecular testing) to evaluate alternative diagnoses, antibiotic resistance, or drug–drug interactions.
	Campylobacteriosis	For Mild Disease and if CD4 Count >200 Cells/mm^3 • No therapy unless symptoms persist for more than several days (CIII).	For Mild-to-Moderate Disease (If Susceptible) • Levofloxacin 750 mg (PO or IV) every 24 hours (BIII), *or* • Moxifloxacin 400 mg (PO or IV) every 24 hours (BIII)	Oral or IV rehydration if indicated (AIII) Anti-motility agents should be avoided (BIII). If no clinical response is observed after 5–7 days, consider a follow-

Opportunistic Infection		Preferred Therapy	Alternative Therapy	Other Comments
		For Mild-to-Moderate Disease (If Susceptible) • Ciprofloxacin 500–750 mg PO (or 400 mg IV) every 12 hours for 7–10 days (BIII), *or* • Azithromycin 500 mg PO daily for 5 days (BIII) (Note: Not for patients with bacteremia [AIII]) For *Campylobacter* Bacteremia • Ciprofloxacin 500–750 mg PO (or 400 mg IV) every 12 hours for ≥14 days if the isolate is sensitive (BIII) plus an aminoglycoside (BIII) For Recurrent infections • Duration of therapy may be extended to 2–6 weeks (BIII).	Add an aminoglycoside to fluoroquinolone in bacteremic patients (BIII).	up stool culture, alternative diagnosis, or antibiotic resistance. In the United States in 2018, 29% of *C. jejuni* isolates were resistant to ciprofloxacin and 2% were resistant to azithromycin; among *C. coli* isolates, 40.5% were resistant to fluoroquinolone and 13.3% are resistant to azithromycin. The rationale for addition of an aminoglycoside to a fluoroquinolone in bacteremic patients is to prevent emergence of quinolone resistance. Effective ART may reduce the frequency, severity, and recurrence of *campylobacter* infections.
	Clostridium difficile infection (CDI)	Fidaxomicin 200 mg PO two times daily for 10 days (AI) Vancomycin 125 mg PO four times daily for 10 days (AI) For severe, life-threatening CDI, see text and references for additional information.	For Nonsevere CDI *If Fidaxomicin or Vancomycin Access Is Limited* • Metronidazole 500 mg (PO) three times daily for 10 days (CII)	Recurrent CDI Treatment is the same as in patients without HIV infection. Bezlotoximab (CIII) or fecal microbiota therapy may be successful and safe to treat recurrent CDI (CIII). See text and references for additional information.
	Salmonellosis	All people with HIV and salmonellosis should receive antimicrobial treatment due to an increase of bacteremia (by 20-fold to 100-fold) and mortality (by up to 7-fold) compared to individuals without HIV (AIII).		Oral or IV rehydration if indicated (AIII) Anti-motility agents should be avoided (BIII). The role of long-term secondary prophylaxis in patients with recurrent *Salmonella* bacteremia is not well established. Must weigh benefit against risks of long-term antibiotic exposure (BIII). Effective ART may reduce the frequency, severity, and recurrence of salmonella infections.
		• Ciprofloxacin 500–750 mg PO (or 400 mg IV) every 12 hours, if susceptible (AIII) Duration of Therapy *For Gastroenteritis Without Bacteremia* • If CD4 count ≥200 cells/mm^3: 7–14 days (BIII) • If CD4 count <200 cells/mm^3: 2–6 weeks (BIII)	• Levofloxacin 750 mg (PO or IV) every 24 hours (BIII), *or* • Moxifloxacin 400 mg (PO or IV) every 24 hours (BIII), *or* • TMP 160 mg-SMX 800 mg (PO or IV) every 12 hours (BIII), *or* • Ceftriaxone 1 g IV every 24 hours (BIII), *or* • Cefotaxime 1 g IV every 8 hours (BIII)	

Opportunistic Infection		Preferred Therapy	Alternative Therapy	Other Comments
		For Gastroenteritis with Bacteremia • If CD4 count ≥200/mm^3: 14 days or longer duration if bacteremia persists or if the infection is complicated (e.g., if metastatic foci of infection are present) (BIII) • If CD4 count <200 cells/mm^3: 2–6 weeks (BIII) Secondary Prophylaxis Should Be Considered • For patients with recurrent *Salmonella* bacteremia (BIII), *or* • For patients with recurrent gastroenteritis (with or without bacteremia) with CD4 count <200 cells/mm^3 with severe diarrhea (BIII)		
	Shigellosis	• Ciprofloxacin 500–750 mg PO (or 400 mg IV) every 12 hours (if MIC <0.12 µg/mL (AIII) Duration of Therapy • Gastroenteritis: 7–10 days (AIII) • Bacteremia: ≥14 days (BIII) • Recurrent infections: Up to 6 weeks (BIII) Note: Increased resistance of *Shigella* to fluoroquinolones is occurring in the United States. Avoid fluoroquinolones if ciprofloxacin MIC is ≥0.12 µg/mL, even if the laboratory identifies the isolate as sensitive. Many *Shigella* strains resistant to fluoroquinolones exhibit resistance to other commonly used antibiotics. Thus, antibiotic sensitivity testing of *Shigella* isolates from HIV-infected individuals should be performed routinely.	• Levofloxacin 750 mg (PO or IV) every 24 hours (BIII), *or* • Moxifloxacin 400 mg (PO or IV) every 24 hours (BIII), *or* • TMP 160 mg-SMX 800 mg (PO or IV) every 12 hours (BIII) (Note: *Shigella* infections acquired outside of the United States have high rates of TMP-SMX resistance), *or* • Azithromycin 500 mg PO daily for 5 days (BIII) (Note: not recommended for patients with bacteremia [AIII].) Note: Azithromycin-resistant *Shigella spp.* has been reported in HIV-infected MSM.	Therapy may slightly shorten duration of illness and/or prevent spread of infection (AIII). Given increasing antimicrobial resistance and limited data showing that antibiotic therapy limits transmission, antibiotic treatment may be withheld in patients with CD4 count >500 cells/mm^3 whose diarrhea resolves prior to culture confirmation of *Shigella* infection (CIII). Oral or IV rehydration if indicated (AIII). Anti-motility agents should be avoided (BIII). If no clinical response after 5–7 days, consider a follow-up stool culture, alternative diagnosis, or antibiotic resistance. Effective ART may decrease the risk of recurrence of *Shigella* infections.

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Bartonellosis	For Bacillary Angiomatosis, Peliosis Hepatis, Bacteremia, and Osteomyelitis • Doxycycline 100 mg PO or IV every 12 hours (AII), *or* • Erythromycin 500 mg PO or IV every 6 hours (AII) CNS Infections • (Doxycycline 100 mg +/- RIF 300 mg) PO or IV every 12 hours (AIII) Confirmed *Bartonella* Endocarditis • (Doxycycline 100 mg IV every 12 hours plus gentamicin 1 mg/kg IV every 8 hours) for 2 weeks, then continue with doxycycline 100 mg IV or PO every 12 hours (BII) Other Severe Infections • (Doxycycline 100 mg PO or IV +/- RIF 300 mg PO or IV) every 12 hours (BIII), *or* • (Erythromycin 500 mg PO or IV every 6 hours) +/- RIF 300 mg PO or IV every 12 hours (BIII) Duration of Therapy • At least 3 months (AII)	For Bacillary Angiomatosis, Peliosis Hepatis, Bacteremia, and Osteomyelitis • Azithromycin 500 mg PO daily (BIII) • Clarithromycin 500 mg PO twice a day (BIII) Confirmed *Bartonella* Endocarditis, but with Renal Insufficiency • (Doxycycline 100 mg IV plus RIF 300 mg PO or IV) every 12 hours for 2 weeks, then continue with doxycycline 100 mg IV or PI every 12 hours (BII)	When RIF is used, take into consideration the potential for significant interaction with ARV drugs and other medications (see Table 5 for dosing recommendations). If relapse occurs after initial (>3 month) course of therapy, long-term suppression with doxycycline or a macrolide is recommended as long as CD4 count is <200 cells/μL (AIII).
Candidiasis (Mucocutaneous)	For Oropharyngeal Candidiasis; Initial Episodes (for 7–14 Days) *Oral Therapy* • Fluconazole 100 mg PO daily (AI) For Esophageal Candidiasis (for 14–21 Days) • Fluconazole 100 mg (up to 400 mg) PO or IV daily (AI), *or* • Itraconazole oral solution 200 mg PO daily (AI) For Uncomplicated Vulvo-Vaginal Candidiasis • Oral fluconazole 150 mg for one dose (AII), *or*	For Oropharyngeal Candidiasis; Initial Episodes (for 7–14 Days) *Oral Therapy* • Itraconazole oral solution 200 mg PO daily (BI), *or* • Posaconazole oral suspension 400 mg PO twice a day for 1 day, then 400 mg daily (BI) *Topical Therapy* • Clotrimazole troches, 10 mg PO five times daily (BI), *or* • Miconazole mucoadhesive buccal 50-mg tablet; apply to mucosal surface over the	Chronic or prolonged use of azoles may promote development of resistance. Higher relapse rate for esophageal candidiasis seen with echinocandins than with fluconazole use. Suppressive therapy usually not recommended (BIII) unless patients have frequent or severe recurrences. If Decision Is to Use Suppressive Therapy *Oropharyngeal Candidiasis* • Fluconazole 100 mg PO daily or three times weekly (BI), or

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	• Topical azoles (clotrimazole, butoconazole, miconazole, tioconazole, or terconazole) for 3–7 days (AII) For Severe or Recurrent Vulvo-Vaginal Candidiasis • Fluconazole 100–200 mg PO daily for ≥7 days (AII), *or* • Topical antifungal ≥7 days (AII)	canine fossa once daily (do not swallow, chew, or crush tablet) (BI), *or* • Nystatin suspension 4–6 mL four times a day or 1–2 flavored pastilles four to five times daily (BII) • Gentian violet (0.00165%) topical application twice daily (BI) For Esophageal Candidiasis (for 14–21 Days) • Voriconazole 200 mg PO or IV twice a day (BI), *or* • Isavuconazole 200 mg PO as a loading dose, followed by 50 mg PO daily (BI), *or* • Isavuconazole 400 mg PO as a loading dose, followed by 100 mg PO daily (BI), *or* • Isavuconazole 400 mg PO once weekly (BI), *or* • Anidulafungin 100 mg IV 1 time, then 50 mg IV daily (BI), *or* • Caspofungin 50 mg IV daily (BI), *or* • Micafungin 150 mg IV daily (BI), *or* • Amphotericin B deoxycholate 0.6 mg/kg IV daily (BI), *or* • Lipid formulation of amphotericin B 3–4 mg/kg IV daily (BIII) For Uncomplicated Vulvo-Vaginal Candidiasis • Itraconazole oral solution 200 mg PO daily for 3–7 days (BII)	• Itraconazole oral solution 200 mg PO daily (CI) *Esophageal Candidiasis* • Fluconazole 100–200 mg PO daily (BI); or • Posaconazole 400 mg PO twice a day (BII) *Vulvo-Vaginal Candidiasis* • Fluconazole 150 mg PO once weekly (CII)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
		For Azole-Refractory *Candida glabrata* Vaginitis • Boric acid vaginal suppository 600 mg once daily for 14 days	
Chagas Disease (American Trypanosomiasis)	For Acute, Early Chronic, and Re-Activated Disease • Benznidazole 5–8 mg/kg/day PO in 2 divided doses for 30–60 days (BIII) (not commercially available in the United States; contact the CDC Drug Service at drugservice@cdc.gov or (404)-639-3670, or the CDC emergency operations center at 770-488-7100).	For Acute, Early Chronic, And Reactivated Disease: • Nifurtimox 8–10 mg/kg/day PO for 90–120 days (CIII) (not commercially available in the United States, contact the CDC Drug Service at drugservice@cdc.gov or (404) 639-3670, or the CDC emergency operations center at (770) 488-7100).	Treatment is effective in reducing parasitemia and preventing clinical symptoms or slowing disease progression. It is ineffective in achieving parasitological cure. Duration of therapy has not been studied in HIV-infected patients. Initiate or optimize ART in patients undergoing treatment for Chagas disease, once they are clinically stable (AIII).
Coccidioidomycosis	Clinically Mild Infections (e.g., Focal Pneumonia) • Fluconazole 400 mg PO daily (BII), *or* • Itraconazole 200 mg PO twice a day (BII) Severe, Non-Meningeal Infection (Diffuse Pulmonary Infection or Severely Ill Patients with Extrathoracic, Disseminated Disease) • Amphotericin B deoxycholate 0.7–1.0 mg/kg IV daily (AII) • Lipid formulation amphotericin B 4–6 mg/kg IV daily (AIII) • Duration of therapy: continue until clinical improvement, then switch to an azole (BIII). Meningeal Infections • Fluconazole 400–800 mg IV or PO daily (AII) Chronic Suppressive Therapy • Fluconazole 400 mg PO daily (AII), *or*	Mild Infections (Focal Pneumonia) *For Patients Who Failed to Respond to Fluconazole or Itraconazole* • Posaconazole 200 mg PO twice a day (BII), *or* • Voriconazole 200 mg PO twice a day (BIII) Severe, Non-Meningeal Infection (Diffuse Pulmonary Infection or Severely Ill Patients with Extrathoracic, Disseminated Disease) • Some specialists will add a triazole (fluconazole or itraconazole, with itraconazole preferred for bone disease) 400 mg per day to amphotericin B therapy and continue triazole once amphotericin B is stopped (BIII). Meningeal Infections • Itraconazole 200 mg PO three times a day for 3 days, then 200 mg PO twice a day (BII), *or*	Some patients with meningitis may develop hydrocephalus and require CSF shunting. Therapy should be continued indefinitely in patients with diffuse pulmonary or disseminated diseases because relapse can occur in 25%–33% of HIV-negative patients. It can also occur in HIV-infected patients with CD4 counts >250 cells/μL (BIII). Therapy should be lifelong in patients with meningeal infections because relapse occurs in 80% of HIV-infected patients after discontinuation of triazole therapy (AII). Itraconazole, posaconazole, and voriconazole may have significant interactions with certain ARV agents. These interactions are complex and can be bi-directional. Refer to Table 5 for dosage recommendations. Therapeutic drug monitoring and dosage adjustment may be necessary to ensure triazole antifungal and antiretroviral efficacy and reduce concentration-related toxicities.

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	• Itraconazole 200 mg PO twice a day (AII)	• Posaconazole 200 mg PO twice a day (BIII), *or* • Voriconazole 200–400 mg PO twice a day (BIII), *or* • Intrathecal amphotericin B deoxycholate, when triazole antifungals are ineffective (AIII) Chronic Suppressive Therapy • Posaconazole 200 mg PO twice a day (BII), *or* • Voriconazole 200 mg PO twice a day (BIII)	Intrathecal amphotericin B should only be given in consultation with a specialist and administered by an individual with experience with the technique.
Community-Acquired Pneumonia (CAP)	Empiric antibiotic therapy should be initiated promptly for patients presenting with clinical and radiographic evidence consistent with bacterial pneumonia. The recommendations listed are suggested empiric therapy. The regimen should be modified as needed once microbiologic results are available (BIII). Providers must also consider the risk of opportunistic lung infections (e.g., PCP, TB), which may alter the empiric therapy. Empiric Outpatient Therapy • A PO beta-lactam plus a PO macrolide (azithromycin or clarithromycin) (AII) *Preferred Beta-Lactams* • High-dose amoxicillin or amoxicillin/clavulanate *Alternative Beta-Lactams* • Cefpodoxime or cefuroxime*, or* • Levofloxacin 750 mg PO once daily (AII), *or* moxifloxacin 400 mg PO once daily (AII), especially for patients with penicillin allergies	Empiric antibiotic therapy should be initiated promptly for patients presenting with clinical and radiographic evidence consistent with bacterial pneumonia. The recommendations listed are suggested empiric therapy. The regimen should be modified as needed once microbiologic results are available (BIII). Providers must also consider the risk of opportunistic lung infections (e.g., PCP, TB), which may alter the empiric therapy. Empiric Outpatient Therapy • A PO beta-lactam plus PO doxycycline (CIII) *Preferred Beta-Lactams* • High-dose amoxicillin or amoxicillin/clavulanate *Alternative Beta-Lactams*: • Cefpodoxime or cefuroxime	Duration For most patients, 5–7 days Patients should be afebrile for 48–72 hours and clinically stable before stopping antibiotics. Longer duration is often required if severe CAP or bacteremia is present, and particularly if due to *S. pneumoniae* or complicated *S. aureus* pneumonia. Fluoroquinolones should be used with caution in patients in whom TB is suspected but is not being treated. Empiric therapy with a macrolide alone is not routinely recommended, because of increasing pneumococcal resistance (up to 30%) (BIII). Patients receiving a macrolide for MAC prophylaxis may have bacterial resistance to macrolide due to chronic exposure. For patients begun on IV antibiotic therapy, switching to PO should be considered when they are clinically improved and able to tolerate oral medications. Antibiotic chemoprophylaxis is generally not recommended because of the potential for

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	Empiric Therapy for Hospitalized Patients with Non-Severe CAP • An IV beta-lactam plus a macrolide (azithromycin or clarithromycin) (AI) *Preferred Beta-Lactams* • Ceftriaxone, cefotaxime, or ampicillin-sulbactam • Levofloxacin 750 mg IV once daily (AI), *or* moxifloxacin, 400 mg IV once daily (AI), especially for patients with penicillin allergies. Empiric Therapy for Hospitalized Patients with Severe CAP • An IV beta-lactam plus IV azithromycin (AI), *or* • An IV beta-lactam plus (levofloxacin 750 mg IV once daily or moxifloxacin 400 mg IV once daily) (AI) *Preferred Beta-Lactams* • Ceftriaxone, cefotaxime, or ampicillin-sulbactam Empiric Therapy for Patients at Risk of *Pseudomonas* Pneumonia • An IV antipneumococcal, antipseudomonal beta-lactam plus (ciprofloxacin 400 mg IV every 8–12 hours or levofloxacin 750 mg IV once daily) (AI) *Preferred Beta-Lactams* • Piperacillin-tazobactam, cefepime, imipenem, or meropenem Empiric Therapy for Patients at Risk for Methicillin-Resistant *Staphylococcus aureus* Pneumonia • Add vancomycin IV or linezolid (IV or PO) to the baseline regimen (AII). • Addition of clindamycin to vancomycin (but not to linezolid) can be considered for severe necrotizing pneumonia to minimize bacterial toxin production (CII).	Empiric Therapy for Hospitalized Patients with Non-Severe CAP • An IV beta-lactam plus doxycycline (CIII) Empiric Therapy for Hospitalized Patients with Severe CAP *For Penicillin-Allergic Patients* • Aztreonam IV plus (levofloxacin 750 mg IV once daily or moxifloxacin 400 mg IV once daily) (BIII) Empiric Therapy for Patients at Risk of *Pseudomonas* Pneumonia • An IV antipneumococcal, antipseudomonal beta-lactam plus an IV aminoglycoside plus azithromycin (BII), *or* • An IV antipneumococcal, antipseudomonal beta-lactam plus an aminoglycoside plus (levofloxacin 750 mg IV once daily or moxifloxacin 400 mg IV once daily) (BIII) *For Penicillin-Allergic Patients* • Replace the beta-lactam with aztreonam (BIII).	developing drug resistance and drug toxicities (AI).

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Cryptococcosis	Cryptococcal Meningitis *Induction Therapy (2 weeks, followed by consolidation therapy)* • Liposomal amphotericin B 3–4 mg/kg IV daily plus flucytosine 25 mg/kg PO four times a day (AI) (Note: Flucytosine dose should be adjusted in patients with renal dysfunction.) • Amphotericin B deoxycholate 0.7–1.0 mg/kg IV daily plus flucytosine 25 mg/kg PO four times a day (AI) (if cost is an issue and the risk of renal dysfunction is low), *or* • If not improved clinically or remain clinically unstable, continue induction therapy until the CSF culture is confirmed to be negative (BIII). *Consolidation Therapy (for at least 8 weeks (AI), followed by maintenance therapy)* • Fluconazole 800 mg PO (or IV) daily (AI) • For clinically stable patients with negative CSF cultures, dose can be reduced to 400 mg PO once daily (AII) • If CSF remains positive (but clinically stable) after 2 weeks of induction therapy, increase fluconazole dose to 1,200 mg and perform LP 2 weeks later (BIII); duration of consolidation therapy should be 8 weeks from the time of negative CSF culture (AI). *Maintenance Therapy* • Fluconazole 200 mg PO daily for ≥1 year from initiation of antifungal therapy (AI) For Non-CNS, Extrapulmonary Cryptococcosis and Diffuse Pulmonary Disease or Patients with Isolated Asymptomatic	Cryptococcal Meningitis *Induction Therapy (for at least 2 weeks, followed by consolidation therapy)* • Amphotericin B lipid complex 5 mg/kg IV daily plus flucytosine 25 mg/kg PO four times a day (BII), *or* • Liposomal amphotericin B 3–4 mg/kg IV daily plus fluconazole 800–1,200 mg PO or IV daily (BIII), *or* • Fluconazole 1,200 mg PO or IV daily plus flucytosine 25 mg/kg PO four times a day (BII), *or* • Fluconazole 800 mg PO or IV daily plus flucytosine 25 mg/kg PO four times a day (BIII), *or* • Amphotericin B deoxycholate 0.7–1.0 mg/kg IV daily plus fluconazole 800–1,200 mg PO or IV daily (BI), *or* • Liposomal amphotericin B 3–4 mg/kg IV daily (BI), *or* • Amphotericin B deoxycholate 0.7–1.0 mg/kg IV once daily alone (BI), *or* • Liposomal amphotericin B 3–4 mg/kg IV once daily plus flucytosine 25 mg/kg PO four times a day for 1 week followed by fluconazole 1,200 mg PO once daily (BIII), *or* • Fluconazole 1,200 mg PO or IV daily (CI) *Consolidation Therapy (for at least 8 weeks (AI), followed by maintenance therapy)* • If patient's CSF culture remains positive at the end of 2 weeks, but the patient is not ill enough to be	Addition of flucytosine to amphotericin B has been associated with more rapid sterilization of CSF and decreased risk for subsequent relapse. Patients receiving flucytosine should have either blood levels monitored (peak level 2 hours after dose should be 25–100 mcg/mL) or at least twice weekly monitoring of complete blood counts for cytopenia. Dosage should be adjusted in patients with renal insufficiency (BII). In resource limited settings, induction of 1 week of amphotericin B deoxycholate with flucytosine followed by high dose fluconazole is preferred (BIII). Opening pressure should always be measured when an LP is performed. Repeated LPs or CSF shunting are essential to effectively manage increased intracranial pressure. Corticosteroids and mannitol are ineffective in reducing ICP and are not recommended (AIII). Some specialists recommend a brief course of tapering dose of corticosteroid for management of severe IRIS symptoms (BIII).

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	Antigenemia Without Meningitis and Serum **CrAg. ≥1:640 by LFA** • Treatment same as for cryptococcal meningitis (BIII) Non-CNS Cryptococcosis with Mild-to-Moderate Symptoms and Focal Pulmonary Infiltrates, or Patients with Isolated Asymptomatic Antigenemia Without Meningitis **and Serum CrAg ≤1:320 by L**FA) • Fluconazole, 400 to 800 mg PO daily for 10 weeks, followed by 200 mg daily for a total of 6 months (BIII)	hospitalized, continue flucytosine for an additional 2 weeks with fluconazole 1,200 mg daily, before starting a single-drug consolidation regimen. • Itraconazole 200 mg PO twice a day for 8 weeks—less effective than fluconazole (CI) *Maintenance Therapy* • No alternative therapy recommendation	
Cryptosporidiosis	• Initiate or optimize ART for immune restoration to CD4 count >100 cells/μL (AII), *and* • Aggressive oral or IV rehydration and replacement of electrolyte loss (AIII), *and* • Symptomatic treatment of diarrhea with anti-motility agents (AIII).	No therapy has been shown to be effective without ART. Trial of these agents may be used in conjunction with, but not instead of, ART: • Nitazoxanide 500–1,000 mg PO twice a day for 14 days (CIII), *or* • Paromomycin 500 mg PO four times daily for 14–21 days (CIII) • With optimized ART, symptomatic treatment and rehydration and electrolyte replacement	Tincture of opium may be more effective than loperamide in management of diarrhea (CIII).
Cytomegalovirus (CMV) Disease	CMV Retinitis Induction Therapy (followed by Chronic Maintenance Therapy) *For Immediate Sight-Threatening Lesions (within 1,500 microns of the fovea)* • Ganciclovir 5 mg/kg every 12 hours IV or valganciclovir 900 mg PO twice a day or for 14–21 days (AI) (some prefer IV ganciclovir initially and transition to PO valganciclovir when there is evidence of clinical response) with or without • Intravitreal injections of ganciclovir (2 mg) or foscarnet (2.4 mg) to	CMV Retinitis *For Immediate Sight-Threatening Lesions (within 1,500 microns of the fovea): Intravitreal therapy as listed in the Preferred section, plus one of the following:* *Alternative Systemic Induction Therapy (followed by Chronic Maintenance Therapy)* • Foscarnet 90 mg/kg IV every 12 hours or 60 mg/kg every 8 hours for 14–21 days (BI), *or*	The choice of therapy for CMV retinitis should be individualized, based on tolerance of systemic medications, prior exposure to anti-CMV drugs, and location of the lesion (AIII). Given the evident benefits of systemic therapy in preventing contralateral eye involvement, reduce CMV visceral disease and improve survival. Whenever feasible, treatment should include systemic therapy. The ganciclovir ocular implant, which is effective for treatment of CMV retinitis, is no longer available.

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	rapidly achieve high intraocular concentration, continue weekly until lesion inactivity is achieved (AIII); plus *For Peripheral Lesions* • Valganciclovir 900 mg PO twice a day for 14–21 days, then 900 mg once daily (AI) *Maintenance Therapy* • Valganciclovir 900 mg PO daily (AI) for 3–6 months until ART induced immune recovery CMV Esophagitis or Colitis • Ganciclovir 5 mg/kg IV every 12 hours; may switch to valganciclovir 900 mg PO every 12 hours once the patient can tolerate oral therapy (BI) • Valganciclovir 900 mg PO every 12 hours may be considered as initial therapy in mild diseases (CIII) • Duration: 21–42 days or until symptoms have resolved (CII) • Maintenance therapy is usually not necessary, but should be considered after relapses (BII). Well-Documented, Histologically Confirmed CMV Pneumonia • Experience for treating CMV pneumonitis in HIV patients is limited. Use of IV ganciclovir or IV foscarnet is reasonable (doses same as for CMV retinitis) (CIII). • The optimal duration of therapy and the role of oral valganciclovir have not been established. CMV Neurological Disease *Note: Treatment should be initiated promptly.* • Ganciclovir 5 mg/kg IV every 12 hours plus (foscarnet 90 mg/kg IV every 12 hours or 60 mg/kg IV every 8 hours) to stabilize disease	• Cidofovir 5 mg/kg/week IV for 2 weeks; saline hydration before and after therapy and probenecid, 2 g PO 3 hours before dose, followed by 1 g PO 2 hours and 8 hours after the dose (total of 4 g) (CI) (Note: This regimen should be avoided in patients with sulfa allergy because of cross hypersensitivity with probenecid.) *Chronic Maintenance (for 3–6 months until ART-induced immune recovery)* • Foscarnet 90–120 mg/kg IV once daily (AI), *or* • Cidofovir 5 mg/kg IV every other week with saline hydration and probenecid as above (BI) CMV Esophagitis or Colitis • Foscarnet 90 mg/kg IV every 12 hours or 60 mg/kg every 8 hours (BI) for patients with treatment-limiting toxicities to ganciclovir or with ganciclovir resistance, *or* • Valganciclovir 900 mg PO every 12 hours in milder disease and if able to tolerate PO therapy (BII), *or* • Duration: 21–42 days or until symptoms have resolved (CII) • For mild disease, if ART can be initiated without delay, consider withholding CMV therapy (CIII).	Routine (i.e., every 3 months) ophthalmologic follow-up is recommended after stopping chronic maintenance therapy for early detection of relapse or IRU, and then periodically after sustained immune reconstitution (AIII). IRU may develop in the setting of immune reconstitution. Treatment of IRU Periocular, intravitreal, or short courses of systemic steroid (BIII) Initial therapy in patients with CMV retinitis, esophagitis, colitis, and pneumonitis should include initiation or optimization of ART (BIII).

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	and maximize response, continue until symptomatic improvement and resolution of neurologic symptoms (CIII) • The optimal duration of therapy and the role of oral valganciclovir have not been established.		
Hepatitis B Virus (HBV) Disease	ART is recommended for all HIV/HBV co-infected patients regardless of CD4 cell count (AII). ART regimen should include 2 drugs that are active against both HBV and HIV, such as [tenofovir 300 mg plus emtricitabine 200 mg (or lamivudine 300 mg)] PO once daily (plus additional drug(s) for HIV) (AIII). Duration Continue treatment indefinitely (CIII)	For Patients Who Refuse or Are Unable to Take ART or Who Are **HIV Long**-Term Non-Progressors • HBV treatment is indicated for patients with elevated ALT and HBV DNA >2,000 IU/mL significant liver fibrosis, advanced liver disease or cirrhosis (AI). • Peginterferon alfa-2a 180 mg SQ once weekly for 48 weeks (CIII), *or* • Peginterferon alfa-2b 1.5 mg/kg SQ once weekly for 48 weeks (CIII) If Tenofovir Cannot Be Used as Part of HIV/HBV Therapy (Because of Current or High Risk of Renal Dysfunction) • Use a fully suppressive ART regimen without tenofovir, and with the addition of entecavir (dose adjustment according to renal function) (BIII).	Directly acting HBV drugs—such as adefovir, emtricitabine, entecavir, lamivudine, telbivudine, or tenofovir—must not be given in the absence of a fully suppressive ART regimen to avoid selection of drug resistance HIV (AI). Cross-resistance to emtricitabine or telbivudine should be assumed in patients with suspected or proven lamivudine resistance. When changing ART regimens, continue agents with anti-HBV activity (BIII). If anti-HBV therapy is discontinued and a flare occurs, therapy should be re-instituted because it can be potentially lifesaving (AIII).
Hepatitis C Virus (HCV) Disease	The field of HCV drug development is evolving rapidly, with a number of investigational drugs currently at late-stage clinical trials, and some will soon be approved for use. Clinicians should refer to the most recent HCV treatment guidelines (http://www.hcvguidelines.org) for the most up-to-date recommendations.		
Herpes Simplex Virus (HSV) Disease	**Orolabial Lesions (for 5–10 Days)** • Valacyclovir 1 g PO twice a day (AIII), *or* • Famciclovir 500 mg PO twice a day (AIII), *or* • Acyclovir 400 mg PO three times a day (AIII)	For Acyclovir-Resistant HSV *Preferred Therapy* • Foscarnet 80–120 mg/kg/day IV in two to three divided doses until clinical response (AI)	Patients with HSV infection can be treated with episodic therapy when symptomatic lesions occur, or with daily suppressive therapy to prevent recurrences. Extemporaneous compounding of topical products can be prepared using trifluridine ophthalmic

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	Initial or Recurrent Genital HSV (for 5–14 days) • Valacyclovir 1 g PO twice a day (AI), *or* • Famciclovir 500 mg PO twice a day (AI), *or* • Acyclovir 400 mg PO three times a day (AI) Severe Mucocutaneous HSV • Initial therapy acyclovir 5 mg/kg IV every 8 hours (AIII) • After lesions begin to regress, change to PO therapy as above. Continue until lesions are completely healed. Chronic Suppressive Therapy *For Patients with Severe Recurrences of Genital Herpes (AI) or Patients Who Want to Minimize Frequency of Recurrences (AI)* • Valacyclovir 500 mg PO twice a day (AI), *or* • Famciclovir 500 mg PO twice a day (AI), *or* • Acyclovir 400 mg PO twice a day (AI) • Continue indefinitely, regardless of CD4 count.	*Alternative Therapy (CIII)* • IV cidofovir (dosage as in CMV retinitis), *or* • Topical trifluridine 1% three times a day, *or* • Topical cidofovir 1% once daily, *or* • Topical imiquimod 5% three times weekly, *or* • Topical foscarnet 1% five times daily Duration of Therapy • 21–28 days or longer	solution and the IV formulation of cidofovir and foscarnet. An expanded access program of oral pritelivir is now available for immunocompromised patients with acyclovir-resistant HSV infection. For more information, see the AiCuris Pritelivir website.
Histoplasmosis	Moderately Severe to Severe Disseminated Disease *Induction Therapy* • For at least 2 weeks or until clinically improved • Liposomal amphotericin B 3 mg/kg IV daily (AI) *Maintenance Therapy* • Itraconazole 200 mg PO three times a day for 3 days, then 200 mg PO twice a day (AII)	Moderately Severe to Severe Disseminated Disease *Induction Therapy (for at least 2 weeks or until clinically improved)* • Amphotericin B lipid complex 5 mg/kg IV daily (AIII), *or* Alternatives to Itraconazole for Maintenance Therapy or **Treatment of Less Severe** Disease • Posaconazole extended release 300 mg PO twice a	Itraconazole, posaconazole, and voriconazole may have significant interactions with certain ARV agents. These interactions are complex and can be bi-directional. Refer to Drug–Drug Interactions in the Adult and Adolescent Antiretroviral Guidelines for dosage recommendations. Therapeutic drug monitoring and dosage adjustment may be necessary to ensure triazole antifungal and ARV efficacy and reduce concentration-related toxicities.

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	Less Severe Disseminated Disease *Induction and Maintenance Therapy* • Itraconazole 200 mg PO three times a day for 3 days, then 200 mg PO twice a day (AII) *Duration of Therapy* • At least 12 months Meningitis *Induction Therapy (4–6 weeks)* • Liposomal amphotericin B 5 mg/kg/day (AIII) *Maintenance Therapy* • Itraconazole 200 mg PO twice a day to three times a day for ≥12 months and until resolution of abnormal CSF findings (AII) **Long**-Term Suppression Therapy *For patients with severe disseminated or CNS infection (AIII) after completion of at least 12 months of therapy and who relapse despite appropriate therapy (BIII)* • Itraconazole 200 mg PO daily (AIII)	day for 1 day, then 300 mg PO once daily (BIII) • Voriconazole 400 mg PO twice a day for 1 day, then 200 mg twice a day (BIII), *or* • Fluconazole 800 mg PO daily (CII) Meningitis (These Recommendations Are Based on Limited Clinical Data for Patients with Intolerance to Itraconazole) • Posaconazole extended release 300 mg PO twice a day for 1 day, then 300 mg PO once daily (BIII) • Voriconazole 400 mg PO twice a day for 1 day, then 200 mg twice a day (BIII), *or* • Fluconazole 800 mg PO daily (CII) **Long**-Term Suppression Therapy • Posaconazole 300 mg extended release tablet PO once daily (BIII) • Voriconazole 200 mg PO twice daily (BIII) • Fluconazole 400 mg PO once daily (CII)	Random serum concentration of itraconazole between 1–2 mcg/mL is recommended. Frequency and severity of toxicities increase when concentration is >4 mcg/mL. Acute pulmonary histoplasmosis in HIV-infected patients with CD4 counts >300 cells/mm^3 should be managed as non-immunocompromised host (AIII).
Human Herpesvirus-8 Diseases (*Kaposi Sarcoma [KS], Primary Effusion Lymphoma [PEL], Multicentric Castleman's Disease [MCD]*)	Mild to Moderate KS (Localized Involvement of Skin and/or Lymph Nodes) • Initiate or optimize ART (AII) Advanced KS (Visceral [AI] or Disseminated Cutaneous KS [BIII]) • Chemotherapy (per oncology consult) plus ART • Liposomal doxorubicin first-line chemotherapy (AI) **Primary Effusion Lymphoma** • Chemotherapy (per oncology consult) plus ART (AIII)	MCD • Rituximab (375 mg/m^2 given weekly for 4–8 weeks) may be an alternative to or used adjunctively with antiviral therapy (CII).	Corticosteroids should be avoided in patients with KS, including those with KS-IRIS (AIII). Corticosteroids are potentially effective as adjunctive therapy for MCD, but should be used with caution, especially in patients with concurrent KS. Patients who received rituximab for MCD may experience subsequent exacerbation or emergence of KS.

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	• PO valganciclovir or IV ganciclovir can be used as adjunctive therapy (CIII) MCD Therapy Options (in Consultation with Specialist, Depending on HIV/HHV-8 Status, Presence of Organ Failure, and Refractory Nature of Disease) ART (AIII) along with one of the following: • Valganciclovir 900 mg PO twice a day for 3 weeks (CII), *or* • Ganciclovir 5 mg/kg IV every 12 hours for 3 weeks (CII), *or* • Valganciclovir PO or Ganciclovir IV plus zidovudine 600 mg PO every 6 hours for 7–21 days (CII) • Rituximab +/- Prednisone (CII) • Monoclonal antibody targeting IL-6 or IL-6 receptor (BII) Concurrent KS and MCD Rituximab plus liposomal doxorubicin (BII)		
Human Papillomavirus (HPV) Disease	Treatment of Condyloma Acuminata (Genital Warts)		HIV-infected patients may have larger or more numerous warts and may not respond as well to therapy for genital warts when compared to HIV-uninfected individuals. Topical cidofovir has activity against genital warts, but the product is not commercially available (CIII). Intralesional interferon-alpha is usually not recommended because of high cost, difficult administration, and potential for systemic side effects (CIII). The rate of recurrence of genital warts is high despite treatment in HIV-infected patients. There is no consensus on the treatment of oral warts. Many treatments for anogenital warts cannot be used in the oral
	Patient-Applied Therapy for Uncomplicated External Warts That Can Be Easily Identified by Patients • Podophyllotoxin (e.g., podofilox 0.5% solution or 0.5% gel): Apply to all lesions twice a day for 3 consecutive days, followed by 4 days of no therapy, repeat weekly for up to 4 cycles, until lesions are no longer visible (BIII), *or* • Imiquimod 5% cream: Apply to lesion at bedtime and remove in the morning on 3 non-consecutive nights weekly for up to 16 weeks, until lesions are no longer visible. Each treatment should be washed with soap and water 6–10 hours after application (BII), *or*	Provider-Applied Therapy for Complex or Multicentric **Lesions, or Lesions** Inaccessible to Patient *Applied Therapy* • Cryotherapy (liquid nitrogen or cryoprobe): Apply until each lesion is thoroughly frozen. Repeat every 1–2 weeks for up to 4 weeks, until lesions are no longer visible (BIII). Some providers allow the lesion to thaw, then freeze a second time in each session (BIII), *or* • Trichloroacetic acid or bichloroacetic acid cauterization: 80%–90% aqueous solution, apply to	

Opportunistic Infection		Preferred Therapy	Alternative Therapy	Other Comments
		• Sinecatechins 15% ointment: Apply to affected areas three times a day for up to 16 weeks, until warts are completely cleared and not visible (BIII).	wart only, allow to dry until a white frost develops. Repeat weekly for up to 6 weeks, until lesions are no longer visible (BIII), *or* • Surgical excision (BIII) or laser surgery (CIII) to external or anal warts, *or* • Podophyllin resin 10%–25% in tincture of benzoin: Apply to all lesions (up to 10 cm^2), then wash off a few hours later, repeat weekly for up to 6 weeks until lesions are no longer visible (CIII).	mucosa. Surgery is the most common treatment for oral warts that interfere with function or for aesthetic reasons.
Isosporiasis (Cystoisosporiasis)		For Acute Infection • TMP-SMX (160 mg/800 mg) PO (or IV) four times a day for 10 days (AII), *or* • TMP-SMX (160 mg/800 mg) PO (or IV) twice a day for 7–10 days (BI) • Can start with twice a day dosing first and increase daily dose and/or duration (up to 3–4 weeks) if symptoms worsen or persist (BIII) • IV therapy may be used for patients with potential or documented malabsorption. Chronic Maintenance Therapy (Secondary Prophylaxis) • In patients with CD4 count <200/μL, TMP-SMX (160 mg/800 mg) PO three times weekly (AI)	For Acute Infection • Pyrimethamine[a] 50–75 mg PO daily plus leucovorin 10–25 mg PO daily (BIII), *or* • Ciprofloxacin 500 mg PO twice a day for 7 days (CI) as a second line alternative Chronic Maintenance Therapy (Secondary Prophylaxis) • TMP-SMX (160 mg/800 mg) PO daily or (320 mg/1,600 mg) three times weekly (BIII) • Pyrimethamine[a] 25 mg PO daily plus leucovorin 5–10 mg PO daily (BIII) • Ciprofloxacin 500 mg three times weekly (CI) as a second-line alternative	Fluid and electrolyte management in patients with dehydration (AIII). Nutritional supplementation for malnourished patients (AIII). Immune reconstitution with ART may result in fewer relapses (AIII).
Leishmaniasis	Visceral	For Initial Infection • Liposomal amphotericin B 2–4 mg/kg IV daily (AII), *or* • Liposomal amphotericin B interrupted schedule (e.g., 4 mg/kg on days 1–5, 10, 17, 24, 31, 38) (AII) • To achieve total dose of 20–60 mg/kg (AII)	For Initial Infection • Other lipid formulation of amphotericin B, dose and schedule as in Preferred Therapy, *or* • Amphotericin B deoxycholate 0.5–1.0 mg/kg IV daily for total dose of 1.5–2.0 g (BII), *or*	ART should be initiated or optimized (AIII). For sodium stibogluconate, contact the CDC Drug Service at (404) 639-3670 or drugservice@cdc.gov. For miltefosine, visit https://www.impavido.com.

Opportunistic Infection		Preferred Therapy	Alternative Therapy	Other Comments
		Chronic Maintenance Therapy (Secondary Prophylaxis); Especially in Patients with CD4 Count <200 cells/μL • Liposomal amphotericin B 4 mg/kg every 2–4 weeks (AII), *or* • Amphotericin B lipid complex (AII) 3 mg/kg every 21 days (AII)	• Sodium stibogluconate (pentavalent antimony) (BII) 20 mg/kg IV or IM daily for 28 days. • Miltefosine—if 30–44 kg: 50 mg two times daily; if ≥45 kg, 50 mg three times a day—for 28 days (CIII) Chronic Maintenance Therapy (Secondary Prophylaxis) • Sodium stibogluconate 20 mg/kg IV or IM every 4 weeks (BII)	
	Cutaneous	• Liposomal amphotericin B 2–4 mg/kg IV daily for 10 days (BIII), *or* • Liposomal amphotericin B interrupted schedule (e.g., 4 mg/kg on days 1–5, 10, 17, 24, 31, 38) to achieve total dose of 20–60 mg/kg (BIII), *or* • Sodium stibogluconate 20 mg/kg IV or IM daily for 3–4 weeks (BIII) Chronic Maintenance Therapy May be indicated in immunocompromised patients with multiple relapses (CIII)	Possible Options • Oral miltefosine (can be obtained via a treatment IND), *or* • Topical paromomycin, *or* • Intralesional sodium stibogluconate, *or* • Local heat therapy No data exist for any of these agents in HIV-infected patients; choice and efficacy dependent on species of *Leishmania.*	None
Malaria		Because *Plasmodium falciparum* malaria can progress within hours from mild symptoms or low-grade fever to severe disease or death, all HIV-infected patients with confirmed or suspected *P. falciparum* infection should be hospitalized for evaluation, initiation of treatment, and observation (AIII). Treatment recommendations for HIV-infected patients are the same as for HIV-uninfected patients (AIII). Choice of therapy is guided by the degree of parasitemia, the species of *Plasmodium*, the patient's clinical status, region of infection, and the likely drug susceptibility of the infected	When suspicion for malaria is low, antimalarial treatment should not be initiated until the diagnosis is confirmed.	For treatment recommendations for specific regions, clinicians should refer to the following web link: http://www.cdc.gov/malaria. or call the CDC Malaria Hotline: (770) 488-7788, Monday–Friday, 8 a.m.–4:30 p.m. ET; or (770-) 488-7100 after hours.

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	species, and can be found at https://www.cdc.gov/malaria.		
Microsporidiosis	For GI Infections Caused by *Enterocytozoon bienuesi* • Initiate or optimize ART with immune restoration to CD4 count >100 cells/mm^3 (AII); *plus* • Manage dehydration and diarrhea with fluid support (AII); and malnutrition and wasting with nutritional supplement (AIII). For Intestinal and Disseminated (Not Ocular) Infections Caused by Microsporidia Other Than *E. bienuesi* and *Vittaforma corneae* • Albendazole 400 mg PO twice daily (AII), continue until CD4 count >200 cells/mm^3 for >6 months after initiation of ART (BIII) For Disseminated Disease Caused by *Trachipleistophora* or *Anncaliia* • Itraconazole 400 mg PO daily plus albendazole 400 mg PO twice daily (CIII) For Ocular Infection • Topical fumagillin bicylohexylammonium (Fumidil B) eyedrops 3 mg/mL in saline (fumagillin 70 μg/mL): two eyedrops every 2 hours for 4 days, then two eyedrops four times daily (investigational use only in United States) (BII) plus albendazole 400 mg PO twice daily, for management of systemic infection (BIII) *If CD4 Count >200 Cells/mm^3* • Continue until symptoms resolved (CIII). *If CD4 Count ≤200 Cells/mm^3* • Continue until resolution of ocular symptoms and CD4 count increases to >200 cells/mm^3 for >6 months in response to ART (BIII).	For GI Infections Caused by *E. bienuesi* • Fumagillin 60 mg/day (BII) and TNP-470 (a synthetic analog of fumagillin) (BIII) may be effective, but neither is available in the United States. • Nitazoxanide (1,000 mg twice daily) may have some effect, but response may be minimal in patients with low CD4 cell counts (CIII).	Anti-motility agents can be used for diarrhea control if required (BIII).

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Mycobacterium avium Complex (MAC) Disease	**At Least 2 Drugs as Initial Therapy** to Prevent or Delay Emergence of Resistance • Clarithromycin 500 mg PO two times daily (AI) plus ethambutol 15 mg/kg PO daily (AI), *or* • If drug interaction or intolerance precludes the use of clarithromycin, (azithromycin 500–600 mg plus ethambutol 15 mg/kg) PO daily (AII) Duration • At least 12 months of therapy, can discontinue if no signs and symptoms of MAC disease and sustained (>6 months) CD4 count >100 cells/mm^3 in response to ART	Some experts recommend addition of a third or fourth drug for patients with high mycobacterial loads (>2 log CFU/mL of blood), or in the absence of effective ART (CIII). Third or Fourth Drug Options May Include • Rifabutin 300 mg PO daily (dose adjustment may be necessary based on drug interactions) (CI), *or* • A fluoroquinolone, such as moxifloxacin 400 mg PO daily (CIII) or levofloxacin 500 mg PO daily (CIII), *or* • An injectable aminoglycoside such as amikacin 10–15 mg/kg IV daily (CIII) or streptomycin 1 g IV or IM daily (CIII)	Testing of susceptibility to clarithromycin and azithromycin is recommended (BIII). NSAIDs can be used for moderate to severe symptoms attributed to IRIS (CIII). If IRIS symptoms persist, short course (i.e., 4 weeks–8 weeks) systemic corticosteroid (equivalent to 20–40 mg prednisone) can be used (CII).
Mycobacterium tuberculosis (TB) Disease	After collecting a specimen for culture and molecular diagnostic tests, empiric TB treatment should be started in individuals with clinical and radiographic presentation suggestive of TB (AIII). Refer to the Dosing Recommendations table in the *Mycobacterium tuberculosis* section for dosing recommendations. Initial Phase (8 weeks or 2 months, given daily by DOT) (AI) • INH (plus pyridoxine) plus (RIF or RFB) plus PZA plus EMB (AI) • If drug susceptibility report shows sensitivity to INH and RFP, then EMB can be discontinued before the end of 2 months (AI).	Treatment for Drug-Resistant TB *Empiric therapy for resistance to rifamycin +/- other drugs:* • INH plus PZA plus EMB plus (moxifloxacin or levofloxacin) plus (linezolid or amikacin) (BII) • Therapy should be modified once rifamycin resistance is confirmed, and based on drug susceptibility results to provide ≥5 drugs (BII). *Resistant to INH* • (Moxifloxacin or levofloxacin) plus (RIF or RFB) plus EMB plus PZA for 6 months (BII) *Resistance to Rifamycin +/- Other Drugs* • Therapy should be individualized based on drug susceptibility results and clinical and microbiologic responses, to include	DOT is recommended for all patients (AII). All rifamycins may have significant pharmacokinetic interactions with ARV drugs; please refer to the Dosing Recommendations table in the *Mycobacterium tuberculosis* section and the Drug–Drug Interactions section in the Adult and Adolescent Antiretroviral Guidelines for dosing recommendations. Therapeutic drug monitoring should be considered in patients receiving rifamycin and interacting ART. Adjunctive corticosteroids for TB meningitis (AII): dexamethasone 0.3–0.4mg/kg/day for 2–4 weeks, then taper by 0.1 mg/kg per week until 01mg/kg, then 4 mg per day, and taper by 1 mg/week for total of 12 weeks. Adjunctive corticosteroid is not recommended for patients with TB pericarditis.

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	Continuation Phase (Duration depends on site and severity of infection [as noted below].) • INH (plus pyridoxine) plus (RIF or RFB) daily (AI) Total Duration of Therapy (For Drug-Susceptible TB) *Pulmonary, Drug-Susceptible, Uncomplicated TB* • 6 months (AI) *Pulmonary TB with Positive Culture After 2 Months of TB Treatment, or Severe Cavitary or Disseminated Extrapulmonary TB* • 9 months (BII) *TB Meningitis*: • 9–12 months (BII) *Extra-Pulmonary TB in Other Sites* • 6 months (BII)	≥5 active drugs, and with close consultation with experienced specialists (AIII).	Paradoxical IRIS that is not severe can be treated with NSAIDs without a change in TB or HIV therapy (BIII). See text for prednisone dosing recommendations for preemptive treatment or management of IRIS.
Pneumocystis Pneumonia (PCP)	Patients who develop PCP despite TMP-SMX prophylaxis can usually be treated with standard doses of TMP-SMX (BIII). Duration of PCP treatment: 21 days (AII) For Moderate-to-Severe PCP • TMP-SMX: (TMP 15–20 mg and SMX 75–100 mg)/kg/day IV given every 6 hours or every 8 hours (AI); may switch to PO formulations after clinical improvement (AI). For Mild-to-Moderate PCP • TMP-SMX: (TMP 15–20 mg and SMX 75–100 mg)/kg/day, given PO in 3 divided doses (AI), *or* • TMP-SMX: (160 mg/800 mg or DS) two tablets PO three times daily (AI)	For Moderate-to-Severe PCP • Pentamidine 4 mg/kg IV daily infused over ≥60 minutes (AI); can reduce dose to 3 mg/kg IV daily in the event of toxicities (BI), *or* • Primaquine 30 mg (base) PO daily plus (clindamycin 600 mg IV every 6 hours or 900 mg IV every 8 hours) or (clindamycin 450 mg PO every 6 hours or 600 mg PO every 8 hours) (AI) For Mild-to-Moderate PCP • Dapsone 100 mg PO daily plus TMP 5 mg/kg PO three times a day (BI), *or* • Primaquine 30 mg (base) PO daily plus (clindamycin 450 mg PO every 6 hours or 600 mg PO every 8 hours) (BI), *or*	Indications for Adjunctive Corticosteroids (AI) PaO_2 <70 mmHg at room air, *or* Alveolar-arterial DO_2 gradient >35 mmHg Prednisone Doses (Beginning as Early as Possible and Within 72 Hours of PCP Therapy) (AI) • Days 1–5: 40 mg PO twice daily • Days 6–10: 40 mg PO daily • Days 11–21: 20 mg PO daily IV methylprednisolone can be administered as 75% of prednisone dose. Benefit of corticosteroid if started after 72 hours of treatment is unknown, but some clinicians will use it for moderate-to-severe PCP (BIII). Whenever possible, patients should be tested for G6PD before

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	Secondary Prophylaxis, After Completion of PCP Treatment • TMP-SMX DS: 1 tablet PO daily (AI), *or* • TMP-SMX (80 mg/400 mg or SS): 1 tablet PO daily (AI)	• Atovaquone 750 mg PO twice daily with food (BI) Secondary Prophylaxis, After Completion of PCP Treatment • TMP-SMX DS: 1 tablet PO three times weekly (BI), *or* • Dapsone 100 mg PO daily (BI), *or* • Dapsone 50 mg PO daily with (pyrimethamine[a] 50 mg plus leucovorin 25 mg) PO weekly (BI), *or* • (Dapsone 200 mg plus pyrimethamine[a] 75 mg plus leucovorin 25 mg) PO weekly (BI), *or* • Aerosolized pentamidine 300 mg monthly via Respirgard II™ nebulizer (BI), *or* • Atovaquone 1,500 mg PO daily (BI), *or* • (Atovaquone 1,500 mg plus pyrimethamine[a] 25 mg plus leucovorin 10 mg) PO daily (CIII)	use of dapsone or primaquine. Alternative therapy should be used in patients found to have G6PD deficiency. Patients who are receiving pyrimethamine[a]/sulfadiazine for treatment or suppression of toxoplasmosis do not require additional PCP prophylaxis (AII). If TMP-SMX is discontinued because of a mild adverse reaction, re-institution should be considered after the reaction resolves (AII). The dose can be increased gradually (desensitization) (BI), reduced, or the frequency modified (CIII). TMP-SMX should be permanently discontinued in patients with possible or definite Stevens-Johnson Syndrome or toxic epidermal necrosis (AII).
Progressive Multifocal **Leukoencephalopathy (PML)**/JC Virus Infections	There is no specific antiviral therapy for JC virus infection. The main treatment approach is to reverse the immunosuppression caused by HIV. Initiate ART immediately in ART-naive patients (AII). Optimize ART in patients who develop PML in phase of HIV viremia on ART (AIII).	None	Corticosteroids may be used for PML-IRIS characterized by contrast enhancement, edema or mass effect, and with clinical deterioration (BIII) (see text for further discussion).
Syphilis (*Treponema pallidum* Infection)	Early-Stage (Primary, Secondary, and Early-**Latent Syphilis)** • Benzathine penicillin G 2.4 million units IM for 1 dose (AII) **Late-Latent Disease (>1 year or of** Unknown Duration, and No Signs of Neurosyphilis)	Early-Stage (Primary, Secondary, and Early-**Latent** Syphilis) *For penicillin-allergic patients* • Doxycycline 100 mg PO twice a day for 14 days (BII), *or*	The efficacy of non-penicillin alternatives has not been evaluated in HIV-infected patients and they should be used only with close clinical and serologic monitoring. Combination of procaine penicillin and probenecid is not recommended for patients who

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	• Benzathine penicillin G 2.4 million units IM weekly for 3 doses (AII) **Late**-Stage (Tertiary–Cardiovascular or Gummatous Disease) • Benzathine penicillin G 2.4 million units IM weekly for 3 doses (AII) (Note: Rule out neurosyphilis before initiation of benzathine penicillin, and obtain infectious diseases consultation to guide management.) Neurosyphilis (Including Otic or Ocular Disease) • Aqueous crystalline penicillin G 18–24 million units per day (administered as 3–4 million units IV q4h or by continuous IV infusion) for 10–14 days (AII) +/- benzathine penicillin G 2.4 million units IM weekly for 3 doses after completion of IV therapy (CIII)	• Ceftriaxone 1 g IM or IV daily for 10–14 days (BII), *or* • Azithromycin 2 g PO for 1 dose (BII) (Note: Azithromycin is not recommended for men who have sex with men or pregnant women [AII].) **Late-Latent Disease (>1 year or of Unknown Duration, and No Signs of Neurosyphilis)** *For penicillin-allergic patients* • Doxycycline 100 mg PO twice a day for 28 days (BIII) Neurosyphilis • Procaine penicillin 2.4 million units IM daily plus probenecid 500 mg PO four times a day for 10–14 days (BII) +/- benzathine penicillin G 2.4 million units IM weekly for 3 doses after completion of above (CIII), *or* • For penicillin-allergic patients: Desensitization to penicillin is the preferred approach (BIII); if not feasible, ceftriaxone, 2 g IV daily for 10–14 days (BII)	are allergic to sulfa-containing medications (AIII). The Jarisch-Herxheimer reaction is an acute febrile reaction accompanied by headache and myalgia that can occur within the first 24 hours after therapy for syphilis. This reaction occurs most frequently in patients with early syphilis, high non-treponemal titers, and prior penicillin treatment.
Talaromycosis (Penicilliosis)	Induction Therapy • Liposomal amphotericin B 3–5 mg/kg/day IV (AI) *Duration* • 2 weeks (AI), followed by consolidation therapy Consolidation Therapy • Itraconazole 200 mg PO twice daily for 10 weeks (AI), followed by chronic maintenance therapy Chronic Maintenance Therapy • Itraconazole 200 mg PO once daily, until CD4 count >100 cells/mm^3 for ≥6 months (AII)	Induction Therapy • Amphotericin B deoxycholate 0.7 mg/kg/day IV for 2 weeks (if liposomal amphotericin B is not available) (AI) *If Amphotericin B is Not Available* • Voriconazole 6 mg/kg IV every 12 hours for 1 day (loading dose), then 4 mg/kg IV every 12 hours (BII), *or* • Voriconazole 600 mg PO twice daily for 1 day (loading dose), then 400 mg PO twice daily (BII)	Itraconazole is not recommended as induction therapy for talaromycosis (AI). ART can be initiated as early as 1 week after initiation of treatment for talaromycosis (BIII). Itraconazole and voriconazole may have significant interactions with certain ARV agents. These interactions are complex and can be bi-directional. Refer to Drug–Drug Interactions in the Adult and Adolescent Antiretroviral Guidelines for dosage recommendations. TDM and dosage adjustment may be necessary to ensure triazole

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
		Duration • 2 weeks (BII) followed by consolidation therapy with itraconazole (preferred) or voriconazole Consolidation Therapy • Voriconazole 200 mg PO twice daily for 10 weeks (BII), followed by chronic maintenance therapy Chronic Maintenance Therapy • Itraconazole should be used (AII). Chronic maintenance therapy with voriconazole has not been studied.	antifungal and ARV efficacy and reduce concentration-related toxicities. The goals of itraconazole and voriconazole trough concentrations are >0.5 mcg/mL and >1.0 mcg/mL, respectively.
Toxoplasma gondii Encephalitis	Treatment of Acute Infection (AI) • Pyrimethamine[a] 200 mg PO 1 time, followed by weight-based therapy: o If <60 kg: pyrimethamine[a] 50 mg PO once daily plus sulfadiazine 1,000 mg PO every 6 hours plus leucovorin 10–25 mg PO once daily o If ≥60 kg: pyrimethamine[a] 75 mg PO once daily plus sulfadiazine 1,500 mg PO every 6 hours plus leucovorin 10–25 mg PO once daily • Leucovorin dose can be increased to 50 mg daily or twice a day. Duration for Acute Therapy • At least 6 weeks (BII); longer duration if clinical or radiologic disease is extensive or response is incomplete at 6 weeks • After completion of acute therapy, all patients should be initiated on chronic maintenance therapy. Chronic Maintenance Therapy • Pyrimethamine[a] 25–50 mg PO daily plus sulfadiazine 2,000–4,000 mg PO daily (in 2–4 divided doses)	Treatment of Acute Infection • Pyrimethamine[a] (leucovorin)* plus clindamycin 600 mg IV or PO every 6 hours (AI), *or* • TMP-SMX (TMP 5 mg/kg and SMX 25 mg/kg) IV or PO twice a day (BI), *or* • Atovaquone 1,500 mg PO twice a day with food plus pyrimethamine[a] (leucovorin)* (BII), *or* • Atovaquone 1,500 mg PO twice a day with food plus sulfadiazine 1,000–1,500 mg PO every 6 hours (weight-based dosing, as in preferred therapy) (BII), *or* • Atovaquone 1,500 mg PO twice a day with food (BII), *or* Chronic Maintenance Therapy • Clindamycin 600 mg PO every 8 hours plus (pyrimethamine[a] 25–50 mg plus leucovorin 10–25 mg) PO daily (BI), *or*	If pyrimethamine is unavailable or there is a delay in obtaining it, TMP-SMX should be utilized in place of pyrimethamine-sulfadiazine (BI). For patients with a history of sulfa allergy, sulfa desensitization should be attempted using one of several published strategies (BI). Atovaquone should be administered until therapeutic doses of TMP-SMX are achieved (CIII). Adjunctive corticosteroids (e.g., dexamethasone) should only be administered when clinically indicated to treat mass effect associated with focal lesions or associated edema (BIII); discontinue as soon as clinically feasible. Anticonvulsants should be administered to patients with a history of seizures (AIII) and continued through acute treatment, but should not be used as seizure prophylaxis (AIII). If clindamycin is used in place of sulfadiazine, additional therapy

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	plus leucovorin 10–25 mg PO daily (AI)	• TMP-SMX DS 1 tablet twice a day (BII), *or* • TMP-SMX DS 1 tablet once daily (BII); *or* • Atovaquone 750–1,500 mg PO twice a day plus (pyrimethamine[a] 25 mg plus leucovorin 10 mg) PO daily (BII), *or* • Atovaquone 750–1,500 mg PO twice a day plus sulfadiazine 2,000–4,000 mg PO daily (in 2–4 divided doses (BII), *or* • Atovaquone 750–1,500 mg PO twice a day with food (BII) * Pyrimethamine[a] and leucovorin doses are the same as for preferred therapy.	must be added to prevent PCP (AII).
Varicella Zoster Virus (VZV) Disease	Primary Varicella Infection (Chickenpox) *Uncomplicated Cases* • Initiate as soon as possible after symptom onset and continue for 5 to 7 days: o Valacyclovir 1 g PO three times a day (AII), *or* o Famciclovir 500 mg PO three times a day (AII) *Severe or Complicated Cases* • Acyclovir 10 mg/kg IV every 8 hours for 7–10 days (AIII) • May switch to oral valacyclovir, famciclovir, or acyclovir after defervescence if no evidence of visceral involvement (BIII). Herpes Zoster (Shingles) *Acute Localized Dermatomal* • For 7–10 days; consider longer duration if lesions are slow to resolve	Primary Varicella Infection (Chickenpox) *Uncomplicated Cases (for 5–7 Days)* • Acyclovir 800 mg PO five times a day (BII) Herpes Zoster (Shingles) *Acute Localized Dermatomal* • For 7–10 days; consider longer duration if lesions are slow to resolve • Acyclovir 800 mg PO 5 times a day (BII)	In managing VZV of the eyes, consultation with an ophthalmologist experienced in management of VZV retinitis is strongly recommended (AIII). Duration of therapy for VZV retinitis is not well defined, and should be determined based on clinical, virologic, and immunologic responses and ophthalmologic responses. Optimization of ART is recommended for serious and difficult-to-treat VZV infections (e.g., retinitis, encephalitis) (AIII). In patients with herpes zoster ophthalmicus who have stromal keratitis and anterior uveitis, topical corticosteroids to reduce inflammation may be necessary. The role of ART has not been established in these cases.

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	• Valacyclovir 1 g PO three times a day (AII), *or* • Famciclovir 500 mg three times a day (AII) **Extensive Cutaneous Lesion or** Visceral Involvement • Acyclovir 10 mg/kg IV every 8 hours until clinical improvement is evident (AII) • May switch to PO therapy (valacyclovir, famciclovir, or acyclovir) after clinical improvement (i.e., when no new vesicle formation or improvement of signs and symptoms of visceral VZV), to complete a 10–14-day course (BIII). ARN • Acyclovir 10 mg/kg IV every 8 hours for 10–14 days, followed by valacyclovir 1g PO three times a day for >14 weeks (AIII), *plus* • Intravitreal ganciclovir 2 mg/0.05 mL twice weekly for 1-2 doses (BIII) PORN • Acyclovir 10 mg/kg IV every 8 hours or ganciclovir 5 mg/kg IV every 12 hours (AIII), *plus* • ≥1 intravitreal antiviral injection: ganciclovir 2 mg/0.05 mL or foscarnet 1.2 mg/0.05 ml twice weekly (AIII) • Initiate or optimize ART (AIII)		

[a] Refer to Daraprim Direct for information on accessing pyrimethamine.

For information regarding the evidence ratings, refer to the Rating System for Prevention and Treatment Recommendations in the Introduction section of the Adult and Adolescent Opportunistic Infection Guidelines.

Key: ARN = acute retinal necrosis; ART = antiretroviral therapy; ARV = antiretroviral; CD4 = CD4 T lymphocyte cell; CDC = Centers for Disease Control and Prevention; CDI = *Clostridium* difficile infection; CFU = colony-forming unit; CNS = central nervous system; CSF = cerebrospinal fluid; CYP3A4 = Cytochrome P450 3A4; DOT = directly observed therapy; DS = double strength; EMB = ethambutol; g = gram; G6PD = Glucose-6-phosphate dehydrogenase; GI = gastrointestinal; ICP = intracranial pressure; IM = intramuscular; IND = investigational new drug; INH = isoniazid; IRIS = immune reconstitution inflammatory syndrome; IRU = immune reconstitution uveitis; IV = intravenous; LP = lumbar puncture; MIC = minimum inhibitory concentrations; mg = milligram; mmHg = millimeters of mercury; MSM = men who have sex with men; NSAID = non-steroidal anti-inflammatory drugs; PCR = polymerase chain reaction; PI = protease inhibitor; PO = oral; PORN = progressive outer retinal necrosis; PZA = pyrazinamide; RFB = rifabutin; RIF = rifampin; SQ = subcutaneous; TVR = telaprevir; TMP-SMX = trimethoprim-sulfamethoxazole

Table 3. Dosing Recommendations for Anti-TB Drugs for Treatment of Active Drug-Sensitive TB

(Last updated February 17, 2022; last reviewed February 17, 2022)

TB Drug	ARV Drugs	Daily Dose
Isoniazid	All ARVs	5 mg/kg (usual dose 300 mg)
Rifampin[a,b] Note: DTG, RAL, and MVC doses need to be adjusted when used with rifampin.	HIV PIs, DOR, ETR, RPV, BIC, CAB, or EVG/c	Not recommended
	TAF	Use with caution[c] at dose indicated below.
	All other ARV drugs	10 mg/kg (usual dose 600 mg)
Rifabutin[a] Note: DOR and RPV[d] doses need to be adjusted when used with rifabutin.	PI with COBI, TAF, RPV (IM), BIC, CAB, EVG/c-containing regimens	Not recommended
	DTG, RAL, DOR, EFV, or RPV (PO only[d])	5 mg/kg (usual dose 300 mg)
	HIV PIs with RTV	150 mg daily[e]
	EFV	450–600 mg
Pyrazinamide	All ARVs	Weight-based dosing • *Weighing 40–55 kg*: 1,000 mg (18.2–25.0 mg/kg) • *Weighing 56–75 kg*: 1,500 mg (20.0–26.8 mg/kg) • *Weighing 76–90 kg*: 2,000 mg (22.2–26.3 mg/kg) • *Weighing >90 kg*: 2,000 mg[f]
Ethambutol	All ARVs	Weight-based dosing • *Weighing 40–55 kg*: 800 mg (14.5–20.0 mg/kg) • *Weighing 56–75 kg*: 1,200 mg (16.0–21.4 mg/kg) • *Weighing 76–90 kg*: 1,600 mg (17.8–21.1 mg/kg) • *Weighing >90 kg*: 1,600 mg[f]

[a] For more detailed guidelines on use of different ARV drugs with rifamycin, clinicians should refer to the Drug–Drug Interactions section of the Adult and Adolescent Antiretroviral Guidelines.

[b] Higher doses may be needed in the treatment of TB meningitis. Expert consultation is advised.

[c] This combination has not been tested in patients to confirm pharmacokinetic and virologic efficacy among patients taking full-dose ARV and TB regimens.

[d] Intramuscular long-acting RPV is not recommended with rifabutin. PO RPV can be used but the dose should be increased to 50 mg daily.

[e] Acquired rifamycin resistance has been reported in patients with inadequate rifabutin levels while on 150 mg twice weekly, dosing together with RTV-boosted PIs. May consider therapeutic drug monitoring (TDM) when rifabutin is used with an RTV-boosted PI and adjust dose accordingly.

[f] Monitor for therapeutic response and consider TDM to assure dosage adequacy in patients weighing >90 kg.

For information regarding the evidence ratings, refer to the Rating System for Prevention and Treatment Recommendations in the Introduction section of the Adult and Adolescent Opportunistic Infection Guidelines.

Key: ARV = antiretroviral; BIC = bictegravir; CAB = cabotegravir; COBI = cobicistat; DOR = doravirine; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; MVC = maraviroc; PI = protease inhibitor; PO = oral; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TB = tuberculosis

Table 4. Indications for Discontinuing and Restarting Opportunistic Infection Secondary Prophylaxis or Chronic Maintenance in HIV-Infected Adults and Adolescents (page 1 of 3) (Last updated July 1, 2021; last reviewed January 12, 2022)

Opportunistic Infection	Indication for Discontinuing Primary Prophylaxis	Indication for Restarting Primary Prophylaxis	Indication for Discontinuing Secondary Prophylaxis/ Chronic Maintenance Therapy	Indication for Restarting Secondary Prophylaxis/Chronic Maintenance
Bacterial Enteric Infections: Salmonellosis	Not applicable	Not applicable	Resolution of *Salmonella* infection and after response to ART with sustained viral suppression and CD4 counts >200 cells/μL **(CII)**	No recommendation
Bartonellosis	Not applicable	Not applicable	• Received at least 3–4 months of treatment, *and* • CD4 count >200 cells/μL for ≥6 months **(CIII)** Some specialists would only discontinue therapy if *Bartonella* titers have also decreased by four-fold **(CIII)**.	No recommendation
Candidiasis (Mucocutaneous)	Not applicable	Not applicable	If used, reasonable to discontinue when CD4 count >200 cells/μL **(AIII)**.	No recommendation
Coccidioidomycosis	CD4 count ≥250 cells/μL for ≥6 months **(CIII)**	Restart at CD4 count <250 cells/ μL **(BIII)**	Only for patients with focal coccidioidal pneumonia **(AII)**: • Clinically responded to ≥12 months antifungal therapy, with CD4 count >250 cells/mm³, and receiving effective ART. • Should continue monitoring for recurrence with serial chest radiographs and coccidioidal serology. For patients with diffuse pulmonary **(BIII)**, disseminated non-meningeal **(BIII),** or meningeal diseases **(AII):** For meningeal diseases **(AII)**: Suppressive therapy should be continued indefinitely, even with increase in CD4 count on ART.	No recommendation
Cryptococcal Meningitis	Not applicable	Not applicable	If the following criteria are fulfilled **(BII)**: • Completed initial (induction and consolidation) therapy, *and* • Received at least 1 year of antifungal therapy, *and* • Remain asymptomatic of cryptococcal infection, *and* CD4 count ≥100 cells/μL, and with suppressed plasma HIV RNA in response to ART	CD4 count <100 cells/ μL **(AIII)**

Table 4. Indications for Discontinuing and Restarting Opportunistic Infection Secondary Prophylaxis or Chronic Maintenance in HIV-Infected Adults and Adolescents (page 2 of 3)

Opportunistic Infection	Indication for Discontinuing Primary Prophylaxis	Indication for Restarting Primary Prophylaxis	Indication for Discontinuing Secondary Prophylaxis/ Chronic Maintenance Therapy	Indication for Restarting Secondary Prophylaxis/ Chronic Maintenance
Cytomegalovirus Retinitis	Not applicable	Not applicable	• CMV treatment for at least 3 to 6 months; and with CD4 count >100 cells/μL for >3 to 6 months in response to ART **(AII)**. • Therapy should be discontinued only after consultation with an ophthalmologist, taking into account anatomic location of lesions, vision in the contralateral eye, and feasibility of regular ophthalmologic monitoring. Routine (i.e., every 3 months) ophthalmologic follow-up is recommended after stopping therapy for early detection of relapse or immune restoration uveitis, and then periodically after sustained immune reconstitution **(AIII)**.	CD4 count <100 cells/μL **(AIII)**
***Histoplasma capsulatum* Infection**	On ART, with CD4 count >150 cells/mm^3 and undetectable HIV-1 viral load for 6 months **(BIII)**	For patients at high risk of acquiring histoplasmosis, restart if CD4 count falls to <150 cells/mm^3 **(CIII)**	If the following criteria **(AI)** are fulfilled: • Received azole therapy for >1 year, *and* • Negative fungal blood cultures, *and* • Serum or urine *Histoplasma* antigen below the level of quantification, *and* • Undetectable HIV viral load, *and* • CD4 count ≥150 cells/mm^3 for ≥6 months in response to ART	CD4 count <150 cells/ mm^3 **(BIII)**
***Isospora belli* Infection**	Not applicable	Not applicable	Sustained increase in CD4 count to >200 cells/μL for >6 months in response to ART and without evidence of *I. belli* infection **(BIII)**	No recommendation
Leishmaniasis: Visceral (and possibly cutaneous leishmaniasis in immunocompromised patients with multiple relapses)	Not applicable	Not applicable	There is no consensus regarding when to stop secondary prophylaxis. Some investigators suggest that therapy can be stopped if CD4 count increases to >200 to 350 cells/μL for 3–6 months in response to ART, but others suggest that therapy should be continued indefinitely.	No recommendation
Microsporidiosis	Not applicable	Not applicable	No signs and symptoms of non-ocular **(BIII)** or ocular **(CIII)** microsporidiosis and CD4 count >200 cells/μL for >6 months in response to ART.	No recommendation
***Mycobacterium avium* Complex Disease**	Initiation of effective ART **(AI)**	CD4 count <50 cells/mm^3: only if not on fully suppressive ART **(AIII)**	If the Following Criteria are Fulfilled **(AI)**: • Completed ≥12 months of therapy, *and* • No signs and symptoms of MAC disease, *and* Have sustained (>6 months) CD4 count >100 cells/mm^3 in response to ART.	CD4 count <100 cells/ mm^3 **(AIII)**

Table 4. Indications for Discontinuing and Restarting Opportunistic Infection Secondary Prophylaxis or Chronic Maintenance in HIV-Infected Adults and Adolescents (page 3 of 3)

Opportunistic Infection	Indication for Discontinuing Primary Prophylaxis	Indication for Restarting Primary Prophylaxis	Indication for Discontinuing Secondary Prophylaxis/ Chronic Maintenance Therapy	Indication for Restarting Secondary Prophylaxis/ Chronic Maintenance
***Pneumocystis* Pneumonia**	CD4 count increased from <200 to >200 cells/mm^3 for >3 months in response to ART **(AI)** Can consider when CD4 count is 100–200 cells/mm^3 if HIV RNA remains below limits of detection for ≥3 months–6 months **(BII)**.	CD4 count <100 cells/mm^3 **(AIII)** CD4 count 100–200 cells/mm^3 and HIV RNA above detection limit of the assay **(AIII)**.	CD4 count increased from <200 cells/mm^3 to >200 cells/mm^3 for >3 months in response to ART **(BII)** Can consider when CD4 count is 100–200 cells/mm^3 if HIV RNA remains below limits of detection for ≥3 months–6 months **(BII)**. If PCP occurs at a CD4 count >200 cells/mm^3 while not on ART, discontinuation of prophylaxis can be considered once HIV RNA levels are suppressed to below limits of detection for ≥3months–6 months **(CIII)**. If PCP occurs at a CD4 count >200 cells/mm^3 while on ART, continue PCP prophylaxis for life, regardless of how high the CD4 cell count rises as a consequence of ART **(BIII)**.	CD4 count <100 cells/mm^3 **(AIII)** CD4 count 100–200 cells/mm^3 and with HIV RNA above detection limit of the assay **(AIII)**.
Talaromycosis (Penicilliosis)	CD4 count >100 cells/mm^3 for >6 months in response to ART **(BII)** *or* If achieved sustained HIV viral suppression for >6 months **(BIII)**	CD4 count <100 cells/mm^3 **(BIII)**—if patient is unable to have ART, or has treatment failure without access to effective ART options, and still resides in or travels to the endemic area	CD4 count >100 cells/mm^3 for ≥6 months in response to ART **(BII)** *or* If achieved sustained HIV viral suppression for >6 months **(BIII)**	CD4 count <100 cells/mm^3 **(BIII)**
***Toxoplasma gondii* Encephalitis**	CD4 count increased to >200 cells/µL for >3 months in response to ART **(AI)** Can consider when CD4 count 100-200 cells/µL if HIV RNA remain below limits of detection for at least 3-6 months **(BII)**	CD4 count <100 cells/µL, **(AIII)** CD4 count 100-200 cells/µL and with HIV RNA above detection limit of the assay **(AIII)**.	Successfully completed initial therapy, rSuccessfully completed initial therapy, receiving maintenance therapy and remain free of signs and symptoms of TE, and CD4 count >200 cells/µL for >6 months in response to ART **(BI)**.	CD4 count <200 cells/µL **(AIII)**

Key to Acronyms: ART = antiretroviral therapy; CD4 = CD4 T lymphocyte cell; CMV = cytomegalovirus; MAC = *Mycobacterium avium* complex; PCP = *Pneumocystis* pneumonia; TE = *Toxoplasma* encephalitis

Evidence Rating:

Strength of Recommendation:

A: Strong recommendation for the statement
B: Moderate recommendation for the statement
C: Optional recommendation for the statement

Quality of Evidence for the Recommendation:

I: One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
II: One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes
III: Expert opinion

In cases where there are no data for the prevention or treatment of an OI based on studies conducted in HIV-infected populations, but data derived from HIV-uninfected patients exist that can plausibly guide management decisions for patients with HIV/AIDS, the data will be rated as III but will be assigned recommendations of A, B, C depending on the strength of recommendation.

Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 1 of 15) (Last updated October 22, 2019; last reviewed January 12, 2022)

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

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

Do not coadminister.

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

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

Coadministration should be avoided, if possible.

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

Use with caution.

Drug combinations are recommended to be used with caution when:

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

Rifamycin Antibiotics-Related Interactions

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

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

Table 6. Common or Serious Adverse Reactions Associated with Systemically Administered Drugs Used to Treat Opportunistic Infections (page 1 of 6) (Last updated October 22, 2019; last reviewed January 12, 2022)

Drug(s)	Common or Serious Adverse Reactions
Acyclovir	Crystalluria associated with high doses, dehydration, or pre-existing renal impairment; nephrotoxicity secondary to obstructive urolithiasis, particularly after high dose rapid IV infusion; neurotoxicity (e.g., agitation, confusion, hallucination, seizure, coma) with high doses, especially in patients with renal impairment and/or older patients; thrombophlebitis at peripheral IV infusion site; nausea; vomiting; headache
Adefovir	Nausea, asthenia, nephrotoxicity (especially in patients with underlying renal insufficiency or predisposing comorbidities, or in patients who are currently taking nephrotoxic drugs)
Albendazole	Nausea, vomiting, hepatotoxicity, hypersensitivity reaction, dizziness, headache, reversible alopecia **Rarely:** Granulocytopenia, agranulocytosis, pancytopenia
Amikacin	Nephrotoxicity, ototoxicity (both hearing loss and vestibular toxicity are possible), neuromuscular blockade (associated with rapid infusion of large aminoglycoside doses), pain upon IM injection
Amoxicillin/Clavulanate and Ampicillin/Sulbactam	Diarrhea, nausea, vomiting, abdominal pain, *Clostridium difficile*-associated diarrhea and colitis, hypersensitivity reactions (immediate or delayed reactions, including anaphylaxis), bone marrow suppression, drug fever, neurotoxicity (seizure) at high doses (especially in patients with renal dysfunction)
Amphotericin B Deoxycholate and Lipid Formulations	Nephrotoxicity, infusion-related reactions (e.g., fever, chills, rigors, back pain, hypotension), hypokalemia, hypomagnesemia, anemia, thrombophlebitis, nausea, vomiting Lower incidence of nephrotoxicity and infusion-related reactions with liposomal formulations.
Anidulafungin	Generally well-tolerated. Hepatotoxicity, histamine-related infusion reactions (flushing, rash, pruritus, hypotension, and dyspnea are rare when infusion rate <1.1 mg/min), hypokalemia, diarrhea
Artemether/Lumefantrine	Generally well-tolerated. Rash, pruritus, nausea, vomiting, abdominal pain, anorexia, diarrhea, arthralgia, myalgia, dizziness, asthenia, headache, QTc prolongation **Rarely:** Hemolytic anemia
Artesunate	Generally well-tolerated. Bradycardia, dizziness, nausea and vomiting, skin rash, pruritus, postartemisinin delayed hemolysis, QTc prolongation
Atovaquone	Rash, nausea, vomiting, diarrhea, hepatotoxicity, headache, hyperglycemia, fever
Atovaquone/Proguanil	Pruritus, rash, nausea, vomiting, abdominal pain, diarrhea, anorexia, erythema multiforme, asthenia, dizziness, headache, oral ulcers, hepatotoxicity
Azithromycin	Nausea, vomiting, diarrhea, hepatotoxicity, ototoxicity (with prolonged use), rash, urticaria, pruritus, abdominal pain, *C. difficile*-associated diarrhea **Rarely:** Torsades de Pointes (greatest risk in patients with underlying QTc prolongation)
Aztreonam	Diarrhea, thrombophlebitis, neutropenia, increased liver enzymes, *C. difficile*-associated diarrhea **Rarely:** Hypersensitivity reaction
Benznidazole	Photosensitivity, allergic dermatitis, paresthesia, peripheral neuropathy, nausea, vomiting, abdominal pain, anorexia, weight loss, bone marrow suppression
Bedaquiline	Nausea, arthralgia, headache, QTc prolongation, elevated transaminases
Capreomycin	Nephrotoxicity, ototoxicity (both hearing loss and vestibular toxicity are possible), pain upon IM injection
Caspofungin	Generally well-tolerated. Fever, thrombophlebitis, histamine-related infusion reactions (flushing, rash, pruritus, facial swelling, hypotension, dyspnea), hypokalemia, anemia, headache, hepatotoxicity, diarrhea

Table 6. Common or Serious Adverse Reactions Associated with Systemically Administered Drugs Used to Treat Opportunistic Infections (page 2 of 6)

Drug(s)	Common or Serious Adverse Reactions
Ceftriaxone	Generally well-tolerated. Cholelithiasis, urolithiasis, pancreatitis, rash, diarrhea, drug fever, hemolytic anemia, *C. difficile*-associated diarrhea and colitis, injection-site reactions after IM injections
Cephalosporins **See above for Ceftriaxone**	Hypersensitivity reaction, rash, nausea, vomiting, diarrhea, *C. difficile*-associated diarrhea and colitis, bone marrow suppression, hemolytic anemia **Rarely:** CNS toxicities (e.g., seizure, confusion) mostly seen with high doses used in patients with renal insufficiency or elderly patients without dose adjustment
Chloroquine and Hydroxychloroquine	Headache, pruritus, skin pigmentation, nausea, vomiting, abdominal pain, diarrhea, anorexia, photosensitivity, visual disturbances including blurry vision and retinal toxicity, auditory disturbances, QTc prolongation, cardiomyopathy, bone marrow suppression, hemolysis (associated with G6PD deficiency), hypersensitivity reaction (including TEN, SJS, and EM), hepatitis, neuropsychiatric changes (including extrapyramidal reactions and suicidal behavior), convulsive seizures, severe hypoglycemia (which may require adjustment of antidiabetic medications) **Rarely:** Neuromyopathy (which may occur with long-term use)
Cidofovir	Nephrotoxicity, proteinuria, ocular hypotony, anterior uveitis/iritis, neutropenia, metabolic acidosis (including Fanconi's syndrome), diarrhea, asthenia, fever, headache, alopecia, anemia Side effects most likely related to co-administration with probenecid are rash, nausea, vomiting, anorexia.
Ciprofloxacin	Nausea, vomiting, abdominal pain, diarrhea, *C. difficile*-associated diarrhea and colitis, headache, dizziness, sleep disturbances, tendonitis and tendon rupture (associated with age >60 and concomitant steroid use), photosensitivity, hypoglycemia, peripheral neuropathy, hepatotoxicity, QTc prolongation, neurotoxicity (especially with high doses, use in elderly patients, or use in patients with renal dysfunction), seizures, and mental health side effects (e.g., disorientation, agitation, memory impairment, delirium) **Rarely:** Aortic dissection
Clarithromycin	Hepatotoxicity, ototoxicity (with high doses or prolonged use), headache, nausea, vomiting, abdominal cramps, diarrhea, *C. difficile*-associated diarrhea and colitis, rash, QTc prolongation, dysgeusia
Clindamycin	Nausea, vomiting, abdominal pain, diarrhea, *C. difficile*-associated diarrhea and colitis, rash, arrhythmia associated with rapid IV infusion, metallic taste (with IV infusion), thrombophlebitis, abnormal liver function tests
Clotrimazole (Troche)	Generally well-tolerated. Nausea, vomiting, anorexia, metallic taste **Rarely:** Increase in serum transaminases
Cycloserine	Neuropsychiatric toxicities (e.g., headache, somnolence, lethargy, vertigo, tremor, dysarthria, irritability, confusion, paranoia, psychosis), seizures (particularly in patients with history of chronic alcoholism), allergic dermatitis, rash
Dapsone	Methemoglobinemia, hemolytic anemia (especially in patients with G6PD deficiency), neutropenia, dermatologic reactions (including rash), sulfone syndrome (fever, exfoliative dermatitis, lymphadenopathy, hepatic necrosis, hemolysis), peripheral neuropathy, hepatotoxicity, drug-induced lupus erythematosus, nephrotic syndrome, phototoxicity
Daclatasvir	Fatigue, headache, nausea, anemia, bradycardia (when co-administered with sofosbuvir and amiodarone)
Dasabuvir, Ombitasvir, Paritaprevir, and Ritonavir	Hepatotoxicity, nausea, pruritus, rash, insomnia, fatigue, asthenia, dyspnea (associated with ribavirin co-administration)
Doxycycline	Photosensitivity reaction, nausea, vomiting, diarrhea, esophageal ulceration, thrombophlebitis (with IV infusion), intracranial hypertension, *C. difficile*-associated diarrhea and colitis, tissue hyperpigmentation **Rarely:** Hepatotoxicity

Table 6. Common or Serious Adverse Reactions Associated with Systemically Administered Drugs Used to Treat Opportunistic Infections (page 3 of 6)

Drug(s)	Common or Serious Adverse Reactions
Elbasvir/Grazoprevir	Fatigue, headache, nausea, ALT elevations, anemia (when given with ribavirin)
Emtricitabine	Generally well-tolerated. Headache, nausea, skin hyperpigmentation, diarrhea, rash
Entecavir	Generally well-tolerated. Headache, fatigue, dizziness, nausea
Erythromycin	Nausea, vomiting, diarrhea, abdominal pain, anorexia, rash, hepatotoxicity, cholestatic jaundice, ototoxicity (hearing loss, tinnitus), rash, QTc prolongation and cardiac arrhythmia, *C. difficile*-associated diarrhea and colitis, thrombophlebitis (with IV infusion)
Ethambutol	Optic neuritis (dose dependent), peripheral neuropathy, headache, nausea, vomiting, anorexia
Ethionamide	Dose-dependent gastrointestinal side effects (nausea, vomiting, diarrhea, abdominal pain, metallic taste, anorexia), dizziness, drowsiness, depression, postural hypotension, hepatotoxicity, hypothyroidism (with or without goiter), gynecomastia, impotence, hypoglycemia
Famciclovir	Generally well-tolerated. Headache, nausea, vomiting, diarrhea, nephrotoxicity (in patients with underlying renal disease)
Flucytosine	Concentration-dependent bone marrow suppression (anemia, neutropenia, thrombocytopenia), diarrhea, nausea, vomiting, rash, hepatotoxicity
Fluconazole	Hepatotoxicity, rash, nausea, vomiting, diarrhea, abdominal discomfort, reversible alopecia (with doses ≥400 mg/day for >2 months), QTc prolongation
Foscarnet	Nephrotoxicity, electrolyte imbalances (e.g., hypocalcemia, hypomagnesemia, hypophosphatemia, hyperphosphatemia, hypokalemia), penile ulceration, nausea, vomiting, anorexia, headache, seizure (associated with electrolyte imbalances), anemia, injection-site associated thrombophlebitis
Fumagillin (Investigational)	**Oral Therapy:** Neutropenia, thrombocytopenia, vertigo, nausea, vomiting, diarrhea, anorexia, abdominal cramps **Ocular Therapy:** Minimal systemic effect or local effect
Ganciclovir	Neutropenia, thrombocytopenia, anemia, injection-site-associated thrombophlebitis, increased serum creatinine, carcinogenic and teratogenic potential, impaired fertility, neuropathy
Glecaprevir/Pibrentasvir	Generally well tolerated with only 0.1% discontinuation due to adverse reaction in clinical trials. Mild headache, fatigue, nausea, diarrhea
Imipenem/Cilastatin	Hypersensitivity reaction (immediate or delayed); nausea; vomiting; diarrhea; *C. difficile*-associated diarrhea and colitis; thrombophlebitis; headache; bone marrow suppression; drug fever; CNS effects (seizure, myoclonus, and confusion) especially with higher doses, in patients with underlying CNS disorders, or with renal insufficiency
Interferon-Alfa and Peginterferon-Alfa	Flu-like syndrome (e.g., fever, headache, fatigue, myalgia), neuropsychiatric disorders (e.g., depression, suicidal ideation), neutropenia, anemia, thrombocytopenia, thyroid dysfunction, injection-site reactions, alopecia, nausea, anorexia, diarrhea, weight loss, development or exacerbation of autoimmune disorders, ocular effects (e.g., retinal hemorrhage, retinal artery or vein obstructions, and cotton wool spots)
Isavuconazonium Sulfate	Hepatotoxicity, cholelithiasis, infusion-related reaction (hypotension, dyspnea, chills, dizziness, paresthesia, and hypoesthesia), hypersensitivity reaction (e.g., anaphylaxis, rash, SJS), nausea, vomiting, diarrhea, headache, hypokalemia, dyspnea, cough. Adverse events primarily reported in immunocompromised patients.
Isoniazid	Hepatotoxicity, peripheral neuropathy, optic neuritis, psychosis, diarrhea, nausea **Rarely:** Psychosis
Itraconazole	Hepatotoxicity, congestive heart failure, edema, hypokalemia, nausea, vomiting, diarrhea, abdominal pain, rash, QTc prolongation, neuropathy
Lamivudine	Generally well-tolerated. Nausea, vomiting.
Ledipasvir/Sofosbuvir	Fatigue, headache, asthenia (most common), nausea, diarrhea, insomnia, mild transient asymptomatic lipase elevation, mild bilirubin elevation

Table 6. Common or Serious Adverse Reactions Associated with Systemically Administered Drugs Used to Treat Opportunistic Infections (page 4 of 6)

Drug(s)	Common or Serious Adverse Reactions
Levofloxacin	Nausea, vomiting, abdominal pain, diarrhea, *C. difficile*-associated diarrhea and colitis, headache, dizziness, sleep disturbances, tendonitis and tendon rupture (associated with age >60 years and concomitant steroid use), photosensitivity, hypoglycemia, peripheral neuropathy, hepatotoxicity, QTc prolongation, neurotoxicity (especially with high doses, use in older patients, or in patients with renal dysfunction), seizures, and mental health side effects (e.g., disorientation, agitation, memory impairment, delirium) **Rarely:** Aortic dissection
Linezolid	Anemia, neutropenia, thrombocytopenia (especially with treatment lasting longer than 2–4 weeks), peripheral neuropathy, optic neuritis with long-term therapy, serotonin syndrome (especially in patients receiving concomitant serotonergic agents), seizure (in patients with a history of seizure or with risk factors for seizure), diarrhea, headache, nausea, vomiting **Rarely:** Lactic acidosis
Mefloquine	Depression, psychosis, anxiety, rash (reports of TEN and SJS), nausea, vomiting, diarrhea, epigastric pain, agitation, dizziness, headache, insomnia, abnormal dreams, QTc prolongation, arrhythmias (extrasystole, sinus bradycardia), agranulocytosis/aplastic anemia
Meropenem	Generally well-tolerated. Hypersensitivity reaction (immediate or delayed), nausea, vomiting, diarrhea, *C. difficile*-associated diarrhea and colitis, thrombophlebitis, headache, bone marrow suppression, drug fever
Micafungin	Generally well-tolerated. Histamine-related infusion reactions (e.g., flushing, rash, pruritus, hypotension, dyspnea) may occur, but these are rare if infusion lasts over 1 hour; anaphylaxis and anaphylactoid reaction, hepatotoxicity, thrombophlebitis, nausea, vomiting, diarrhea, hypokalemia **Rarely:** Hemolysis
Miconazole Buccal Tablets	Dysgeusia, diarrhea, nausea, vomiting, upper abdominal pain, headache, local reactions (oral discomfort, burning, pain, tongue/mouth ulceration, gingival pruritus, swelling, dry mouth) **Rarely:** Hypersensitivity reaction (may occur in patients with known hypersensitivity reaction to milk product concentrate)
Miltefosine	Nausea, vomiting, diarrhea, headache, motion sickness, leukocytosis, thrombocytosis, nephrotoxicity, retinal degeneration, elevated transaminases and bilirubin, teratogenic potential, impaired fertility
Moxifloxacin	Nausea, vomiting, abdominal pain, diarrhea, *C. difficile*-associated diarrhea and colitis, headache, dizziness, sleep disturbances, tendonitis and tendon rupture (associated with age >60 years and concomitant steroid use), photosensitivity, hypoglycemia, peripheral neuropathy, hepatotoxicity, QTc prolongation, neurotoxicity (especially with high doses, use in elderly patients or in patients with renal dysfunction), seizures, and mental health side effects such as disorientation, agitation, memory impairment, delirium **Rarely:** Aortic dissection
Nifurtimox	Anorexia, weight loss, nausea, vomiting, abdominal pain, headache, dizziness, mood changes, insomnia, myalgia, peripheral neuropathy, rash, pruritus, memory loss
Nitazoxanide	Generally well-tolerated. Nausea, vomiting, diarrhea, abdominal pain, headache
Nystatin (Oral Preparations)	Unpleasant taste, nausea, vomiting, anorexia, diarrhea **Rarely:** Hypersensitivity reaction
Paromomycin	Nausea, vomiting, cramps, anorexia, rash, headache **Rarely:** Nephrotoxicity and ototoxicity (inflammatory bowel disease and renal insufficiency may increase risk)

Table 6. Common or Serious Adverse Reactions Associated with Systemically Administered Drugs Used to Treat Opportunistic Infections (page 5 of 6)

Drug(s)	Common or Serious Adverse Reactions
Penicillin G	**All Penicillin G Preparations:** Hypersensitivity reactions (immediate or delayed reactions, including anaphylaxis), bone marrow suppression, nausea, vomiting, diarrhea, *C. difficile*-associated diarrhea and colitis, drug fever **Benzathine Penicillin G and Procaine Penicillin G:** IM injection-site reactions (pain and erythema), procaine neuropsychiatric reactions (with high dose), neurovascular damage (due to inadvertent intravascular instead of IM injection) **Aqueous Crystalline Penicillin G (IV):** Thrombophlebitis, neurotoxicity at high doses, especially in patients with renal dysfunction
Pentamidine	**IV Infusion:** Nephrotoxicity, infusion-related hypotension, thrombophlebitis, QTc prolongation, arrhythmias (including Torsades de Pointes), pancreatitis, hypoglycemia, hyperglycemia, diabetes mellitus, hepatotoxicity, electrolyte abnormalities, leucopenia, thrombocytopenia **Aerosolized Therapy:** Bronchospasm, cough, dyspnea, tachypnea, metallic taste **Rarely:** Pancreatitis
Pentavalent Antimony (Sodium Stibogluconate)	Nausea, vomiting, abdominal pain, anorexia, headache, hepatotoxicity, arthralgia, myalgia, cardiac toxicity with >20 mg/kg dose (prolonged QTc and T wave inversion), rash, thrombophlebitis, leukopenia, anemia, thrombocytopenia **Rarely:** Pancreatitis
Posaconazole	Nausea, vomiting, diarrhea, abdominal pain, headache, hepatotoxicity, hypokalemia, QTc prolongation, rash **IV Infusion:** Thrombophlebitis, cyclodextrin accumulation (especially in patients with eGFR <50 mL/min, but an observational study did not show an increased risk of nephrotoxicity)
Piperacillin-Tazobactam	Generally well-tolerated. Hypersensitivity reaction, rash, diarrhea, nausea, vomiting, *C. difficile*-associated diarrhea and colitis, thrombophlebitis, impaired platelet aggregation, seizure (with high doses used in patients with renal insufficiency) **Rarely:** Thrombocytopenia
Primaquine	Methemoglobinemia, hemolytic anemia (especially in patients with G6PD deficiency), leukopenia, neutropenia, abdominal cramps, nausea, vomiting, QTc prolongation, pruritus, rash, dizziness
Pyrazinamide	Hepatotoxicity, hyperuricemia, arthralgia, myalgia, nausea, vomiting, rash
Pyrimethamine	Neutropenia, thrombocytopenia, megaloblastic anemia, rash
Quinidine Glucuronate	QTc prolongation, lightheadedness, nausea, vomiting, diarrhea, abdominal pain, drug-induced SLE, headache, rash, hemolysis (with G6PD deficiency), hepatotoxicity, heartburn/esophagitis, cinchonism (tinnitus, vertigo, blurred vision)
Quinine	Headache, nausea, vomiting, diarrhea, cinchonism (tinnitus, vertigo, blurred vision), hypersensitivity reaction, hypoglycemia, thrombocytopenia, QTc prolongation
Ribavirin	Hemolytic anemia, dyspnea, hyperbilirubinemia, fatigue, myalgia, headache, nausea, vomiting, anorexia, dyspepsia, rash, dry cough, teratogenicity, hypersensitivity reaction, hepatotoxicity
Rifabutin	Hepatotoxicity, anterior uveitis (dose dependent), red-orange discoloration of body fluids, rash, arthralgia, neutropenia, nausea, vomiting, abdominal pain, diarrhea, anorexia
Rifampin	Hepatotoxicity (cholestatic hepatitis), red-orange discoloration of body fluids, thrombocytopenia, hemolytic anemia, rash, hypersensitivity reactions with flu-like syndrome, nausea, vomiting, anorexia, abdominal pain, flatulence, diarrhea, renal failure, headache, confusion
Rifapentine	Hypersensitivity reaction, hepatotoxicity, anemia, lymphopenia, neutropenia, arthralgia, conjunctivitis, headache, vomiting, nausea, diarrhea, rash, pruritus, anorexia and lymphadenopathy, red-orange discoloration of body fluids, *C. difficile*-associated diarrhea and colitis

Table 6. Common or Serious Adverse Reactions Associated with Systemically Administered Drugs Used to Treat Opportunistic Infections (page 6 of 6)

Drug(s)	Common or Serious Adverse Reactions
Sofosbuvir	Generally well-tolerated. Fatigue, headache, nausea, insomnia, anemia, bilirubin elevation (associated with ribavirin co-administration), asymptomatic CK elevation and lipase elevation, pancytopenia, depression (associated with Peg-IFN co-administration)
Streptomycin	Nephrotoxicity, ototoxicity (both hearing loss and vestibular toxicity are possible), neuromuscular blockade (associated with rapid infusion of large aminoglycoside doses), pain upon IM injection
Sulfadiazine	Rash (including SJS, EM, and TEN), anemia, neutropenia, thrombocytopenia, crystalluria (with or without urolithiasis), renal insufficiency, nausea, vomiting, drug fever, hepatotoxicity, headache, peripheral neuritis, tinnitus, vertigo, insomnia
Tafenoquine	Dizziness, nausea, vomiting, headache, hypersensitivity reactions, decreased hemoglobin, methemoglobinemia, hemolytic anemia (associated with G6PD deficiency; may cause harm to fetuses and breastfeeding infants who are GDPD deficient), psychiatric adverse reactions (in patients with history of psychiatric illness)
Telavancin	Taste disturbance, nausea, vomiting, diarrhea, red-man syndrome with rapid infusion (flushing, urticaria, pruritus, rash), nephrotoxicity, QTc prolongation, headache, dizziness, *C. difficile*-associated colitis
Telbivudine	Generally well-tolerated. Nausea, vomiting, abdominal pain, increase in creatine kinase, headache, dizziness, fatigue, diarrhea, myopathy, myalgia, cough, fever, dyspepsia, abdominal pain
Tenofovir DF	Renal insufficiency, proximal renal tubulopathy (with hypophosphatemia, hypouricemia, normoglycemic glycosuria), decrease in bone mineral density, nausea
Tenofovir Alafenamide	Lower incidence of renal or bone toxicities than with tenofovir DF
Tetracycline	Photosensitivity, tooth discoloration when taken by infants and children aged <8 years, reduced skeletal development, pruritus, esophageal ulceration, nausea, vomiting, diarrhea, hepatotoxicity, rash, increased BUN, intracranial hypertension
Trimethoprim-Sulfamethoxazole	Rash (including SJS, EM, and TEN), photosensitivity, anemia, neutropenia, thrombocytopenia, hepatotoxicity, dose dependent increase in serum creatinine (without change in GFR), interstitial nephritis, nausea, vomiting, crystalluria (in patients with inadequate hydration), hyperkalemia (more common with high-dose TMP), drug fever
Valacyclovir	Generally well-tolerated. Nausea; vomiting; headache; crystalluria (with high dose or in patients with renal impairment); neurotoxicity (e.g., agitation, confusion, hallucination, seizure, coma) with high doses, especially in patients with renal impairment; abdominal pain
Valganciclovir	Neutropenia, thrombocytopenia, anemia, nausea, vomiting, diarrhea, confusion, pyrexia, tremor, acute renal failure, carcinogenic and teratogenic potential, impaired fertility
Vancomycin	Infusion-related reactions (associated with infusion rate and can include flushing, hypotension, and rash), thrombophlebitis, rash, neutropenia, ototoxicity (associated with excessive concentration), nephrotoxicity (associated with high daily dose and high trough concentrations) **Rarely:** Thrombocytopenia
Velpatasvir/Sofosbuvir	Generally well tolerated. Headache, fatigue, and anemia (associated with ribavirin co-administration)
Voriconazole	Visual disturbances (associated with initial dosing), optic neuritis (associated with >28 days treatment), skin photosensitivity, hepatotoxicity, fever, nausea, rash, vomiting, chills, tachycardia, QTc prolongation, peripheral edema, headache, delirium, hallucination, encephalopathy (associated with trough >5.5 mcg/mL), fluorosis and periostitis with high dose and/or prolonged use, cyclodextrin accumulation (associated with use of IV formulation in patients with CrCl <50 mL/min, but an observational study did not show an increased risk of nephrotoxicity) **Rarely:** Peripheral neuropathy

Key: ALT = alanine aminotransferase; AST = aspartate aminotransferase; BUN = blood urea nitrogen; CK = creatine kinase; CNS = central nervous system; CrCl = creatinine clearance; eGFR = estimated glomerular filtration rate; EM = erythema multiforme; G6PD = glucose-6-phosphate dehydrogenase; GFR = glomerular filtration rate; IM = intramuscular; IV = intravenous; Peg-IFN = peginterferon alpha; SJS = Stevens-Johnson syndrome; SLE = systemic lupus erythematosus; TEN = toxic epidermal necrolysis

Table 7. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections That Require Dosage Adjustment in Patients with Renal Insufficiency (page 1 of 8) (Last updated October 22, 2019; last reviewed January 12, 2022)

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		CrCl (mL/min)*	Dose
Acyclovir	**IV Dose** *Serious HSV:* • 5 mg/kg IV every 8 hours *VZV Infections:* • 10 mg/kg IV every 8 hours	26–50	100% of dose IV every 12 hours
		10–25	100% of dose IV every 24 hours
		<10	50% of dose IV every 24 hours
		HD	50% of dose every 24 hours; administer dose after HD on day of dialysis.
	PO Dose for Herpes Zoster: 800 mg PO five times/day	10–25	800 mg PO every 8 hours
		<10	800 mg PO every 12 hours
		HD	800 mg PO every 12 hours; administer dose after HD on day of dialysis
Adefovir	10 mg PO every 24 hours	30–49	10 mg PO every 48 hours
		10–29	10 mg PO every 72 hours
		HD	10 mg PO weekly; administer dose after HD
Amikacin For mycobacterial infections	IV 15 mg/kg per day *or* 25 mg/kg three times per week	Use with caution in patients with renal insufficiency and family history of ototoxicity.	Adjust dose based on serum concentrations with target peak concentration 35–45 mcg/mL and trough concentration <4 mcg/mL. Administer dose after HD on day of dialysis.
Amphotericin B	0.7–1.0 mg/kg IV per day (amphotericin B deoxycholate) *or* 3–6 mg/kg IV per day (lipid formulation)	N/A	No dosage adjustment necessary; consider alternative antifungals if renal insufficiency occurs during therapy despite adequate hydration.
Capreomycin	15 mg/kg IV or IM per day	Use with caution in patients with renal insufficiency.	Adjust dose based on serum concentrations with target peak concentration 35–45 mcg/mL and trough concentration <4 mcg/mL. Administer dose after HD on day of dialysis.
Chloroquine (Base)	**For Treatment of Acute Malaria:** • 1 g (600 mg base) PO for 1 dose, followed by 500 mg (300 mg base) PO at 6, 24, and 48 hours (for a total dose of 1,500 mg)	<10	50% of dose
Cidofovir	5 mg/kg IV on Day 0, repeat 5 mg/kg IV dose on Day 7, then 5 mg/kg IV every 2 weeks Give each dose with probenecid and saline hydration (see Table 2 for dosing instructions).	Pretreatment SCr >1.5 mg/dL *or* CrCl <55 mL/min *or* Proteinuria ≥100 mg/dL (≥2 +)	Cidofovir **is not recommended**.
		If SCr increases by 0.3–0.4 mg/dL above baseline	Decrease to 3 mg/kg IV per dose
		If SCr increases >0.5 mg/dL above baseline *or* Proteinuria ≥3 +	Discontinue therapy

Table 7. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections That Require Dosage Adjustment in Patients with Renal Insufficiency (page 2 of 8)

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		CrCl (mL/min)*	Dose
Ciprofloxacin	500–750 mg PO every 12 hours *or* 400 mg IV every 8–12 hours	30–50	500–750 mg PO every 12 hours *or* 400 mg IV every 12 hours
		<30	250–500 mg PO every 24 hours *or* 400 mg IV every 24 hours
		HD or PD	250–500 mg PO every 24 hours *or* 200–400 mg IV every 24 hours; administer after HD or PD on day of dialysis.
Clarithromycin	500 mg PO every 12 hours	30–60	Usual dose except when used with an HIV PI or with COBI, then reduce dose by 50%.
		<30	250 mg PO twice daily *or* 500 mg PO once daily If used with an HIV PI or COBI, reduce dose by 75% (or consider using azithromycin as alternative).
Cycloserine	10–15 mg/kg/day PO in two divided doses (maximum 1,000 mg/day); start at 250 mg once daily and increase dose per tolerability	50–80	Usual dose; consider monitoring serum concentration and toxicities.
		<50 (not on HD)	Monitor serum concentrations (target peak concentration 20–35 mcg/mL) and adjust dose accordingly. Use with caution in patients with ESRD who are not on dialysis.
		HD	250 mg PO once daily or 500 mg PO three times per week; monitor serum cycloserine concentration (target peak concentration 20–35 mcg/mL).
Emtricitabine (FTC)	One 200–mg tablet PO once daily *or* 240 mg solution PO once daily	30–49	**Oral Tablets:** 200 mg every 48 hours **Oral Solution:** 120 mg every 24 hours
		15–29	**Oral Tablets:** 200 mg every 72 hours **Oral Solution:** 80 mg every 24 hours
		<15 or HD (administer dose after dialysis)	**Oral Tablets:** 200 mg every 96 hours **Oral Solution:** 60 mg every 24 hours
Emtricitabine/Tenofovir Alafenamide (FTC/TAF) (FDC Trade Name: Descovy) **Note:** Please refer to product information for dosing recommendations for other ARV FDC products containing FTC/TAF.	One (FTC 200 mg/TAF 25 mg) tablet PO once daily	<30	Coformulated tablet **is not recommended**.

Table 7. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections That Require Dosage Adjustment in Patients with Renal Insufficiency (page 3 of 8)

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		CrCl (mL/min)*	Dose
Emtricitabine/Tenofovir Disoproxil Fumarate (FTC/TDF) (FDC Trade Name: Truvada) **Note:** Please refer to product information for dosing recommendations for other ARV FDC products containing FTC/TDF.	One (FTC 200 mg/TDF 300 mg) tablet PO daily	30–49	1 tablet PO every 48 hours (monitor for worsening renal function or consider switching to TAF)
		<30 or HD	**Do not use** coformulated tablet in patients with CrCl <30 mL/min. Use formulation for each component drug and adjust dose according to recommendations for the individual drugs.
Entecavir	**Usual Dose:** 0.5 mg PO once daily **For Treatment of 3TC-Refractory HBV or for Patients with Decompensated Liver Disease:** 1 mg PO once daily	30 to <50	**Usual Renal Dose Adjustment:** • 0.25 mg PO every 24 hours, *or* • 0.5 mg PO every 48 hours **3TC-Refractory or Decompensated Liver Disease:** • 0.5 mg PO every 24 hours, *or* • 1 mg PO every 48 hours
		10 to <30	**Usual Renal Dose Adjustment:** • 0.15 mg PO every 24 hours, *or* • 0.5 mg PO every 72 hours **3TC-Refractory or Decompensated Liver Disease:** • 0.3 mg PO every 24 hours, *or* • 1 mg PO every 72 hours
		<10 or HD or CAPD (administer after HD or CAPD on dialysis day)	**Usual Renal Dose Adjustment:** • 0.05 mg PO every 24 hours, *or* • 0.5 mg PO once every seven days **3TC-Refractory or Decompensated Liver Disease:** • 0.1 mg PO every 24 hours, *or* • 1 mg PO once every seven days
Ethambutol	**For MAI:** 15 mg/kg PO daily **For MTB:** 15–25 mg/kg PO daily (See Table 3 for additional MTB dosing recommendations.)	<30 or HD	Usual dose PO three times weekly (in patients on HD, give dose after dialysis) Consider TDM to guide optimal dosing.
Ethionamide	15–20 mg/kg PO daily (usually 250–500 mg PO once or twice daily)	<30 or HD	250–500 mg PO once daily
Famciclovir	**For Herpes Zoster:** 500 mg PO every 8 hours **For HSV:** 500 mg PO every 12 hours	40–59	500 mg PO every 12 hours
		20–39	500 mg PO every 24 hours
		<20	250 mg PO every 24 hours
		HD	250 mg PO only on HD days, administer after HD

Table 7. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections That Require Dosage Adjustment in Patients with Renal Insufficiency (page 4 of 8)

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		CrCl (mL/min)*	Dose
Fluconazole	200–1,200 mg PO or IV every 24 hours (dose and route of administration depends on type of OI)	≤50	50% of dose every 24 hours
		HD	Administer full dose after HD on days of dialysis
Flucytosine	25 mg/kg PO every 6 hours TDM is recommended for all patients to guide optimal dosing (target peak serum concentration 2 hours after dose: 30–80 mcg/mL).	21–40	25 mg/kg PO every 12 hours
		10–20	25 mg/kg PO every 24 hours
		<10	25 mg/kg PO every 48 hours
		HD	25–50 mg/kg PO every 48–72 hours; administer dose after HD
Foscarnet	**Induction Therapy for CMV Infection:** 180 mg/kg/day IV in two divided doses **Maintenance Therapy for CMV Infection or for Treatment of HSV Infections:** 90–120 mg/kg IV once daily	Dosage adjustment needed according to calculated CrCl/kg; consult product label for dosing table.	Dosage adjustment needed according to calculated CrCl/kg; consult product label for dosing table.
Ganciclovir	**Induction Therapy:** 5 mg/kg IV every 12 hours	50–69	2.5 mg/kg IV every 12 hours
		25–49	2.5 mg/kg IV every 24 hours
		10–24	1.25 mg/kg IV every 24 hours
		<10 or HD	1.25 mg/kg IV three times per week; administer dose after HD on days of dialysis
	Maintenance Therapy: 5 mg/kg IV every 24 hours	50–69	2.5 mg/kg IV every 24 hours
		25–49	1.25 mg/kg IV every 24 hours
		10–24	0.625 mg/kg IV every 24 hours
		<10 or HD	0.625 mg/kg IV three times per week; administer dose after HD on days of dialysis
Lamivudine (3TC)	300 mg PO every 24 hours	30–49	150 mg PO every 24 hours
		15–29	150 mg PO once, then 100 mg PO every 24 hours
		5–14	150 mg PO once, then 50 mg PO every 24 hours
		<5 or HD	50 mg PO once, then 25 mg PO every 24 hours; administer dose after HD on dialysis day
Lamivudine/Tenofovir Disoproxil Fumarate (3TC/TDF) (FDC Trade Names: Cimduo or Temixys) **Note:** Please refer to product information for dosing recommendations for other ARV FDC products containing 3TC/TDF.	One (3TC 300 mg/TDF 300 mg) tablet PO every 24 hours	<50	Coformulated tablet **is not recommended**.
Ledipasvir/Sofosbuvir	One (ledipasvir 90 mg/sofosbuvir 400 mg) tablet PO once daily	<30	Co-formulated tablet **is not recommended**. No dose has been established because of up to 20-fold higher sofosbuvir metabolite observed at this level of renal impairment.

Table 7. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections That Require Dosage Adjustment in Patients with Renal Insufficiency (page 5 of 8)

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		CrCl (mL/min)*	Dose
Levofloxacin	500 mg (low dose) or 750-1,000 mg (high dose) IV or PO daily	20–49	**Low Dose:** 500 mg once, then 250 mg every 24 hours, IV or PO **High Dose:** 750 mg every 48 hours IV or PO
		<20 or CAPD or HD (administer dose after HD or CAPD on days of dialysis)	**Low Dose:** • 500 mg once, then 250 mg every 48 hours, IV or PO • Dose can be adjusted based on serum concentrations. **High Dose:** 750 mg once, then 500 mg every 48 hours, IV or PO
Para-aminosalicylic acid	8–12 g/day PO in two to three divided doses	<30 or HD	4 g PO twice daily; administer after HD on days of dialysis
Paromomycin	500 mg PO every 6 hours	<10	Minimal systemic absorption. No dosage adjustment necessary, but monitor for worsening renal function and ototoxicity in patients with ESRD.
Peginterferon Alfa-2a	180 mcg SQ once weekly	<30	135 mcg SQ once weekly
		HD	135 mcg SQ once weekly
Peginterferon Alfa-2b	1.5 mcg/kg SQ once weekly	30–50	Reduce dose by 25%
		10–29 and HD	Reduce dose by 50%
Penicillin G (Potassium or Sodium)	**Neurosyphilis, Ocular Syphilis, or Otosyphilis:** • 3–4 million units IV every 4 hours, *or* • 18–24 million units IV daily as continuous infusion	10–50	2–3 million units every 4 hours *or* 12–18 million units as continuous infusion
		<10	2 million units every 4–6 hours *or* 8–12 million units as continuous infusion
		HD or CAPD	2 million units every 6 hours *or* 8 million units as continuous infusion
Pentamidine	4 mg/kg IV every 24 hours	10–50	3 mg/kg IV every 24 hours
		<10	4 mg/kg IV every 48 hours
Posaconazole	**IV:** 300 mg twice daily on Day 1; then 300 mg once daily **Delayed-Release Tablet:** 300 mg PO once daily **Oral Suspension:** 400 mg PO twice daily	<50	No dosage adjustment of oral dose in patients with renal insufficiency. Higher variability in serum concentrations observed in patients with CrCl <20 ml/min. Monitor posaconazole concentrations (target trough concentration >1.25 mcg/mL). IV posaconazole **is not recommended** by the manufacturer because of potential toxicity due to accumulation of sulfobutylether cyclodextrin (vehicle of IV product). However, an observational study did not find worsening in renal function in patients with CrCl <50 ml/min given sulfobutylether cyclodextrin. Switch patients with CrCl <50 ml/min to oral posaconazole when feasible.
Pyrazinamide	See Table 3 for weight-based dosing guidelines.	<30 or HD	25–35 mg/kg/dose three times per week; administer dose after HD on dialysis days

Table 7. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections That Require Dosage Adjustment in Patients with Renal Insufficiency (page 6 of 8)

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		CrCl (mL/min)*	Dose
Quinidine Gluconate (Salt) **Note:** 10 mg quinidine gluconate salt = 6.25 mg quinidine base	10 mg/kg (salt) IV over one to two hours, then 0.02 mg/kg/min (salt) IV for up to 72 hours or until able to take oral meds	<10	75% of usual dose
		HD	75% of usual dose; some clinicians recommend supplementation with 100–200 mg IV after HD on days of dialysis. Consider TDM for all patients to optimize dosing.
Quinine Sulfate	650 mg salt (524 mg base) PO every 8 hours	<10 or HD	650 mg once, then 325 mg PO every 12 hours
Ribavirin	**For Genotypes 1 and 4:** 1,000–1,200 mg PO per day in two divided doses (based on weight; see Table 2 for full dosing recommendation) **For Genotypes 2 and 3:** 400 mg PO twice daily	30–50	Alternate dosing 200 mg PO and 400 mg PO every other day
		<30 or HD	200 mg PO daily (based on limited data)
Rifabutin	5 mg/kg PO daily (usually 300 mg PO daily) See Table 3 and Drug-Drug Interactions in the Adult and Adolescent Antiretroviral Guidelines for dosage adjustment based on interactions with ARVs.	<30	Consider 50% of dose once daily if toxicity is suspected. Monitor serum concentration and adjust dose as needed.
Rifampin	10 mg/kg PO daily (usually 600 mg PO daily)	<30 or HD	600 mg once daily, or 600 mg three times per week
Sofosbuvir	400 mg PO daily	<30	**Not recommended.** Up to 20-fold higher sofosbuvir metabolite observed in patients with this level of renal impairment.
Streptomycin	15 mg/kg IM or IV every 24 hours *or* 25 mg/kg IM or IV three times per week	Use with caution in patients with renal insufficiency.	Adjust dose based on serum concentrations. Administer dose after dialysis on day of dialysis.
Sulfadiazine	1,000–1,500 mg PO every 6 hours (1,500 mg every 6 hours for patients >60 kg)	10–50	1,000–1,500 mg PO every 12 hours (ensure adequate hydration)
		<10 or HD	1,000–1,500 mg PO every 24 hours; administer dose after HD on days of dialysis
Telavancin	10 mg/kg IV every 24 hours	31-50	7.5 mg/kg IV every 24 hours (decreased clinical cure rate with CrCl <50 ml/minute; use with caution)
		10-30	10 mg/kg IV every 48 hours (decreased clinical cure rate with CrCl <50 ml/minute; use with caution)
		<10	Insufficient clinical data to recommend routine use. Use with caution due to decreased clinical cure rate with CrCl <50 mL/minute. If no other option, consider 10 mg/kg every 48 hours IV or 10 mg/kg IV post-HD three times a week (based on observational study [n = 10]).

Table 7. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections That Require Dosage Adjustment in Patients with Renal Insufficiency (page 7 of 8)

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		CrCl (mL/min)*	Dose
Telbivudine	600 mg PO daily	30–49	**Oral Tablets:** 600 mg PO every 48 hours **Oral Solution:** 400 mg PO every 24 hours
		<30	**Oral Tablets:** 600 mg PO every 72 hours **Oral Solution:** 200 mg PO every 24 hours
		HD	**Oral Tablets:** 600 mg PO every 96 hours; administer dose after dialysis. **Oral Solution:** 120 mg PO every 24 hours; administer dose after HD on dialysis day
Tenofovir Alafenamide (TAF)	25 mg PO daily	<15	**Not recommended**
		<15 on HD	No dosage adjustment required. Administer dose after HD on dialysis days.
Tenofovir Disoproxil Fumarate (TDF)	300 mg PO daily	30–49	300 mg PO every 48 hours (consider switching to TAF for treatment of HBV)
		10–29	300 mg PO every 72–96 hours (consider switching to alternative agent for treatment of HBV)
		<10 and not on dialysis	**Not recommended**
		HD	300 mg PO once weekly; administer dose after dialysis
Tetracycline	250 mg PO every 6 hours Consider using doxycycline in patients with renal dysfunction.	10–49	250 mg PO every 12–24 hours
		<10	250 mg PO every 24 hours
		HD	250 mg PO every 24 hours; administer dose after dialysis
Trimethoprim/ Sulfamethoxazole (TMP-SMX)	**For PCP Treatment:** • 5 mg/kg (of TMP component) IV every 6-8 hours, *or* • Two TMP-SMX DS tablets PO every 8 hours	15–30	5 mg/kg (TMP) IV every 12 hours, or two TMP-SMX DS tablets PO every 12 hours
		<15	5 mg/kg (TMP) IV every 24 hours, or one TMP-SMX DS tablet PO every 12 hours (or two TMP-SMX DS tablets every 24 hours)
		HD	5 mg/kg/day (TMP) IV, or two TMP-SMX DS tablets PO; administer dose after HD on dialysis day. Consider TDM to optimize therapy (target TMP concentrations: 5–8 mcg/mL)
	For PCP Prophylaxis: • One TMP-SMX DS tablet PO daily; • One TMP-SMX DS tablet PO three times per week; *or* • One TMP-SMX SS tablet PO daily	15–30	Reduce dose by 50%
		<15	Reduce dose by 50% or use alternative agent
	For Toxoplasmosis Encephalitis (TE) Treatment: 5 mg/kg (TMP component) IV or PO every 12 hours	15–30	5 mg/kg (TMP component) IV or PO every 24 hours
		<15	5 mg/kg (TMP component) IV or PO every 24 hours or use alternative agent

Table 7. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections That Require Dosage Adjustment in Patients with Renal Insufficiency (page 8 of 8)

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		CrCl (mL/min)*	Dose
Trimethoprim/ Sulfamethoxazole (TMP-SMX), continued	**For TE Chronic Maintenance Therapy:** • One TMP-SMX DS tablet twice daily, *or* • One TMP-SMX DS tablet daily	15–30	Reduce dose by 50%
		<15	Reduce dose by 50% or use alternative agent
	For Toxoplasmosis Primary Prophylaxis: One TMP-SMX DS tablet PO daily	15-30	Reduce dose by 50%
		<15	Reduce dose by 50% or use alternative agent
Valacyclovir	**For Herpes Zoster:** 1 g PO three times daily	30–49	1 g PO every 12 hours
		10–29	1 g PO every 24 hours
		<10	500 mg PO every 24 hours
		HD	500 mg PO every 24 hours; dose after HD on dialysis days
Valganciclovir	**Induction Therapy:** 900 mg PO twice daily **Maintenance Therapy:** 900 mg PO once daily	40–59	**Induction:** 450 mg PO twice daily **Maintenance:** 450 mg PO daily
		26–39	**Induction:** 450 mg PO daily **Maintenance:** 450 mg PO every 48 hours
		10–25	**Induction:** 450 mg PO every 48 hours **Maintenance:** 450 mg PO twice weekly
		<10 and not on dialysis	**Induction: Not recommended** **Maintenance: Not recommended**
		HD **Note:** Clinical efficacy of these doses has not been established.	**Induction:** 200 mg (oral powder formulation) PO three times per week after HD **Maintenance:** 100 mg (oral powder formulation) PO three times per week after HD
Voriconazole	6 mg/kg IV every 12 hours for two doses, then 4 mg/kg IV every 12 hours *or* 200–300 mg PO every 12 hours	<50	IV voriconazole **is not recommended** by the manufacturer because of potential toxicity due to accumulation of sulfobutylether cyclodextrin (vehicle of IV product). An observational study did not find worsening in renal function in patients with CrCl <50 mL/min. Switch patients with CrCl <50 mL/min to oral voriconazole when feasible. No need for dosage adjustment when the oral dose is used. Adjust dose based on serum concentrations.

Key: 3TC = lamivudine; ARV = antiretroviral; CAPD = continuous ambulatory peritoneal dialysis; CMV = cytomegalovirus; COBI = cobicistat; CrCl = creatinine clearance; DS = double strength, ESRD = end-stage renal disease; FDC = fixed-dose combination; FTC = emtricitabine; HBV = hepatitis B virus; HD = hemodialysis; HSV = herpes simplex virus; IM = intramuscular; IV = intravenous; MAI = *Mycobacterium avium intracellulare*; MTB = *Mycobacterium tuberculosis*; N/A = not applicable; OI = opportunistic infection; PD = peritoneal dialysis; PCP = Pneumocystis pneumonia; PI = protease inhibitor; PO = orally; SCr = serum creatinine; SQ = subcutaneous; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TDM = therapeutic drug monitoring; TMP-SMX = trimethoprim-sulfamethoxazole; VZV = varicella zoster virus

*** Creatinine Clearance Calculation**

Male:	Female:
$\frac{(140 - \text{age in years}) \times (\text{weight in kg})}{72 \times (\text{serum creatinine})}$	$\frac{(140 - \text{age in years}) \times (\text{weight in kg}) \times (0.85)}{72 \times (\text{serum creatinine})}$

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 1 of 8) (Last updated February 11, 2020; last reviewed January 12, 2022)

Drug	FDA Category[a]	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Acyclovir	B	No teratogenicity in mice, rats, rabbits at human levels. Extensive experience in human pregnancy (>700 first-trimester exposures reported to registry); well-tolerated.	Treatment of frequent or severe symptomatic herpes outbreaks or varicella
Adefovir	C	No increase in malformations at 23 times (rats) and 40 times (rabbits) human dose. Limited experience with use human in pregnancy.	**Not recommended** because of limited data in pregnancy. Report exposures during pregnancy to the Antiretroviral Pregnancy Registry.
Albendazole	C	Embryotoxic and teratogenic (skeletal malformations) in rats and rabbits, but not in mice or cows. Limited experience in human pregnancy.	**Not recommended**, especially in first trimester. Primary therapy for microsporidiosis in pregnancy should be ART.
Amikacin	C	Not teratogenic in mice, rats, rabbits. Theoretical risk of ototoxicity in fetus; reported with streptomycin but not amikacin.	Drug-resistant TB, severe MAC infections
Amoxicillin, Amoxicillin/ Clavulanate, and **Ampicillin/ Sulbactam**	B	Not teratogenic in animals. Extensive experience in human pregnancy does not suggest an increase in AEs.	Susceptible bacterial infections
Amphotericin B	B	Not teratogenic in animals or in human experience. Preferred over azole antifungals in first trimester if similar efficacy expected.	Documented invasive fungal disease
Antimonials, Pentavalent (Stibogluconate, Meglumine)	Not FDA approved	Antimony not teratogenic in rats, chicks, sheep. Three cases reported of use in human pregnancy in second trimester with good outcome. Labeled as **contraindicated** in pregnancy.	Use for therapy of visceral leishmaniasis not responsive to amphotericin B or pentamidine.
Artesunate, Artemether, and **Artemether/ Lumefantrine**	C	Embryotoxicity, cardiovascular and skeletal anomalies in rats and rabbits. Embryotoxic in monkeys. Human experience, primarily in the second and third trimesters, has not identified increased AEs.	Recommended by WHO as first-line therapy in second/third trimester for *P. falciparum* and severe malaria. Pending more data, use for malaria in first trimester **only if other drugs are not available or have failed**. Report cases of exposure to a WHO Anti-Malarial Pregnancy Exposure Registry when available.
Atovaquone	C	Not teratogenic in rats or rabbits, limited human experience	Alternate agent for PCP, *Toxoplasma gondii*, malaria infections
Azithromycin	B	Not teratogenic in animals. Moderate experience with use in human pregnancy does not suggest AEs.	Preferred agent for MAC prophylaxis or treatment (with ethambutol), *Chlamydia trachomatis* infection in pregnancy
Aztreonam	B	Not teratogenic in rats, rabbits. Limited human experience, but other beta-lactam antibiotics have not been associated with adverse pregnancy outcomes.	Susceptible bacterial infections
Bedaquiline	B	Not teratogenic in rats, rabbits. No experience in human pregnancy.	Multidrug resistant TB when effective treatment regimen cannot otherwise be provided
Benznidazole	Not FDA approved	No animal studies. Increase in chromosomal aberrations in children with treatment; uncertain significance. No human pregnancy data.	Not indicated for chronic *T. cruzi* in pregnancy. Seek expert consultation if acute or symptomatic infection in pregnancy requiring treatment.

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 2 of 8)

Drug	FDA Category[a]	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Boceprevir	B	Not teratogenic in rats, rabbits. No human pregnancy data.	Treatment of HCV currently generally not indicated in pregnancy
Capreomycin	C	Increase in skeletal variants in rats. Limited experience in human pregnancy; theoretical risk of fetal ototoxicity.	Drug-resistant TB
Caspofungin	C	Embryotoxic, skeletal defects in rats, rabbits. No experience with human use.	Invasive *Candida* or *Aspergillus* infections refractory to amphotericin and azoles
Cephalosporins	B	Not teratogenic in animals. Extensive experience in human pregnancy has not suggested increase in adverse outcomes.	Bacterial infections; alternate treatment for MAC
Chloroquine	C	Associated with anophthalmia, micro-ophthalmia at fetotoxic doses in animals. Not associated with increased risk in human pregnancy at doses used for malaria.	Drug of choice for malaria prophylaxis and treatment of sensitive species in pregnancy
Cidofovir	C	Embryotoxic and teratogenic (meningocele, skeletal abnormalities) in rats and rabbits. No experience in human pregnancy.	**Not recommended**
Ciprofloxacin and **Other Quinolones**	C	Arthropathy in immature animals; not embryotoxic or teratogenic in mice, rats, rabbits, or monkeys. More than 1,100 cases of quinolone use in human pregnancy have not been associated with arthropathy or birth defects.	Severe MAC infections; multidrug resistant TB, anthrax, bacterial infections
Clarithromycin	C	Cardiovascular defects noted in one strain of rats and cleft palate in mice at high doses, not teratogenic in rabbits or monkeys. Two human studies, each with >100 first-trimester exposures, did not show increase in defects but one study found an increase in spontaneous abortion.	Treatment or secondary MAC prophylaxis, if other choices exhausted
Clindamycin	B	No concerns specific to pregnancy in animal or human studies.	Treatment of anaerobic bacterial infections and used with quinine for chloroquine-resistant malaria; alternate agent for secondary prophylaxis of *Toxoplasma*
Clofazimine	C	Not teratogenic in mice, rats, or rabbits. Limited experience reported (19 cases); no anomalies noted but red-brown skin discoloration reported in several infants exposed throughout pregnancy.	No indications
Clotrimazole Troches	C	Not teratogenic in animals at exposures expected from treatment of oral or vaginal *Candida*. No increase in adverse pregnancy outcomes with vaginal use.	Oral or vaginal *Candida* infections and prophylaxis
Cycloserine	C	Not teratogenic in rats. No data available from human studies.	Drug-resistant TB
Dapsone	C	No animal data. Limited human experience does not suggest teratogenicity; might displace bound bilirubin in the neonate, increasing the risk of kernicterus. Case reports of hemolytic anemia in fetus/infant with maternal treatment.	Alternative for primary or secondary PCP prophylaxis
Dasabuvir/ Ombitasvir/ Paritaprevir/ Ritonavir	Not assigned	No AEs in mice, rats, rabbits during pregnancy or lactation. No data in human pregnancy or breastfeeding.	Therapy in pregnancy **is not recommended** because ribavirin, which is recommended for concomitant use with this drug, is contraindicated in pregnancy.

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 3 of 8)

Drug	FDA Category[a]	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Diphenoxylate	C	Limited animal and human data do not indicate teratogenicity.	Symptomatic treatment of diarrhea
Doxycycline and **Other Tetracyclines**	D	Risk of hepatic toxicity increased with tetracyclines in pregnancy; staining of fetal bones and teeth contraindicates use in pregnancy.	No indications
Elbasvir/ Grazoprevir	Not assigned	No AEs in rats, rabbits during pregnancy or lactation. No data in human pregnancy or breastfeeding.	May be considered for use in patients who do not need ribavirin if benefits felt to outweigh unknown risks. However, this drug **is not recommended** for patients who need ribavirin based on HCV subtype or resistance because ribavirin is contraindicated in pregnancy.
Emtricitabine	B	No concerns in pregnancy from limited animal and human data.	As part of fully suppressive combination ARV regimen for treatment of HIV, HBV. Report exposures during pregnancy to the Antiretroviral Pregnancy Registry.
Entecavir	C	Animal data do not suggest teratogenicity at human doses; however, limited experience in human pregnancy.	**Not recommended** because of limited data in pregnancy. Use as part of fully suppressive ARV regimen with ARV agents active against both HIV and HBV. Report exposures during pregnancy to the Antiretroviral Pregnancy Registry.
Erythromycin	B	Hepatotoxicity with erythromycin estolate in pregnancy; other forms acceptable. No evidence of teratogenicity.	Bacterial and chlamydial infections
Ethambutol	B	Teratogenic, at high doses, in mice, rats, rabbits. No evidence of teratogenicity in 320 cases of human use for treatment of TB.	Active TB and MAC treatment; avoid in first trimester if possible
Ethionamide	C	Increased rate of defects (omphalocele, exencephaly, cleft palate) in rats, mice, and rabbits with high doses; not seen with usual human doses. Limited human data; case reports of CNS defects.	Active TB; avoid in first trimester if possible
Famciclovir	B	No evidence of teratogenicity in rats or rabbits, limited human experience.	Recurrent genital herpes and primary varicella infection. Report exposures during pregnancy to the Famvir Pregnancy Registry (1-888-669-6682).
Fluconazole	C	Abnormal ossification, structural defects in rats, mice at high doses. Case reports of rare pattern of craniofacial, skeletal and other abnormalities in five infants born to four women with prolonged exposure during pregnancy; no increase in defects seen in several series after single dose treatment.	Single dose may be used for treatment of vaginal *Candida* though topical therapy preferred. **Not recommended** for prophylaxis during early pregnancy. Can be used for invasive fungal infections after first trimester; amphotericin B preferred in first trimester if similar efficacy expected.
Flucytosine	C	Facial clefts and skeletal defects in rats; cleft palate in mice, no defects in rabbits. No reports of use in first trimester of human pregnancy; may be metabolized to 5-fluorouracil, which is teratogenic in animals and possibly in humans.	Use after first trimester if indicated for life-threatening fungal infections.

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 4 of 8)

Drug	FDA Category[a]	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Foscarnet	C	Skeletal variants in rats, rabbits and hypoplastic dental enamel in rats. Single case report of use in human pregnancy in third trimester.	Alternate agent for treatment or secondary prophylaxis of life-threatening or sight-threatening CMV infection.
Fumagillin	Not FDA approved	Caused complete litter destruction or growth retardation in rats, depending on when administered. No data in human pregnancy.	Topical solution can be used for ocular microsporidial infections.
Ganciclovir and **Valganciclovir**	C	Embryotoxic in rabbits and mice; teratogenic in rabbits (cleft palate, anophthalmia, aplastic kidney and pancreas, hydrocephalus). Case reports of safe use in human pregnancy after transplants, treatment of fetal CMV.	Treatment or secondary prophylaxis of life-threatening or sight-threatening CMV infection. Preferred agent for therapy in children.
Glecaprevir/ Pibrentasvir	Not assigned	No AEs of glecaprevir in rats or of pibrentasvir in mice, rabbits during pregnancy and lactation. No data in human pregnancy or breastfeeding.	Use may be considered for hepatitis C if benefits outweigh unknown risks.
Imipenem and **Meropenem**	C/B	Not teratogenic in animals; limited human experience.	Serious bacterial infections
Imiquimod	B	Not teratogenic in rats and rabbits; eight case reports of human use, only two in first trimester.	Because of limited experience, other treatment modalities such as cryotherapy or trichloroacetic acid recommended for wart treatment during pregnancy.
Influenza Vaccine	C	Not teratogenic. Live vaccines, including intranasal influenza vaccine, are contraindicated in pregnancy.	All pregnant women should receive injectable influenza vaccine because of the increased risk of complications of influenza during pregnancy. Ideally, HIV-infected women should be on ART before vaccination to limit potential increases in HIV RNA levels with immunization.
Interferons Alfa, Beta, and Gamma	C	Abortifacient at high doses in monkeys, mice; not teratogenic in monkeys, mice, rats, or rabbits. Approximately 30 cases of use of interferon-alfa in pregnancy reported; 14 in first trimester without increase in anomalies; possible increased risk of intrauterine growth retardation.	Not indicated. Treatment of HCV currently generally **not recommended** in pregnancy.
Isavuconazole	C	Increased perinatal mortality in rats at exposures below human exposure levels. Dose-related skeletal defects in rats at exposures below human exposure levels. No data in human pregnancy or breastfeeding.	Use alternate antifungals, especially in first trimester.
Isoniazid	C	Not teratogenic in animals. Possible increased risk of hepatotoxicity during pregnancy; prophylactic pyridoxine 50 mg/day should be given to prevent maternal and fetal neurotoxicity.	Active TB; prophylaxis for exposure or skin test conversion
Itraconazole	C	Teratogenic in rats and mice at high doses. Case reports of craniofacial, skeletal abnormalities in humans with prolonged fluconazole exposure during pregnancy; no increase in defect rate noted among >300 infants born after first-trimester itraconazole exposure.	Only for documented systemic fungal disease, not prophylaxis. Consider using amphotericin B in first trimester if similar efficacy expected.
Kanamycin	D	Associated with club feet in mice, inner ear changes in multiple species. Hearing loss in 2.3% of 391 children after long-term *in utero* therapy.	Drug-resistant TB

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 5 of 8)

Drug	FDA Category[a]	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Ketoconazole	C	Teratogenic in rats, increased fetal death in mice, rabbits. Inhibits androgen and corticosteroid synthesis; may impact fetal male genital development; case reports of craniofacial, skeletal abnormalities in humans with prolonged fluconazole exposure during pregnancy.	None
Lamivudine	C	Not teratogenic in animals. No evidence of teratogenicity with >3,700 first-trimester exposures reported to the Antiretroviral Pregnancy Registry.	HIV and HBV therapy, only as part of a fully suppressive combination ARV regimen. Report exposures to the Antiretroviral Pregnancy Registry.
Ledipasvir/ Sofosbuvir	B	No evidence of teratogenicity in rats or rabbits. No experience in human pregnancy.	Treatment of HCV generally not indicated in pregnancy.
Leucovorin (Folinic Acid)	C	Prevents birth defects of valproic acid, methotrexate, phenytoin, aminopterin in animal models. No evidence of harm in human pregnancies.	Use with pyrimethamine when use of pyrimethamine cannot be avoided.
Linezolid	C	Not teratogenic in animals. Decreased fetal weight and neonatal survival at expected human exposures, possibly related to maternal toxicity. Limited human experience.	Serious bacterial infections
Loperamide	B	Not teratogenic in animals. No increase in birth defects among infants born to 89 women with first-trimester exposure in one study; another study suggests a possible increased risk of hypospadias with first-trimester exposure, but confirmation required.	Symptomatic treatment of diarrhea after the first trimester
Mefloquine	C	Animal data and human data do not suggest an increased risk of birth defects, but miscarriage and stillbirth may be increased.	Second-line therapy of chloroquine-resistant malaria in pregnancy, if quinine/clindamycin not available or not tolerated. Weekly as prophylaxis in areas with chloroquine-resistant malaria.
Meglumine	Not FDA approved	See **Antimonials, pentavalent**	Therapy of visceral leishmaniasis not responsive to amphotericin B or pentamidine
Metronidazole	B	Multiple studies do not indicate teratogenicity. Studies on several hundred women with first-trimester exposure found no increase in birth defects.	Anaerobic bacterial infections, bacterial vaginosis, trichomoniasis, giardiasis, amebiasis
Micafungin	C	Teratogenic in rabbits; no human experience.	**Not recommended**
Miltefosine	Not FDA approved	Embryotoxic in rats, rabbits; teratogenic in rats. No experience with human use.	**Not recommended**
Nifurtimox	Not FDA approved	Not teratogenic in mice and rats. Increased chromosomal aberrations in children receiving treatment; uncertain significance. No experience in human pregnancy.	Not indicated in chronic infection; seek expert consultation if acute infection or symptomatic reactivation of *T. cruzi* in pregnancy.
Nitazoxanide	B	Not teratogenic in animals; no human data.	Severely symptomatic cryptosporidiosis after the first trimester
Ombitasvir/ Paritaprevir/ Ritonavir	Not assigned	No AEs in mice, rats, rabbits during pregnancy or lactation. No data in human pregnancy or breastfeeding.	Ribavirin, recommended to be used with this drug, is contraindicated in pregnancy so therapy in pregnancy **not recommended**.
Para-Aminosalicylic Acid (PAS)	C	Occipital bone defects in one study in rats; not teratogenic in rabbits. Possible increase in limb, ear anomalies in one study with 143 first-trimester exposures; no specific pattern of defects noted, several studies did not find increased risk.	Drug-resistant TB

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 6 of 8)

Drug	FDA Category[a]	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Paromomycin	C	Not teratogenic in mice and rabbits. Limited human experience, but poor oral absorption makes toxicity, teratogenicity unlikely.	Amebic intestinal infections, possibly cryptosporidiosis
Penicillin	B	Not teratogenic in multiple animal species. Vast experience with use in human pregnancy does not suggest teratogenicity, other adverse outcomes.	Syphilis, other susceptible bacterial infections
Pentamidine	C	Embryocidal but not teratogenic in rats, rabbits with systemic use. Limited experience with systemic use in human pregnancy.	Alternate therapy for PCP and leishmaniasis
Piperacillin-Tazobactam	B	Not teratogenic in limited animal studies. Limited experience in pregnancy but penicillins generally considered safe.	Bacterial infections
Pneumococcal Vaccine	C	No studies in animal pregnancy. Polysaccharide vaccines generally considered safe in pregnancy. Well-tolerated in third-trimester studies.	Initial or booster dose for prevention of invasive pneumococcal infections. Pregnant women with HIV should be on ART before vaccination to limit potential increases in HIV RNA levels with immunization.
Podophyllin and **Podofilox**	C	Increased embryonic and fetal deaths in rats, mice but not teratogenic. Case reports of maternal, fetal deaths after use of podophyllin resin in pregnancy; no clear increase in birth defects with first-trimester exposure.	Because alternative treatments for genital warts in pregnancy are available, use **is not recommended**; however, inadvertent use in early pregnancy is not indication for abortion.
Posaconazole	C	Embryotoxic in rabbits; teratogenic in rats at similar to human exposures. No experience in human pregnancy.	**Not recommended**
Prednisone	B	Dose-dependent increased risk of cleft palate in mice, rabbits, hamsters; dose-dependent increase in genital anomalies in mice. Human data inconsistent regarding increased risk of cleft palate. Risk of growth retardation, low birth weight may be increased with chronic use; monitor for hyperglycemia with use in third trimester.	Adjunctive therapy for severe PCP; multiple other non-HIV-related indications
Primaquine	C	No animal data. Limited experience with use in human pregnancy; theoretical risk for hemolytic anemia if fetus has G6PD deficiency.	Alternate therapy for PCP, chloroquine-resistant malaria
Proguanil	C	Not teratogenic in animals. Widely used in malaria-endemic areas with no clear increase in adverse outcomes.	Alternate therapy and prophylaxis of *P. falciparum* malaria
Pyrazinamide	C	Not teratogenic in rats, mice. Limited experience with use in human pregnancy.	Active TB
Pyrimethamine	C	Teratogenic in mice, rats, hamsters (cleft palate, neural tube defects, and limb anomalies). Limited human data have not suggested an increased risk of birth defects; because folate antagonist, use with leucovorin.	Treatment and secondary prophylaxis of toxoplasmic encephalitis; alternate treatment of PCP
Quinidine Gluconate	C	Generally considered safe in pregnancy; high doses associated with preterm labor. One case of fetal VIII-nerve damage reported.	Alternate treatment of malaria, control of fetal arrhythmias
Quinine Sulfate	C	High doses, often taken as an abortifacient, have been associated with birth defects, especially deafness, in humans and animals. Therapeutic doses have not been associated with an increased risk of defects in humans or animals. Monitor for hypoglycemia.	Treatment of chloroquine-resistant malaria

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 7 of 8)

Drug	FDA Category[a]	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Ribavirin	X	Dose-dependent risk of multiple defects (craniofacial, central nervous system, skeletal, anophthalmia) in rats, mice, hamsters starting at below human doses. Reports of treatment during second half of pregnancy in nine women without incident; first 49 cases in registry did not suggest increased risk, but limited data.	**Contraindicated** in early pregnancy; no clear indications in pregnancy. Report exposures during pregnancy to the Ribavirin Pregnancy Registry (1-800-593-2214).
Rifabutin	B	Not teratogenic in rats and rabbits; no specific concerns for human pregnancy.	Treatment or prophylaxis of MAC, active TB
Rifampin	C	Teratogenic at high doses in mice (cleft palate) and rats (spina bifida) but not in rabbits. No clear teratogenicity in humans.	Active TB
Rifapentine	C	Embryofetal toxicity with increased rate of malformations and fetal loss noted in rats and rabbits. Limited experience in human pregnancy and lactation.	Use alternate drugs in pregnancy if possible.
Simeprevir	C	Decreased fetal weights and increased skeletal variants in mice at 4 times human exposure. Increased deaths and decreased fetal and neonatal growth and developmental delay after *in utero* exposure in rats. No experience in human pregnancy.	Treatment of HCV currently generally **not recommended** in pregnancy.
Sinecatechin Ointment	C	No evidence of teratogenicity in rats and rabbits after oral or intravaginal dosing. No experience in human pregnancy.	**Not recommended** based on lack of data.
Sofosbuvir	B	No evidence of teratogenicity in rats or rabbits. No experience in human pregnancy.	Treatment of HCV generally not indicated in pregnancy. Regimens including ribavirin and interferon are **contraindicated** in pregnancy.
Sofosbuvir/ Velpatasvir	Not assigned	No AEs in mice, rats, rabbits during pregnancy or lactation. No data in human pregnancy or breastfeeding.	Could be used if benefits felt to outweigh unknown risks in patients not needing ribavirin. Ribavirin is **contraindicated** in pregnancy, so not recommended for patients needing ribavirin based on subtype or resistance.
Sofusbuvir/ Velpatasvir +/- Voxilaprevir	Not assigned	No AEs in mice, rats, rabbits during pregnancy or lactation. No data in human pregnancy or breastfeeding.	Could be used if benefits felt to outweigh unknown risks.
Streptomycin	D	No teratogenicity in mice, rats, guinea pigs. Possible increased risk of deafness and VIII-nerve damage; no evidence of other defects.	Alternate therapy for active TB
Sulfadiazine	B	Sulfonamides teratogenic in some animal studies. No clear teratogenicity in humans; potential for increased jaundice, kernicterus if used near delivery.	Secondary prophylaxis of toxoplasmic encephalitis
Telaprevir	B	Not teratogenic in mice, rats. No human pregnancy data.	Treatment of HCV currently generally not indicated in pregnancy.
Telbivudine	B	Not teratogenic in rats, rabbits. Limited experience in human pregnancy.	**Not recommended** because of limited data in pregnancy. Use as part of fully suppressive ARV regimen with ARV agents active against both HIV and HBV. Report exposures during pregnancy to the Antiretroviral Pregnancy Registry.

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 8 of 8)

Drug	FDA Category[a]	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Tenofovir	B	No evidence of birth defects in rats, rabbits, or monkeys at high doses; chronic administration in immature animals of multiple species at 6–50 times human doses has led to dose-specific bone changes ranging from decreased mineral density to severe osteomalacia and fractures. Clinical studies in humans (particularly children) show bone demineralization with chronic use; clinical significance unknown. No evidence of increased birth defects in nearly 2,000 first-trimester exposures in women.	Component of fully suppressive ARV regimen in pregnant women. Report exposures during pregnancy to the Antiretroviral Pregnancy Registry.
Trichloroacetic Acid and **Bichloroacetic Acid**	Not rated	No studies. Used topically so no systemic absorption expected.	Topical therapy of non-cervical genital warts
Trifluridine	C	Not teratogenic in rats, rabbits. Minimal systemic absorption expected with topical ocular use.	Topical agent for treatment of ocular herpes infections
Trimethoprim-Sulfamethoxazole	C	Teratogenic in rats and mice. Possible increase in congenital cardiac defects, facial clefts, neural tube and urinary defects with first-trimester use. Unclear if higher levels of folate supplementation lower risk. Theoretical risk of elevated bilirubin in the neonate if used near delivery.	Therapy of PCP during pregnancy. Primary and secondary PCP prophylaxis in the second/third trimester; consider aerosolized pentamidine in first trimester. Recommend fetal ultrasound at 18–20 weeks after first-trimester exposure.
Valacyclovir	B	Not teratogenic in mice, rats, and rabbits. Experience with valacyclovir in pregnancy limited; prodrug of acyclovir, which is considered safe for use in pregnancy.	Treatment of HSV and varicella infections in pregnancy
Vancomycin	C	Not teratogenic in rats, rabbits. Limited human experience.	Serious bacterial infections
Voriconazole	D	Embryotoxic in rats, rabbits. Teratogenic in rats (cleft palate, hydronephrosis, and ossification defects). No experience with human use.	**Not recommended**

[a] FDA has discontinued the assignment of drugs to pregnancy-risk letter categories in favor of a narrative approach. This table includes both previously assigned risk categories for older drugs and key findings based on FDA narratives for unassigned newer drugs.

Key: AE = adverse effect; ART = antiretroviral therapy; ARV = antiretroviral; CMV = cytomegalovirus; CNS = central nervous system; FDA = Food and Drug Administration; G6PD = glucose-6-phosphate dehydrogenase; HBV = hepatitis B virus; HCV = hepatitis C virus; HSV = herpes simplex virus; MAC = *Mycobacterium avium* complex; PCP = *Pneumocystis* pneumonia; TB = tuberculosis; VIII nerve = vestibulocochlear nerve; WHO = World Health Organization