Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV

Developed by the National Institutes of Health, the Centers for Disease Control and Prevention, and the HIV Medicine Association of the Infectious Diseases Society of America Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV—A Working Group of the NIH Office of AIDS Research Advisory Council (OARAC)

How to Cite the Adult and Adolescent Opportunistic Infection Guidelines:

Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. National Institutes of Health, Centers for Disease Control and Prevention, HIV Medicine Association, and Infectious Diseases Society of America. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection. Accessed (insert date) [include page numbers, table number, etc., if applicable].

It is emphasized that concepts relevant to HIV management evolve rapidly. The Panels have a mechanism to update recommendations on a regular basis, and the most recent information is available on the Clinicalinfo website (https://clinicalinfo.hiv.gov/).

Table of Contents

Table 1. Chemoprophylaxis to Prevent First Episode of Opportunistic Disease

Updated: September 25, 2023
Reviewed: January 10, 2024

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 with HIV section.

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.

Table 1. Chemoprophylaxis to Prevent First Episode of Opportunistic Disease

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 600 mg plus pyridoxine 25–50 mg) PO daily for 3 months (AI) See the Dosing Recommendations for Anti-TB Drugs table 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 the Dosing Recommendations for Anti-TB Drugs table 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)

Table 1. Chemoprophylaxis to Prevent First Episode of Opportunistic Disease

Opportunistic Infections	Indication	Preferred	Alternative
Syphilis	Individuals exposed sexually within ≤90 days of the diagnosis of primary, secondary, or early latent syphilis in a sex partner, regardless of serologic status (AII), *or* Individuals exposed >90 days before syphilis diagnosis in a sex 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 one dose (AII)	For penicillin-allergic patients: • Doxycycline 100 mg PO twice daily for 14 days (BII), *or* • Ceftriaxone 1 g IM or IV daily for 10–14 days (BII)
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*

Table 1. Chemoprophylaxis to Prevent First Episode of Opportunistic Disease

Opportunistic Infections	Indication	Preferred	Alternative
			• 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 HIV-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy)

Updated: November 14, 2023
Reviewed: January 10, 2024

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 when 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	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).

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

Opportunistic Infection		Preferred Therapy	Alternative Therapy	Other Comments
		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).	If no clinical response is observed after 5–7 days, consider a follow-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% were 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).
		• Ciprofloxacin 500–750 mg PO (or 400 mg IV) every 12 hours, if susceptible (AIII)	• Levofloxacin 750 mg (PO or IV) every 24 hours (BIII), *or*	

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

Opportunistic Infection		Preferred Therapy	Alternative Therapy	Other Comments
		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) *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)	• Moxifloxacin 400 mg (PO or IV) every 24 hours (BIII), *or* • TMP-SMX (160 mg/ 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)	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.
	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 individuals with HIV 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-SMX (160 mg/ 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].)	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-

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
		Note: Azithromycin-resistant *Shigella* spp. has been reported in MSM with HIV.	up stool culture, alternative diagnosis, or antibiotic resistance. Effective ART may decrease the risk of recurrence of *Shigella* infections.
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 plus RIF 300 mg PO or IV) every 12 hours for 6 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, Osteomyelitis, and Other Severe Infection • Azithromycin 500 mg PO daily (BIII) • Clarithromycin 500 mg PO twice a day (BIII) 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)	When RIF is used, take into consideration the potential for significant interaction with ARV drugs and other medications (see Table 4 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 the CD4 count is <200 cells/mm^3 (AIII).
Candidiasis (Mucocutaneous)	For Oropharyngeal Candidiasis; Initial Episodes (for 7–14 Days) *Oral Therapy* • Fluconazole 100 mg PO daily (AI) For Esophageal Candidiasis (for	For Oropharyngeal Candidiasis; Initial Episodes (for 7–14 Days) *Oral Therapy* • Itraconazole oral solution 200 mg PO daily (BI), *or*	Chronic or prolonged use of azoles may promote development of resistance. Higher relapse rate for esophageal candidiasis is seen with echinocandins than with fluconazole use. Suppressive therapy is usually not recommended

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

	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* • 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)	• 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 canine fossa once daily (do not swallow, chew, or crush tablet) (BI), *or* • Nystatin suspension 4–6 mL four times a day or one to two 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 one time, then 50 mg IV daily (BI), *or* • Caspofungin 50 mg IV daily (BI), *or* • Micafungin 150 mg IV daily (BI), *or*	(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 • 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)

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
		• 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) For Azole-Refractory *Candida glabrata* Vaginitis • Boric acid vaginal suppository 600 mg once daily for 14 days	
Chagas Disease (American Trypanosomiasis)	For Acute or Reactivated Disease • Benznidazole 5–8 mg/kg/day PO in two divided doses for 60 days (BIII) (commercially available at http://www.benznidazoletablets.com/en; most experts recommend a daily maximum of 300 mg), *or* • Nifurtimox (Lampit®) 8–10 mg/kg/day PO in three divided doses for 60 days (BIII) (commercially available through retail sources)	None	Treatment is effective in reducing parasitemia and preventing clinical symptoms or slowing disease progression. These drugs have limited efficacy, however, in achieving parasitological cure. Treatment is not recommended for patients with advanced chagasic cardiomyopathy. Duration of therapy has not been studied in patients with HIV. Initiation or optimization of ART is recommended for all people with HIV with concomitant *Trypanosoma cruzi* (AIII).
Coccidioidomycosis	Mild to Moderate Pulmonary Infection • Fluconazole 400 mg PO daily (AII), *or* • Itraconazole 200 mg three times a day for 3 days, then 200 mg PO twice a day (AII)	Mild to Moderate Pulmonary Infection *For Patients Who Failed to Respond to Fluconazole or*	Some patients with meningitis may develop hydrocephalus and require CSF shunting.

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	• Duration of therapy: clinical response to 3–6 months of therapy, and CD4 count ≥250 cells/mm^3, and viral suppression on ARV (AII) Severe Pulmonary or Extrapulmonary Infection (except meningitis) • Lipid formulation amphotericin B 3–5 mg/kg IV daily (AIII); or • Amphotericin B deoxycholate 0.7–1.0 mg/kg IV daily (AII) • Continue until clinical improvement, then switch to an azole (BIII). Therapy should be continued for at least 12 months and usually much longer, and should be continued in patients with HIV viremia or with CD4 count <250 cells/mm^3 (BIII) Meningeal Infections • Fluconazole 400–800 mg IV or PO daily (AII) • Duration of therapy: lifelong (AII)	*Itraconazole* • Posaconazole delayed release tablet 300 mg PO twice a day for first day, then 300 mg PO once daily (BIII), *or* • Voriconazole 400 mg PO twice daily for first day, then 200 mg PO twice a day (BIII) Severe Pulmonary or Extrapulmonary Infection (except meningitis) • 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 (CIII). Meningeal Infections • Itraconazole 200 mg PO two or three times daily (BII), *or* • Voriconazole 200–400 mg PO twice a day (BIII), *or* • Posaconazole delayed release tablet 300 mg PO twice on first day, then 300 mg PO daily (CIII), *or* • Isavuconazole sulfate 372 mg PO every 8 hrs for six doses, then 372 mg daily (CIII) • Intrathecal amphotericin B deoxycholate, when triazole antifungals are ineffective (AIII)	Therapy should be lifelong in patients with meningeal infections because relapse occurs in 80% of patients with HIV after discontinuation of triazole therapy (AII). See Table 4 for antifungal drug–drug interactions. Itraconazole, posaconazole, and voriconazole may have significant interactions with certain ARV agents. These interactions are complex and can be bidirectional. 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 antiretroviral efficacy and reduce concentration-related toxicities. 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	Empiric antibiotic therapy should be initiated promptly for patients presenting with clinical and radiographic	Duration For most patients, 5–7 days Patients should be afebrile

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	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 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*	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 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	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 developing drug resistance and drug toxicities (AI).

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	• 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).	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).	
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).	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*	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,

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

	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 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 LFA**) • Fluconazole, 400 to 800 mg PO daily for 10 weeks, followed by 200 mg daily for a total of 6 months (BIII)	• 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 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	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 managing 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).

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Cryptosporidiosis	• Aggressive oral and/or IV rehydration and replacement of electrolyte loss (AIII), *and* • Symptomatic treatment of diarrhea with anti-motility agents (AIII), *and* • ART initiation to achieve immune restoration to CD4 count >100 cells/mm^3 (AII).	No therapy has been shown to be effective without ART. Consider trial of these agents in conjunction with ART, rehydration, and symptomatic treatment: • Nitazoxanide 500–1,000 mg PO twice a day with food for at least 14 days (CIII), *or* • Paromomycin 500 mg PO four times daily for 14–21 days (CIII)	Tincture of opium may be more effective than loperamide in management of diarrhea (CIII). Because diarrhea can cause lactase deficiency, patients should avoid milk products (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 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	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* • 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)*	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). Initial therapy in patients with CMV retinitis, esophagitis, colitis, and pneumonitis should include initiation or optimization of ART (BIII). 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.

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	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 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.	• 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)
Hepatitis B Virus (HBV) Disease	ART is recommended for all patients with HIV/HBV coinfection regardless of CD4 cell count and HBV DNA level (AIII). The ART regimen must include two drugs that are active against both HBV and HIV (AIII). If CrCl ≥60 mL/min: • (TDF 300 mg plus [FTC 200 mg or 3TC 300 mg]) or (TAF [10 or 25 mg][a]	For Persons Not on ART • Anti-HBV therapy is indicated for those who meet criteria for treatment according to the AASLD Hepatitis B Guidance. • Peginterferon alfa-2a 180 mcg SQ once weekly for 48 weeks (CIII), *or*	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-resistant HIV (AII). Chronic administration of 3TC or FTC as the only active drug against HBV

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	plus FTC 200 mg) PO once daily (AII) Note: TAF 10 mg is in the STR tablets of EVG/COBI/TAF/FTC and DRV/COBI/TAF/FTC; when TAF is used with other ARVs, the dose is 25 mg. If CrCl 30–59 mL/min: • TAF (10 or 25 mg)[a] plus FTC 200 mg PO once daily (AII) If CrCl <30 mL/min, not on HD: • Renally dosed entecavir (in place of TDF or TAF), with a fully suppressive ART regimen, *or* • ART with renally dose-adjusted TDF and FTC or 3TC can be used (BIII) if recovery of renal function is unlikely. If on HD: • (TDF or TAF) plus (FTC or 3TC) can be used. Refer to Table 6 for dosing recommendations. TAF and FTC do not require renal dose adjustment in people receiving HD. Duration • Continue treatment indefinitely (BIII).	• Peginterferon alfa-2b 1.5 mcg/kg SQ once weekly for 48 weeks (CIII)	should be avoided because of the high rate of selection of HBV drug-resistance mutations (AI). People with 3TC-resistant HBV will have cross-resistance to telbivudine and FTC, and partial resistance to entecavir. These agents should not be used among people found to have 3TC-resistant HBV (AI). If 3TC resistance is suspected or documented, TDF or TAF should be added to the ART regimen (BIII). When changing ART regimens, continue agents with anti-HBV activity (AIII). If anti-HBV therapy is discontinued and a flare occurs, therapy should be re-instituted because it can be potentially lifesaving (AIII). Because HBV reactivation can occur during treatment for HCV with direct-acting antivirals in the absence of anti-HBV therapy, all people with HIV/HBV coinfection who will be treated for HCV infection should be on HBV-active ART at the time of HCV treatment initiation (AIII). If immunosuppressive therapy is given, HBV reactivation can occur. For people who are HBsAg-positive, treatment for HBV infection should be administered (AII).

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Hepatitis C Virus (HCV) Disease	For Treatment-Naive Patients Without Cirrhosis (Any Genotype or No Pre-Treatment Genotype) • Glecaprevir/pibrentasvir FDC (100 mg/40 mg per tablet), three tablets daily for 8 weeks (AI), *or* • Sofosbuvir/velpatasvir FDC (400 mg/100 mg per tablet), one tablet daily for 12 weeks (AI) Characteristics that exclude patients from receiving simplified approach to therapy are outlined in Box 1 of the Hepatitis C Virus section. For Treatment-Naive Patients with Compensated Cirrhosis (Recommendations Based on Genotypes) *Genotypes 1, 2, 4–6* • Glecaprevir/pibrentasvir FDC (100 mg/40 mg per tablet), three tablets daily for 8 weeks (AIII), *or* • Sofosbuvir/velpatasvir FDC (400 mg/100 mg per tablet), one tablet daily for 12 weeks (AI) *Genotype 3* • Glecaprevir/pibrentasvir FDC (100 mg/40 mg per tablet), three tablets daily for 8 weeks (AIII) For Treatment of Acute HCV Infection • Glecaprevir/pibrentasvir FDC (100 mg/40 mg per tablet), three tablets daily for 8 weeks (AII) *or* • Sofosbuvir/velpatasvir FDC (400 mg/100 mg per tablet), one tablet daily for 12 weeks (AII)	For Treatment-Naive Patients with Compensated Cirrhosis (Recommendations Based on Genotypes) *Genotypes 1, 2, 4–6* • Glecaprevir/pibrentasvir FDC (100 mg/40 mg per tablet), three tablets daily for 12 weeks (CI) *Genotype 3* • Glecaprevir/pibrentasvir FDC (100 mg/40 mg per tablet), three tablets daily for 12 weeks (CI) *or* • Sofosbuvir/velpatasvir FDC (400 mg/100 mg per tablet), one tablet daily with or without ribavirin for 12 weeks pending results of NS5A RAS testing (CI)	Simplified approach to HCV treatment can be used in treatment-naive patients with any genotype and without cirrhosis. This approach includes standardized treatment, with no on-treatment testing or in-person follow-up and limited follow-up to confirm SVR. See Hepatitis C Virus section to review a summary of drug–drug interactions between HCV therapy and ARV drugs. HCV treatment should not be withheld solely due to perceived lack of adherence to ART or untreated HIV (BIII). Effort should be made to document SVR (HCV RNA less than lower limits of quantification) at least 12 weeks after completion of therapy (AI). Patients without cirrhosis who achieve SVR do not require continued liver disease monitoring. Recommendations for treatment after DAA failure are not provided. The reader is referred to the corresponding section in the AASLD/IDSA HCV treatment guidance.
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*	For Acyclovir-Resistant	Patients with HSV infection can be treated with episodic therapy when symptomatic lesions occur, or with daily suppressive therapy to prevent recurrences.

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	• Acyclovir 400 mg PO three times a day (AIII) 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.	HSV *Preferred Therapy* • Foscarnet 80–120 mg/kg/day IV in two to three divided doses until clinical response (AI) *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	Extemporaneous compounding of topical products can be prepared using trifluridine ophthalmic 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)	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	Itraconazole, posaconazole, and voriconazole may have significant interactions with certain ARV agents. These interactions are complex and can be bidirectional. Refer to Drug–Drug Interactions in the Adult and Adolescent Antiretroviral Guidelines for dosage recommendations. Therapeutic drug monitoring and dosage adjustment may

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	Maintenance Therapy • Itraconazole 200 mg PO three times a day for 3 days, then 200 mg PO twice a day (AII) **Less Se**vere 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)	**Treatment of Less Severe** Disease • 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) 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)	be necessary to ensure triazole antifungal and ARV efficacy and reduce concentration-related toxicities. 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 patients with HIV 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	MCD • Rituximab (375 mg/m^2 given weekly for 4–8 weeks) may be an alternative to or used	Corticosteroids should be avoided in patients with KS, including those with KS-IRIS (AIII). Corticosteroids are potentially effective as

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	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) • 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)	adjunctively with antiviral therapy (CII).	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.
Human Papillomavirus (HPV) Disease	Treatment of Condyloma Acuminata (Genital Warts)		Patients with HIV may have larger or more numerous warts and may not respond as well to therapy for genital warts when compared to individuals without HIV. Topical cidofovir has activity against genital warts, but the product is not commercially available (CIII).
	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*	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	

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	• Imiquimod 5% cream: Apply to lesion at bedtime and remove in the morning on 3 nonconsecutive 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* • 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).	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 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).	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 patients with HIV. There is no consensus on the treatment of oral warts. Many treatments for anogenital warts cannot be used in the oral 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 cells/mm^3, TMP-SMX	For Acute Infection • Pyrimethamine[b] 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)	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).

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

Opportunistic Infection		Preferred Therapy	Alternative Therapy	Other Comments
		(160 mg/800 mg) PO three times weekly (AI)	• 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	
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) Chronic Maintenance Therapy (Secondary Prophylaxis); Especially in Patients with CD4 Count <200 cells/mm^3 • Liposomal amphotericin B 4 mg/kg every 2–4 weeks (AII), *or* • Amphotericin B lipid complex (AII) 3 mg/kg every 21 days (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* • 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)	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.
	Cutaneous	For Initial Infection • 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	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 patients with HIV; choice and efficacy are dependent on species of	None

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	immunocompromised patients with multiple relapses (CIII)	*Leishmania.*	
Malaria	Because *Plasmodium falciparum* malaria can progress within hours from mild symptoms or low-grade fever to severe disease or death, all patients with HIV with confirmed or suspected *P. falciparum* infection should be hospitalized for evaluation, initiation of treatment, and observation (AIII). Treatment recommendations for patients with HIV are the same as for patients without HIV (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 species, and can be found at https://www.cdc.gov/malaria.	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 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.
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 supplements (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 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 counts (CIII).	Anti-motility agents can be used for diarrhea control if required (BIII).

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	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/mm³* • Continue until symptoms resolve (CIII). *If CD4 Count ≤200 Cells/mm³* • Continue until resolution of ocular symptoms and CD4 count increases to >200 cells/mm³ for >6 months in response to ART (BIII).		
Mpox	For Severe Disease or at Risk for Severe Disease (See Other Comments for Definition) • Tecovirimat 600 mg PO every 12 hours (<120 kg) or every 8 hours (≥120 kg) for 14 days (BIII) within 30 minutes of a fatty meal; *or* • Tecovirimat 200 mg IV every 12 hours for 14 days (<120 kg) or 300 mg IV every 12 hours (≥120 kg) if concern exists regarding altered GI absorption capacity, inability to take PO, or extent of organ systems affected by mpox (BIII) *Adjunctive Therapy for Severe Disease or at Risk for Severe Disease* • Cidofovir 5 mg/kg/week IV for two doses with saline hydration before and after therapy and probenecid 2 g PO 3 hours before the dose followed by 1 g PO 2 hours after the dose and 1 g PO 8 hours after the dose (total of 4 g) (BIII), *or* • Brincidofovir 200 mg PO once weekly for two doses (BIII), *or*		ART should be initiated as soon as possible (AIII). For severe disease, consider early intervention with adding one of the adjunctive therapies at the time of first medical encounter, in consultation with CDC or an expert in mpox treatment (CIII). Patients with severe immunocompromise might benefit from extended treatment (i.e., >14 days) of preferred and/or adjunctive therapies if new confirmed mpox lesions occur or existing lesions worsen despite treatment. Vaccination with any live virus vaccines should be delayed until 3 months after VIGIV administration (CIII). People who received VIGIV shortly after a live virus vaccination should be revaccinated 3 months after

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	• VIGIV 6,000–9,000 units/kg IV single dose (BIII) *Preferred Therapy for Ocular Mpox* • Tecovirimat 600 mg PO every 12 hours (<120 kg) or every 8 hours (≥120 kg) for 14 days (CIII) within 30 minutes of a fatty meal, *and* • Trifluridine (Viroptic) 1 drop into affected eye(s) every 2 hours when awake (max: 9 drops/day) until reepithelialization, then every 4 hours (min: 5 drops/day) for 7 days or until all periocular lesions have healed (CIII) o Prolonged use of trifluridine beyond 21 days might cause corneal epithelial toxicity and should be avoided (AII).		administration of the immune globulin (CIII). Definition for Severe Disease or at Risk for Severe Disease: People with HIV who are not virologically suppressed or who have CD4 counts <350 cells/mm^3 are considered at high risk for severe mpox. Severe mpox might manifest as hemorrhagic disease; large number of lesions, such that they are confluent; sepsis; encephalitis; ocular or periorbital infections; or other conditions requiring hospitalization.
Mycobacterium avium Complex (MAC) Disease	**At Least Two 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, a short course (i.e., 4 weeks–8 weeks) of a systemic corticosteroid (equivalent to 20–40 mg prednisone) can be used (CII).

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
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 for Anti-TB Drugs 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). 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)	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 ≥5 active drugs, and with close consultation with experienced specialists (AIII).	DOT is recommended for all patients (AII). All rifamycins may have significant pharmacokinetic interactions with ARV drugs; please refer to the Dosing Recommendations for Anti-TB Drugs 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 0.1 mg/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. 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-	For Moderate to Severe PCP • Pentamidine 4 mg/kg IV daily infused over	Indications for Adjunctive Corticosteroids (AI) • PaO_2 <70 mmHg at room air, *or*

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

	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 three divided doses (AI), *or* • TMP-SMX: (160 mg/800 mg or DS) two tablets PO three times daily (AI) Secondary Prophylaxis, After Completion of PCP Treatment • TMP-SMX DS: One tablet PO daily (AI), *or* • TMP-SMX (80 mg/400 mg or SS): One tablet PO daily (AI)	≥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* • Atovaquone 750 mg PO twice daily with food (BI) Secondary Prophylaxis, After Completion of PCP Treatment • TMP-SMX DS: One 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*	• 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 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

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
		• Atovaquone 1,500 mg plus pyrimethamine[a] 25 mg plus leucovorin 10 mg PO daily (CIII)	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 to achieve viral suppression in patients who develop PML and receive ART but remain viremic (AIII).	None	Corticosteroids may be used for PML-IRIS (BIII). The optimal corticosteroid regimen has not been established but should be tailored to individual patients. ART should not be discontinued during PML-IRIS (AIII).
Syphilis (*Treponema pallidum* Infection)	Early-Stage (Primary, Secondary, and Early-**Latent** Syphilis) • Benzathine penicillin G 2.4 million units IM for one dose (AII) **Late-Latent Disease (>1 Year) or of** Unknown Duration • Benzathine penicillin G 2.4 million units IM weekly for three doses (AII) **Late**-Stage (Tertiary–Cardiovascular or Gummatous Disease) • Benzathine penicillin G 2.4 million units IM weekly for three doses (AII) Note: Rule out neurosyphilis before initiation of benzathine penicillin. Persons with CSF abnormalities should be treated with a regimen for neurosyphilis [AII].) Neurosyphilis, Otic, or Ocular Syphilis • 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 x 1 dose after completion of IV therapy (CIII)	Early-Stage (Primary, Secondary, and Early-**Latent** Syphilis) *For Penicillin-Allergic Patients* • Doxycycline 100 mg PO twice daily for 14 days (BII), or • Ceftriaxone 1 g IM or IV daily for 10–14 days (BII) **Late-Latent Disease** (>1 **Year) or of Unknown** Duration *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) *or*	The efficacy of non-penicillin alternatives has not been evaluated in patients with HIV, and they should be used only with close clinical and serologic monitoring. Persons with penicillin allergy whose compliance or follow-up cannot be ensured should be desensitized and treated with benzathine penicillin (AII). For management of early syphilis during pregnancy, limited evidence indicates a second dose of benzathine penicillin G 2.4 million units IM one week after the single dose treatment may be of benefit for congenital syphilis prevention (BII). 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,

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
		• For penicillin-allergic patients, desensitization to penicillin is the preferred approach (BIII); if not feasible and the patient is not pregnant, ceftriaxone 2 g IV daily for 10–14 days (BII).	and prior penicillin treatment. Procaine penicillin has been discontinued by the manufacturer as of June 13, 2023 (see FDA Drug Shortages).
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) *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.	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 bidirectional. 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 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.

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Toxoplasma gondii Encephalitis	Treatment of Acute Infection (AI) • Pyrimethamine[a] 200 mg PO one 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) plus leucovorin 10–25 mg PO daily (AI)	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) 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* • TMP-SMX DS one tablet twice a day (BII), *or* • TMP-SMX DS one 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*	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 must be added to prevent PCP (AII).

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
		• Atovaquone 750–1,500 mg PO twice a day with food (BII) * Pyrimethamine[a] and leucovorin doses are the same as for preferred therapy.	
Varicella Zoster Virus (VZV) Disease	Primary Varicella Infection (Chickenpox) *Uncomplicated Cases* • Initiate as soon as possible after symptom onset and continue for 5–7 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. • 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)	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 five 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.

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
	• 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- to 14-day course (BIII). ARN • Acyclovir 10 mg/kg IV every 8 hours for 10–14 days, followed by valacyclovir 1 g 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] TAF 10 mg dose is in the fixed-dose combination tablets of elvitegravir/cobicistat/TAF/FTC and darunavir/cobicistat/TAF/FTC; when TAF is used with other antiretrovirals, the dose is 25 mg.

[b] 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: +/- = with or without; 3TC = lamivudine; AASLD = American Association for the Study of Liver Diseases; ARN = acute retinal necrosis; ART = antiretroviral therapy; ARV = antiretroviral; CD4 = CD4 T lymphocyte; CDC = Centers for Disease Control and Prevention; CDI = *Clostridium difficile* infection; CFU = colony-forming unit; CNS = central nervous system; COBI = cobicistat; CrCl = creatinine clearance; CSF = cerebrospinal fluid; DAA = direct-acting antiviral; DOT = directly observed therapy; DRV = darunavir; DS = double strength; EMB = ethambutol; EVG = elvitegravir; FDA = U.S. Food and Drug Administration; FDC = fixed-dose combination; FTC = emtricitabine; G6PD = glucose-6-phosphate dehydrogenase; GI = gastrointestinal; HBeAg = hepatitis B e antigen; HBV = hepatitis B virus; HCV = hepatitis C virus; HD = hemodialysis; ICP = intracranial pressure; IDSA = Infectious Diseases Society of America; IL-6 = interleukin-6; IM = intramuscular; IND = investigational new drug; INH = isoniazid; IRIS = immune reconstitution inflammatory syndrome; IRU = immune reconstitution uveitis; IV = intravenous; LFA = lateral flow assay; LP = lumbar puncture; MIC = minimum inhibitory concentrations; MSM = men who have sex with men; NSAID = non-steroidal anti-inflammatory drugs; PCR = polymerase chain reaction; PO = oral; PORN = progressive outer retinal necrosis; PZA = pyrazinamide; RFB = rifabutin; RIF = rifampin; SMX = sulfamethoxazole; SQ = subcutaneous; SS = single strength; STR = single-tablet regimen; SVR = sustained virologic response; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TMP = trimethoprim; VIGIV = vaccinia immune globulin intravenous

Table 3. Indications for Discontinuing and Restarting Opportunistic Infection Secondary Prophylaxis or Chronic Maintenance in Adults and Adolescents with HIV

Updated: July 1, 2021
Reviewed: January 10, 2024

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/mm^3 (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/mm^3 (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/mm^3, 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): • 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):	CD4 count <100 cells/ mm^3 (AIII)

Table 3. Indications for Discontinuing and Restarting Opportunistic Infection Secondary Prophylaxis or Chronic Maintenance in Adults and Adolescents with HIV

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
			• 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/mm^3 and with suppressed plasma HIV RNA in response to ART	
Cytomegalovirus Retinitis	Not applicable	Not applicable	• CMV treatment for at least 3 to 6 months; and with CD4 count >100 cells/mm^3 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/mm^3 (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 (BIII)

Table 3. Indications for Discontinuing and Restarting Opportunistic Infection Secondary Prophylaxis or Chronic Maintenance in Adults and Adolescents with HIV

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
			• CD4 count ≥150 cells/mm^3 for ≥6 months in response to ART	
Isospora belli Infection	Not applicable	Not applicable	Sustained increase in CD4 count to >200 cells/mm^3 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/mm^3 for 3 to 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/mm^3 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)
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 to 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	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).

Table 3. Indications for Discontinuing and Restarting Opportunistic Infection Secondary Prophylaxis or Chronic Maintenance in Adults and Adolescents with HIV

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
			limits of detection for ≥3 months to 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).	
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/mm^3 for >3 months in response to ART (AI) Can consider when CD4 count 100–200 cells/mm^3 if HIV RNA remain below limits of detection for at least 3-6 months (BII)	CD4 count <100 cells/mm^3, (AIII) CD4 count 100–200 cells/μL and with HIV RNA above detection limit of the assay (AIII).	Successfully completed initial therapy, receiving maintenance therapy and remain free of signs and symptoms of TE, and CD4 count >200 cells/mm^3 for >6 months in response to ART (BI).	CD4 count <200 cells/mm^3 (AIII)

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; CD4 = CD4 T lymphocyte cell; CMV = cytomegalovirus; MAC = *Mycobacterium avium* complex; PCP = *Pneumocystis* pneumonia; TE = *Toxoplasma* encephalitis

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Updated: September 25, 2023
Reviewed: January 10, 2024

This table lists the known, predicted, or suspected pharmacokinetic (PK) interactions between drugs used for the treatment or prevention of HIV-associated opportunistic infections (OIs). Many of the drugs listed in this table may also interact with antiretroviral (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 rationales for these recommendations are summarized below:

Do not coadminister.

There is either strong evidence or strong likelihood that the PK 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. Therapeutic drug monitoring, if available, may facilitate any necessary dose adjustments.

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-Related Induction Interactions

Rifamycin antibiotics are potent inducers of Phase 1 and Phase 2 drug metabolizing reactions. They also affect various transporters. When a rifamycin antibiotic must be combined with an interacting drug, close monitoring for clinical efficacy of the coadministered agent is advised. Therapeutic drug monitoring, if available, may facilitate any necessary dose adjustments.

- *Rifampin (also known as rifampicin):* Interactions may not be apparent in the first several days of rifampin therapy. However, with daily doses of rifampin, enzyme induction increases over a

week or more. Based on limited data, larger daily doses of rifampin (e.g., 1,200 mg or more) appear to produce the same maximum induction as lower doses, but the induction effect occurs more rapidly.

- *Rifabutin:* In general, rifabutin as a cytochrome P450 3A4 (CYP3A4) inducer is about 40% of the potency of rifampin, but this can vary by substrate and enzymatic reaction. Rifabutin is also a substrate of CYP3A4 and may be subject to changes in drug exposure when given concomitantly with 3A4 inhibitors or inducers. Rifabutin dosage modification, therapeutic drug monitoring, and/or more frequent monitoring for rifabutin-related toxicities may be needed.
- *Rifapentine:* In general, daily rifapentine is at least as potent an inducer as rifampin. However, the potential for drug interactions with once-weekly rifapentine is not well studied. Reduced exposure of concurrent drugs that are CYP3A4 substrates is likely to occur with once-weekly rifapentine, with the extent varying by drug.

Azole- and Macrolide-Related Inhibition Interactions

Azole antifungals, including fluconazole, isavuconazole, itraconazole, posaconazole, and voriconazole, are substrates and potent inhibitors of metabolic pathways, including cytochrome P450 enzymes and/or drug transporters (e.g., p-glycoprotein). Interactions involving azole antifungals are common. When an azole antifungal must be combined with an interacting drug, close monitoring for clinical toxicity and efficacy of the azole and/or the coadministered agent may be needed. Therapeutic drug monitoring, if available, may facilitate any necessary dose adjustments.

Macrolides have been shown to form complexes with drug-oxidizing enzymes, including cytochrome P450 enzymes, which render an inhibitory effect. In general, erythromycin and clarithromycin are moderate to strong inhibitors, while azithromycin's propensity for causing clinically relevant drug interactions is lowest, as it does not form complexes with cytochrome P450 enzymes that lead to enzyme inactivation.

Pharmacodynamic Interactions

Pharmacodynamic interactions are not addressed in this table. For example, many of the drug classes listed below independently possess a risk for QTc prolongation, including azoles, macrolides, and certain anti-tuberculosis and antimalarial medications. Coadministration of drugs in these classes may require monitoring for QTc prolongation, particularly in patients with predisposing risk factors.

Therapeutic Drug Monitoring

Drug interactions can alter oral absorption or systemic clearance of drugs. More than one interaction can occur at the same time, with potentially opposing effects. Therapeutic drug monitoring (TDM), if available, may facilitate any necessary dose adjustments in these complicated patients. TDM allows the clinician to make informed, individualized decisions about dose adjustments that are more precise than standardized dose adjustments based upon anticipated, average effects.

Drugs that are marked with an asterisk (*) in the table below are known to have assays (for clinical and/or research purposes) available within the United States and typically in Europe as well. When TDM is appropriate, clinicians should contact their clinical laboratory to determine assay availability and turnaround time for their institution.

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.

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.
	Erythromycin	↑ lumefantrine expected	Coadministration should be avoided, if possible. 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]	Daily and Weekly Rifapentine ↓ artemether, DHA, and lumefantrine	Do not coadminister.

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
		expected	
	Voriconazole	↑ lumefantrine expected	Coadministration should be avoided, if possible. If coadministered, monitor for lumefantrine toxicities.
Atovaquone*	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]	Daily and Weekly Rifapentine ↓ atovaquone expected	Do not coadminister.
Bedaquiline*	Clarithromycin	↑ bedaquiline expected	Do not coadminister. Consider azithromycin in place of clarithromycin.
	Erythromycin	↑ bedaquiline expected	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 coadministered, monitor for

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
			bedaquiline toxicities. If coadministration is required for >14 days, weigh the benefits of therapy against the risks of bedaquiline toxicities.
	Posaconazole	↑ bedaquiline expected	Coadministration should be avoided, if possible. If coadministered, monitor for bedaquiline toxicities.
	Rifabutin[a]	↔ bedaquiline ↓ rifabutin possible	If coadministered, separate time of administration; perform rifabutin TDM and adjust dose accordingly.
	Rifampin[a]	Bedaquiline AUC ↓ 53%	Do not coadminister.
	Rifapentine[a]	Daily Rifapentine Bedaquiline AUC ↓ 55% Weekly Rifapentine ↓ bedaquiline expected	Do not coadminister.
	Voriconazole	↑ bedaquiline expected	Coadministration should be avoided, if possible. If coadministered, monitor for bedaquiline toxicities.
Brincidofovir	Clarithromycin	↑ brincidofovir expected	Coadministration should be avoided, if possible. If coadministered, postpone clarithromycin for at least 3 hours after brincidofovir and monitor for brincidofovir toxicities. Consider azithromycin in place of clarithromycin.
	Erythromycin	↑ brincidofovir expected	Coadministration should be avoided, if possible. If coadministered, postpone erythromycin for at least 3 hours after brincidofovir and monitor for brincidofovir toxicities. Consider azithromycin in place of erythromycin.
	Rifampin	↑ brincidofovir expected	Coadministration should be avoided, if possible. If

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
			coadministered, postpone rifampin for at least 3 hours after brincidofovir and monitor for brincidofovir toxicities.
Caspofungin	Rifabutin[a]	↓ 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]	Daily Rifapentine ↓ caspofungin expected Weekly Rifapentine ↓ 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).
Chloroquine*	Clarithromycin	↑ chloroquine expected	Do not coadminister. Consider azithromycin in place of clarithromycin.
	Erythromycin	↑ chloroquine expected	Do not coadminister. Consider azithromycin in place of erythromycin.
	Fluconazole	↑ chloroquine possible	Coadministration should be avoided, if possible. If coadministered, 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.

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	Rifabutin[a]	↓ chloroquine expected	Monitor for chloroquine efficacy.
	Rifampin[a]	↓ chloroquine expected	Monitor for chloroquine efficacy.
	Rifapentine[a]	Daily and Weekly Rifapentine ↓ 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.
	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.
	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; perform itraconazole and clarithromycin TDM 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

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
			clarithromycin. If coadministered, monitor for toxicities of clarithromycin; perform clarithromycin TDM and adjust dose accordingly.
	Quinine	↑ quinine expected ↑ clarithromycin possible	Do not coadminister. Consider azithromycin in place of clarithromycin.
	Rifabutin[a]	Clarithromycin AUC ↓ 44% 14-OH clarithromycin 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, perform clarithromycin and rifabutin TDM and adjust dose accordingly. Monitor for rifabutin toxicities.
	Rifampin[a]	Clarithromycin concentration ↓ 87% Rifampin AUC ↑ 60%	Do not coadminister. Use azithromycin in place of clarithromycin.
	Rifapentine[a]	Daily and Weekly Rifapentine ↓ clarithromycin expected ↑ 14-OH clarithromycin and rifapentine expected	Daily Rifapentine Do not coadminister. Use azithromycin in place of clarithromycin. Weekly Rifapentine Use with caution. Consider azithromycin in place of clarithromycin. If coadministered, monitor for rifapentine toxicities and clarithromycin efficacy; perform clarithromycin and rifapentine TDM and adjust doses accordingly.
	Voriconazole	↑ clarithromycin expected	Coadministration should be avoided, if possible. Consider azithromycin in place of clarithromycin. If coadministered, monitor for toxicities of clarithromycin; perform clarithromycin TDM and adjust dose accordingly.
Dapsone*	Rifabutin[a]	Dapsone AUC ↓ 27% to 40%	Coadministration should be avoided, if possible. Consider alternatives for dapsone.

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	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]	Daily and Weekly Rifapentine ↓ dapsone expected	Coadministration should be avoided, if possible. Consider alternatives for dapsone.
Doxycycline	Atovaquone	See Atovaquone.	See Atovaquone.
	Rifabutin[a]	↓ 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]	Daily Rifapentine ↓ doxycycline expected Weekly Rifapentine ↓ doxycycline possible	Use with caution. Monitor closely for doxycycline efficacy or consider alternative therapy.
Erythromycin	Artemether/Lumefantrine	See Artemether/Lumefantrine.	See Artemether/Lumefantrine.
	Bedaquiline	See Bedaquiline.	See Bedaquiline.
	Chloroquine	See Chloroquine.	See Chloroquine.
	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.
	Mefloquine	↑ mefloquine possible	Do not coadminister. Consider azithromycin in place of erythromycin.
	Posaconazole	↑ erythromycin expected	Do not coadminister. Consider azithromycin in place of erythromycin.

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	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 and rifabutin toxicities; perform rifabutin TDM and adjust dose accordingly.
	Rifampin[a]	↓ erythromycin expected	Consider azithromycin in place of erythromycin. If coadministered, monitor for erythromycin efficacy.
	Rifapentine[a]	Daily and Weekly Rifapentine ↓ 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.
	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 expected	Use with caution. Monitor for rifabutin toxicities. Perform rifabutin TDM; may need to decrease rifabutin dose to 150 mg/day.

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	Rifampin[a]	Fluconazole AUC ↓ 23% to 56%	Monitor for antifungal efficacy; may need to increase fluconazole dose.
	Rifapentine[a]	Daily and Weekly Rifapentine ↓ fluconazole expected	Monitor for antifungal efficacy; may need to increase fluconazole dose.
Glecaprevir/ Pibrentasvir	Rifabutin[a]	↓ glecaprevir and pibrentasvir possible	Coadministration should be avoided, if possible. Consider alternative agents.
	Rifampin[a]	Glecaprevir AUC ↓ 88% Pibrentasvir AUC ↓ 87%	Do not coadminister.
	Rifapentine[a]	Daily and Weekly Rifapentine ↓ glecaprevir and pibrentasvir expected	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.
	TAF	↔ TFV concentration when coadministered as EVG/c/TAF/FTC	No dose adjustment necessary
Isavuconazole *	Artemether/Lumefantrine	See Artemether/Lumefantrine.	See Artemether/Lumefantrine.
	Bedaquiline	See Bedaquiline.	See Bedaquiline.
	Chloroquine	See Chloroquine.	See Chloroquine.
	Clarithromycin	See Clarithromycin.	See Clarithromycin.
	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 antifungal activity and rifabutin toxicity. Perform rifabutin TDM and adjust dose accordingly.

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	Rifampin[a]	Isavuconazole AUC ↓ 97%	Do not coadminister. Consider alternative antifungal and/or antimycobacterial agent(s).
	Rifapentine[a]	Daily and Weekly Rifapentine ↓ 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.
	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; perform itraconazole TDM and adjust dose accordingly.
	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]	Daily and Weekly Rifapentine ↓ itraconazole expected	Do not coadminister. Consider alternative antifungal and/or antimycobacterial agent(s).
Linezolid*	Rifabutin[a]	↓ linezolid possible	Monitor for linezolid efficacy.
	Rifampin[a]	Linezolid AUC ↓ 32%	Monitor for linezolid efficacy. Perform linezolid TDM and adjust dose accordingly.
	Rifapentine[a]	Daily Rifapentine ↓ linezolid expected Weekly Rifapentine	Daily Rifapentine Monitor for linezolid efficacy. Perform linezolid TDM and adjust dose accordingly.

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
		↓ linezolid possible	Weekly Rifapentine Monitor for linezolid efficacy.
Mefloquine*	Artemether/Lumefantrine	See Artemether/Lumefantrine.	See Artemether/Lumefantrine.
	Clarithromycin	See Clarithromycin.	See Clarithromycin.
	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]	Daily and Weekly Rifapentine ↓ 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.
	Chloroquine	See Chloroquine.	See Chloroquine.
	Clarithromycin	See Clarithromycin.	See Clarithromycin.
	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.

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	Rifabutin[a]	Posaconazole AUC ↓ 49% Rifabutin AUC ↑ 72%	Coadministration should be avoided, if possible. If coadministered, perform posaconazole and rifabutin TDM and adjust doses accordingly; monitor for clinical response to posaconazole and rifabutin toxicities.
	Rifampin[a]	↓ posaconazole expected	Do not coadminister when treating invasive fungal infections. If coadministered for treatment of noninvasive fungal infections, perform posaconazole TDM and adjust dose accordingly; monitor for clinical response.
	Rifapentine[a]	Daily and Weekly Rifapentine: ↓ posaconazole expected	Daily Rifapentine Do not coadminister when treating invasive fungal infections. If coadministered for treatment of noninvasive fungal infections, perform posaconazole TDM and adjust dose accordingly; monitor for clinical response. Weekly Rifapentine Coadministration should be avoided, if possible. If coadministered, perform posaconazole TDM 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 for rifabutin toxicity.
	Rifampin[a]	Quinine AUC ↓ 75% to 85%	Do not coadminister.

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	Rifapentine[a]	Daily and Weekly Rifapentine ↓ 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.
	Clarithromycin	See Clarithromycin.	See Clarithromycin.
	Dapsone	See Dapsone.	See Dapsone.
	Doxycycline	See Doxycycline.	See Doxycycline.
	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.
	Linezolid	See Linezolid.	See Linezolid.
	Mefloquine	See Mefloquine.	See Mefloquine.
	Posaconazole	See Posaconazole.	See Posaconazole.
	Quinine	See Quinine.	See Quinine.
	Sofosbuvir/Velpatasvir	↓ velpatasvir, sofosbuvir expected	Do not coadminister.
	TAF	↓ TAF, TFV, TFV-DP expected ↑ TFV-DP expected versus TDF alone	If coadministered, monitor for HIV and HBV treatment efficacy. Note: Interpretation extrapolated from TAF and rifampin (see Rifampin). FDA labeling recommends not to coadminister.
	TDF	↔ TDF, TFV, TFV-DP expected	No dosage adjustment necessary.

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	Voriconazole	Voriconazole AUC ↓ 79% Rifabutin AUC ↑ 4-fold	Do not coadminister. Consider alternative antifungal and/or antimycobacterial agent(s). Coadministration may be considered if both voriconazole and rifabutin TDM is available 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.
	Dapsone	See Dapsone.	See Dapsone.
	Doxycycline	See Doxycycline.	See Doxycycline.
	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.
	Linezolid	See Linezolid.	See Linezolid.
	Mefloquine	See Mefloquine.	See Mefloquine.
	Posaconazole	See Posaconazole.	See Posaconazole.
	Quinine	See Quinine.	See Quinine.
	Sofosbuvir/Velpatasvir	Sofosbuvir AUC ↓ 72% Velpatasvir AUC ↓ 82%	Do not coadminister.
	TAF	TAF Plus Rifampin • TAF AUC ↓ 56% • TFV AUC ↓ 53% • TFV-DP AUC ↓ 36% Intracellular TFV-DP concentration is 4.2-	If coadministered, monitor for HIV and HBV treatment efficacy. Note: FDA labeling recommends not to coadminister.

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
		fold greater than with TDF alone.	
	TDF	TDF Plus Rifampin 600 mg Daily ↔ TFV	No dosage adjustment necessary
	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.
	Dapsone	See Dapsone.	See Dapsone.
	Doxycycline	See Doxycycline.	See Doxycycline.
	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.
	Linezolid	See Linezolid.	See Linezolid.
	Mefloquine	See Mefloquine.	See Mefloquine.
	Posaconazole	See Posaconazole.	See Posaconazole.
	Quinine	See Quinine.	See Quinine.
	TAF	Daily and Weekly Rifapentine ↓ TAF, TFV, TFV-DP possible	If coadministered, monitor for HIV and HBV treatment efficacy. Note: FDA labeling recommends not to coadminister.

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	TDF	↔ TDF, TFV, TFV-DP expected	No dosage adjustment necessary
	Sofosbuvir/Velpatasvir	↓ sofosbuvir, velpatasvir expected	Do not coadminister.
	Voriconazole	↓ voriconazole expected	Do not coadminister. Consider alternative antifungal and/or antimycobacterial agent(s).
Sofosbuvir*/ Velpatasvir	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 necessary
	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	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	See Sofosbuvir/Velpatasvir.	See Sofosbuvir/Velpatasvir.
Tenofovir* Disoproxil Fumarate	Rifabutin[a]	See Rifabutin.	See Rifabutin.
	Rifampin[a]	See Rifampin.	See Rifampin.
	Rifapentine[a]	See Rifapentine.	See Rifapentine.
	Glecaprevir/Pibrentasvir	See Glecaprevir/Pibrentasvir.	See Glecaprevir/Pibrentasvir.
	Sofosbuvir/Velpatasvir	See Sofosbuvir/Velpatasvir.	See Sofosbuvir/Velpatasvir.
Voriconazole*	Artemether/Lumefantrine	See Artemether/Lumefantrine.	See Artemether/Lumefantrine.
	Bedaquiline	See Bedaquiline.	See Bedaquiline.
	Chloroquine	See Chloroquine.	See Chloroquine.

Table 4. Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections

Primary Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	Clarithromycin	See Clarithromycin.	See Clarithromycin.
	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] Refer to the subsection Rifamycin-Related Induction Interactions in the Table 4 introduction above.

* Drugs marked with asterisk (*) are those which are known to have assays available (for clinical and/or research purposes) within the United States and typically in Europe. When TDM is appropriate, clinicians should contact their clinical laboratory to determine assay availability and turnaround time for their institution.

Key to Symbols

↑ = increase
↓ = decrease
↔ = no substantial change

Key: 14-OH = active metabolite of clarithromycin; AUC = area under the curve; C_{min} = minimum concentration; C_{ss} = concentration at steady state; des-Rbt = desacetyl rifabutin; DHA = dihydroartemisinin; DRV/r = darunavir/ritonavir; EFV = efavirenz; EVG/c = elvitegravir/cobicistat; FDA = U.S. Food and Drug Administration; FTC = emtricitabine; HBV = hepatitis B virus; RPV = rilpivirine; SOF = sofosbuvir; $t_{1/2}$ = half-life; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TDM = therapeutic drug monitoring; TFV= tenofovir; TFV-DP = tenofovir diphosphate; VEL = velpatasvir; VOX = voxilaprevir

↓ = decrease
↔ = no substantial change

Table 5. Serious and/or Common Adverse Reactions Associated with Systemically Administered Drugs Used to Treat or Prevent Opportunistic Infections

Updated: September 25, 2023
Reviewed: January 10, 2024

This table should not be considered a comprehensive list of all possible adverse reactions to each medication. For additional information, clinicians should consult other appropriate resources, such as the U.S. Food and Drug Administration prescribing information. For persons of childbearing potential, please refer to Table 7. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy for information regarding adverse effect potential of these medications during pregnancy.

Drug(s)	Adverse Reactions
Acyclovir	• Crystalluria and nephrotoxicity secondary to obstructive urolithiasis, particularly after rapid high-dose IV infusion. Risk is increased with dehydration or pre-existing renal impairment. o Administer IV fluid hydration to reduce the risk for nephrotoxicity. • Neurotoxicity with high doses (agitation, confusion, hallucination, seizure, coma), especially in patients with renal impairment and/or older patients • Thrombophlebitis at peripheral IV infusion site • Nausea, vomiting, and headache
Adefovir	• Nephrotoxicity, especially in patients with underlying renal insufficiency, predisposing comorbidities, or taking concomitant nephrotoxic drugs • Nausea and asthenia
Albendazole	• Hepatotoxicity • Reversible alopecia • Nausea, vomiting, headache, and dizziness • Bone marrow suppression (i.e., pancytopenia, aplastic anemia, agranulocytosis, and leukopenia) (rare) o Patients with liver disease, including hepatic echinococcosis, appear to be at higher risk.
Amikacin	• Nephrotoxicity o Administer IV fluid hydration to reduce the risk for nephrotoxicity. • Ototoxicity, both hearing loss and vestibular toxicity, are possible. • Neuromuscular blockade, especially with myasthenia or Parkinson's disease and rapid infusion of large doses (rare)
Amphotericin B Deoxycholate **and Lipid Formulations**	• Nephrotoxicity (lower incidence with liposomal formulations) o Administer IV fluid hydration to reduce the risk for nephrotoxicity. • Hypokalemia, hypomagnesemia, and hypocalcemia

Table 5. Serious and/or Common Adverse Reactions Associated with Systemically Administered Drugs Used to Treat or Prevent Opportunistic Infections

Drug(s)	Adverse Reactions
	• Infusion-related reactions, including fever, chills, rigors, flank or back pain, and hypotension (lower incidence with liposomal formulations) • Thrombophlebitis • Transaminase and bilirubin elevations • Headache, nausea, vomiting, and diarrhea • Heart failure (rarely reported) • Anemia (rare)
Anidulafungin	• Refer to the row on Echinocandins.
Artemether/Lumefantrine	• QTc prolongation • Fever, chills, fatigue, arthralgia, and myalgia • Headache, dizziness, asthenia, and insomnia • Nausea, vomiting, diarrhea, abdominal pain, and anorexia • Rash and pruritus • Delayed hemolytic anemia (rare)
Artesunate	• Acute renal failure requiring dialysis • Hemoglobinuria and jaundice • Post-treatment hemolysis that may require transfusion • QTc prolongation and bradycardia • Hypersensitivity reactions (anaphylaxis) • Dizziness, nausea, and vomiting
Atovaquone	• Hepatotoxicity • Rash, nausea, vomiting, and diarrhea • Fever, headache, and insomnia
Atovaquone/Proguanil	• Abdominal pain, nausea, vomiting, anorexia, diarrhea, headache, asthenia, dizziness, and rash • Reversible transaminase elevations
Azithromycin	• Ototoxicity with prolonged use • Hepatotoxicity • Hypersensitivity reactions • Nausea, vomiting, diarrhea, and abdominal pain • QTc prolongation
Benznidazole	• Photosensitivity and hypersensitivity reactions (including allergic dermatitis, TEN, and DRESS)

Table 5. Serious and/or Common Adverse Reactions Associated with Systemically Administered Drugs Used to Treat or Prevent Opportunistic Infections

Drug(s)	Adverse Reactions
	• Paresthesia and peripheral neuropathy, headache, and insomnia • Bone marrow suppression • Embryo-fetal toxicity • Nausea, vomiting, abdominal pain, anorexia, and weight loss
Bedaquiline	• QTc prolongation • Hepatotoxicity • Nausea, vomiting, anorexia, diarrhea, elevated amylase, arthralgia, headache, and skin rash
Bezlotoxumab	• Exacerbation of congestive heart failure • Nausea, pyrexia, and headache
Brincidofovir	• Elevations in hepatic transaminases and bilirubin • Nausea, vomiting, and diarrhea • Embryo-fetal toxicity, male infertility
Caspofungin	• Refer to the row on Echinocandins.
Chloroquine and Hydroxychloroquine	• Auditory and visual disturbances, including blurry vision. Retinal toxicity may occur with long-term use. • QTc prolongation • Cardiomyopathy • Bone marrow suppression and hemolysis • Neuropsychiatric changes, including extrapyramidal reactions, suicidal behavior, and convulsive seizures • Hypersensitivity reactions (including TEN, SJS, and EM) • Severe hypoglycemia which may require adjustment of antidiabetic medications • Photosensitivity, pruritus, skin pigmentation, and exacerbation of psoriasis • Headache, nausea, vomiting, diarrhea, anorexia, abdominal pain, and hepatitis • Neuromyopathy (may occur with long-term use) (rare)
Cidofovir	• Nephrotoxicity, proteinuria, azotemia, proximal tubular dysfunction (normoglycemic glycosuria, hypophosphatemia), and metabolic acidosis (including Fanconi's syndrome) o Administer IV fluid hydration and oral probenecid to reduce the risk for nephrotoxicity. • Neutropenia and anemia • Ocular hypotony and anterior uveitis/iritis • Possibly carcinogenic and teratogenic; may cause hypospermia

Table 5. Serious and/or Common Adverse Reactions Associated with Systemically Administered Drugs Used to Treat or Prevent Opportunistic Infections

Drug(s)	Adverse Reactions
	• Gastrointestinal intolerance and diarrhea • Asthenia, fever, headache, and alopecia • Side effects most likely related to co-administration with probenecid are rash, nausea, vomiting, anorexia, and gout exacerbation.
Ciprofloxacin	• Refer to the row on Fluoroquinolones.
Clarithromycin	• Hepatotoxicity • Ototoxicity, including reversible hearing loss and tinnitus, with high doses or prolonged use • QTc prolongation • Increased risk of cardiac complications or death in patients with heart disease • Diarrhea • Headache, nausea, vomiting, diarrhea, abdominal cramps, and dysgeusia
Clindamycin	• Diarrhea, including *C. difficile*–associated diarrhea and colitis • Metallic taste (with IV infusion), thrombophlebitis, and arrhythmia with rapid IV infusion • Hypersensitivity reactions (including SJS and TEN) • Nausea, vomiting, abdominal pain, and abnormal liver function tests
Clotrimazole (Troche)	• Nausea, vomiting, anorexia, and metallic taste
Cycloserine	• Neuropsychiatric toxicities, including convulsions, psychosis, somnolence, confusion, inability to concentrate, hyperreflexia, headache, tremor, vertigo, paresis, dysarthria, depression (with suicidal ideation), peripheral neuropathy, and seizures (particularly with higher doses and in patients with history of chronic alcoholism) o Administer with pyridoxine. • Hypersensitivity reactions (including SJS), allergic dermatitis, and rash
Dapsone	• Methemoglobinemia, hemolytic anemia, neutropenia, and agranulocytosis o Do not use in patients with moderate to severe G6PD deficiency. • Sulfone syndrome (fever, exfoliative dermatitis, lymphadenopathy, hepatic necrosis, and hemolysis) • Phototoxicity and severe cutaneous reactions (including SJS and TEN) • Drug-induced lupus erythematosus • Hepatotoxicity and nephrotic syndrome • Peripheral neuropathy • Nausea and anorexia
Doxycycline	• Pill-induced esophagitis/esophageal ulceration • Intracranial hypertension

Table 5. Serious and/or Common Adverse Reactions Associated with Systemically Administered Drugs Used to Treat or Prevent Opportunistic Infections

Drug(s)	Adverse Reactions
	• Photosensitivity and skin hyperpigmentation • Thrombophlebitis (with IV infusion) • Nausea and vomiting
Echinocandins (Anidulafungin, Caspofungin, Micafungin)	• Histamine-related infusion reactions (flushing, rash, pruritus, hypotension, and dyspnea) and thrombophlebitis • Hypersensitivity reactions (including anaphylaxis and anaphylactoid reaction) • Abnormal liver enzymes and hepatotoxicity • Hypokalemia • Embryo-fetal toxicity • Diarrhea, nausea, vomiting, fever, and headache • Hemolysis (micafungin) (rare)
Emtricitabine	• Headache, nausea, and diarrhea • Skin hyperpigmentation and rash (palms and soles)
Entecavir	• Headache, fatigue, dizziness, and nausea
Ethambutol	• Optic neuritis (dose- and duration-dependent) and peripheral neuropathy • Headache, nausea, vomiting, anorexia, abdominal pain, and hyperuricemia/gout flare
Ethionamide	• Postural hypotension, hepatotoxicity, hypothyroidism (with or without goiter), and hypoglycemia • Dizziness, drowsiness, confusion, clumsiness, visual disturbances, and depression o Administer with pyridoxine. • Dose-dependent gastrointestinal side effects, including nausea, vomiting, anorexia, diarrhea, abdominal pain, and metallic taste • Photosensitivity and severe cutaneous reactions (including SJS, TEN, and DRESS) • Gynecomastia, acne, hair loss, and impotence
Famciclovir	• Nephrotoxicity (in patients with underlying renal disease) • Headache, nausea, vomiting, and diarrhea
Fidaxomicin	• Nausea, vomiting, and abdominal pain
Flucytosine	• Concentration-dependent (>100 mcg/mL) bone marrow suppression (anemia, neutropenia, agranulocytosis, and thrombocytopenia) • Hepatotoxicity • Diarrhea, nausea, vomiting, and headache • Rash, pruritus, and photosensitivity
Fluconazole	• Hepatotoxicity, nausea, vomiting, diarrhea, and abdominal pain

Table 5. Serious and/or Common Adverse Reactions Associated with Systemically Administered Drugs Used to Treat or Prevent Opportunistic Infections

Drug(s)	Adverse Reactions
	• QTc prolongation • Reversible alopecia (with doses ≥400 mg/day for >2 months)
Fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin)	• Restlessness, insomnia, nightmares, confusion, anxiety, paranoia, tremors, seizure, hallucinations, depression, suicidal thoughts, and attempted and completed suicide • Tendonitis and tendon rupture (associated with age over 60, concurrent corticosteroids, diabetes, and kidney, heart, and lung transplant) • Diarrhea including *C. difficile*–associated diarrhea and colitis • QTc prolongation • Photosensitivity/phototoxicity • Anemia, thrombocytopenia, and leukopenia • Arthralgia and myalgia • Peripheral neuropathy and retinal detachment • Hyper- and hypoglycemia, including hypoglycemic coma • Nausea, diarrhea, bloating, headache, dizziness, and malaise • Vasculitis • Aortic dissection (rare) • Transaminase elevations and interstitial nephritis (rare) • Severe cutaneous reactions (including SJS and TEN) (rare)
Foscarnet	• Nephrotoxicity and electrolyte imbalances (e.g., hypocalcemia, hypomagnesemia, hypophosphatemia, hyperphosphatemia, hypokalemia) o Administer IV fluid hydration to reduce the risk for nephrotoxicity. • Paresthesia and seizure (associated with electrolyte imbalances) • Anemia • Nausea, vomiting, anorexia, and headache • Genital ulceration • Thrombophlebitis
Ganciclovir	• Neutropenia, thrombocytopenia, anemia, and pancytopenia • Carcinogenic and teratogenic potential and impaired fertility • Nephrotoxicity • Neuropathy • Thrombophlebitis
Glecaprevir/Pibrentasvir	• Risk of hepatitis B virus reactivation • Hepatic decompensation/failure in patients with advanced liver disease • Mild headache, fatigue, nausea, and diarrhea

Table 5. Serious and/or Common Adverse Reactions Associated with Systemically Administered Drugs Used to Treat or Prevent Opportunistic Infections

Drug(s)	Adverse Reactions
	• Altered glucose tolerance in diabetic patients
Interferon-Alfa and Peginterferon-Alfa	• Neuropsychiatric effects (e.g., depression, suicidal ideation) • Neutropenia, anemia, and thrombocytopenia • Flu-like syndrome (e.g., fever, headache, fatigue, myalgia) • Hepatitis exacerbations, thyroid dysfunction, and alopecia • Nausea, anorexia, diarrhea, and weight loss • Development or exacerbation of autoimmune diseases and ocular effects (e.g., retinal hemorrhage, retinal artery or vein obstructions, and cotton wool spots) • Ischemic and hemorrhagic cerebrovascular events, cardiovascular and pulmonary effects, hyper- and hypoglycemia, diabetes, severe infection, and colitis • Hypersensitivity reactions
Isavuconazonium Sulfate (Isavuconazole)	• Hepatotoxicity and cholelithiasis • Infusion-related reactions (hypotension, dyspnea, chills, dizziness, paresthesia, and hypoesthesia) • Hypersensitivity reactions (including SJS) • Embryo-fetal toxicity • Shortening of QT interval • Nausea, vomiting, diarrhea, headache, hypokalemia, dyspnea, and cough
Isoniazid	• Hepatotoxicity and asymptomatic elevation in aminotransferase enzymes • Peripheral neuropathy, paresthesia, seizures, and optic neuritis o Administer with pyridoxine • Nausea, diarrhea, and flushing • Arthralgia and lupus-like syndrome • Psychosis (rare) • Hypersensitivity reactions (including TEN and DRESS) (rare)
Itraconazole	• Congestive heart failure, edema, and hypokalemia • QTc prolongation • Hepatotoxicity • Hearing loss • Neuropathy • Gynecomastia • Nausea, vomiting, diarrhea, and abdominal pain
Lamivudine	• Nausea and vomiting

Table 5. Serious and/or Common Adverse Reactions Associated with Systemically Administered Drugs Used to Treat or Prevent Opportunistic Infections

Drug(s)	Adverse Reactions
Levofloxacin	• Refer to the row on Fluoroquinolones.
Linezolid	• Anemia, neutropenia, and thrombocytopenia (especially with treatment lasting longer than 2–4 weeks and renal insufficiency) • Peripheral neuropathy and optic neuritis with long-term therapy • Nausea, vomiting, diarrhea, and headache • Serotonin syndrome (rare) • Seizure (in patients with a history of seizure or with risk factors for seizure) (rare) • Lactic acidosis, hypoglycemia, and hyponatremia (rare)
Mefloquine	• Depression, psychosis, anxiety, agitation, dizziness, headache, insomnia, and abnormal dreams • QTc prolongation and arrhythmias (extrasystole and sinus bradycardia) • Agranulocytosis and aplastic anemia • Nausea, vomiting, diarrhea, and epigastric pain
Micafungin	• Refer to the row on Echinocandins.
Miconazole Buccal Tablets	• Dysgeusia, diarrhea, nausea, vomiting, upper abdominal pain, and headache • Local reactions (e.g., oral discomfort, burning, pain, tongue/mouth ulceration, gingival pruritus, swelling, and dry mouth) • Hypersensitivity reaction (may occur in patients with known hypersensitivity reaction to milk product concentrate)
Miltefosine	• Nephrotoxicity and elevated transaminases and bilirubin • Retinal degeneration • Leukocytosis and thrombocytopenia • Embryo-fetal toxicity and impaired fertility, scrotal pain, and impaired ejaculation • Nausea, vomiting, diarrhea, anorexia, headache, and motion sickness • Severe cutaneous reactions (including SJS)
Moxifloxacin	• Refer to the row on Fluoroquinolones.
Nifurtimox	• Patients with a history of brain injury, seizures, psychiatric disease, and serious behavioral alterations may experience worsening of their conditions. • Vomiting, abdominal pain, headache, decreased appetite, weight loss, nausea, pyrexia, rash, polyneuropathy, insomnia, dizziness, and vertigo • Carcinogenic and teratogenic potential and impaired fertility • Hypersensitivity reactions with hypotension, angioedema, dyspnea, pruritus, rash or other severe skin reactions
Nitazoxanide	• Nausea, vomiting, diarrhea, abdominal pain, headache, and chromaturia

Table 5. Serious and/or Common Adverse Reactions Associated with Systemically Administered Drugs Used to Treat or Prevent Opportunistic Infections

Drug(s)	Adverse Reactions
Nystatin (Oral Preparations)	• Unpleasant taste, nausea, vomiting, anorexia, and diarrhea
Paromomycin	• Nausea, vomiting, abdominal cramps, anorexia, rash, and headache • Nephrotoxicity (rare) o Inflammatory bowel disease and renal insufficiency may increase risk.
Penicillin G	All Penicillin G Preparations • Hypersensitivity (immediate or delayed reactions, including anaphylaxis), bone marrow suppression, nausea, vomiting, diarrhea, and drug fever • Jarisch-Herxheimer reaction when used for syphilis (occurs most frequently in persons with early syphilis, high non-treponemal antibody titers, and prior penicillin treatment) Benzathine Penicillin G • IM injection-site reactions (pain and erythema), procaine neuropsychiatric reactions (with high dose), and 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—and hyperkalemia or hypernatremia at high doses (depending on formulation)
Pentamidine	• Nephrotoxicity, infusion-related hypotension, and thrombophlebitis • QTc prolongation, arrhythmias (including Torsades de pointes), and electrolyte abnormalities • Hypoglycemia, hyperglycemia, and diabetes mellitus • Hepatotoxicity and GI intolerance • Leukopenia and thrombocytopenia • Embryotoxic • Rash • Pancreatitis (rare) Aerosolized Therapy • Bronchospasm, cough, dyspnea, tachypnea, and metallic taste
Posaconazole	• Hepatotoxicity, QTc prolongation, and hypokalemia • Pseudohyperaldosteronism (hypokalemia and hypertension) • Nausea, vomiting, diarrhea, abdominal pain, and headache IV Infusion • Thrombophlebitis, SBECD accumulation, and worsening renal function with IV formulation (especially in patients with eGFR <50 mL/min per package labeling, but observational studies with IV voriconazole suggest that this may not be a concern)

Table 5. Serious and/or Common Adverse Reactions Associated with Systemically Administered Drugs Used to Treat or Prevent Opportunistic Infections

Drug(s)	Adverse Reactions
Primaquine	• Methemoglobinemia, hemolytic anemia (use with caution in patients with mild-moderate G6PD deficiency; do not use if severe G6PD deficiency), leukopenia, and neutropenia • QTc prolongation • Abdominal cramps, nausea, vomiting, and dizziness
Pyrazinamide	• Hepatotoxicity • Polyarthralgia and myalgia • Hyperuricemia/gout flare • Thrombocytopenia and sideroblastic anemia • Nausea, vomiting, flushing, rash, and photosensitivity
Pyrimethamine	• Neutropenia, thrombocytopenia, and megaloblastic anemia o Administer with leucovorin. • Anorexia, vomiting, and rash
Quinine	• QTc prolongation and cardiac arrythmias • Cinchonism (tinnitus, vertigo, and blurred vision) • Hemolytic anemia (especially in patients with G6PD deficiency), thrombocytopenia, and agranulocytosis • Vision abnormalities (e.g., photophobia, altered color perception, and blindness) • Hypersensitivity reactions (including SJS and TEN) • Hypoglycemia • Headache, nausea, vomiting, and diarrhea
Rifabutin	• Uveitis (concentration-dependent) • Neutropenia and thrombocytopenia • Arthralgia • Hepatotoxicity • Rash • Nausea, vomiting, abdominal pain, diarrhea, and anorexia • Red-orange discoloration of body fluids
Rifampin	• Hepatotoxicity (cholestatic hepatitis) • Thrombocytopenia and hemolytic anemia • Renal failure • Hypersensitivity reactions with flu-like syndrome • Interstitial pulmonary disease

Table 5. Serious and/or Common Adverse Reactions Associated with Systemically Administered Drugs Used to Treat or Prevent Opportunistic Infections

Drug(s)	Adverse Reactions
	• Nausea, vomiting, anorexia, abdominal pain, flatulence, diarrhea, headache, confusion, and flushing, rash • Red-orange discoloration of body fluids
Rifapentine	• Hepatotoxicity • Anemia, neutropenia, and lymphopenia • Hypersensitivity reactions • Arthralgia • Rash and pruritis • Nausea, vomiting, diarrhea, and anorexia • Red-orange discoloration of body fluids
Sofosbuvir/Velpatasvir	• Risk of hepatitis B virus reactivation • Headache, fatigue, and anemia (associated with ribavirin co-administration) • Altered glucose tolerance in diabetic patients
Streptomycin	• Neurotoxicity including irreversible ototoxicity (both hearing loss and vestibular toxicity) • Nephrotoxicity • Neuromuscular blockade and respiratory paralysis (associated with rapid infusion of large aminoglycoside doses)
Sulfadiazine	• Severe cutaneous reactions (including SJS, EM, and TEN) and photosensitivity • Anemia, neutropenia, agranulocytosis, and thrombocytopenia • Crystalluria (nephrolithiasis, urolithiasis) and nephrotoxicity • Hepatotoxicity • Drug fever • Peripheral neuritis, tinnitus, vertigo, and insomnia • Nausea, vomiting, and headache
Tafenoquine	• Decreased hemoglobin and methemoglobinemia and hemolytic anemia o Do not use in patients with G6PD deficiency; may cause harm to fetuses and breastfeeding infants who are G6PD deficient. • Psychiatric adverse reactions (in patients with history of psychiatric illness) • Hypersensitivity reactions (angioedema and urticaria) • Visual disturbances • Dizziness, nausea, vomiting, and headache
Tecovirimat	• Headache, nausea, abdominal pain, and vomiting IV formulation

Table 5. Serious and/or Common Adverse Reactions Associated with Systemically Administered Drugs Used to Treat or Prevent Opportunistic Infections

Drug(s)	Adverse Reactions
	• Infusion site pain, swelling, erythema, and extravasation • Contains hydroxypropyl-β-cyclodextrin, which may accumulate in patients with renal impairment and has the potential to cause renal toxicity
Tenofovir disoproxil fumarate	• Renal insufficiency and Fanconi syndrome (proximal renal tubulopathy with hypophosphatemia, hypouricemia, proteinuria, and normoglycemic glycosuria) • Decrease in bone mineral density • Nausea and vomiting
Tenofovir alafenamide	• Headache, abdominal pain, fatigue, and nausea • Lower incidence of renal or bone toxicities than with tenofovir disoproxil fumarate
Trimethoprim-Sulfamethoxazole	• Cutaneous reactions (in some cases SJS, EM, and TEN) and photosensitivity • Anemia, neutropenia, agranulocytosis, and thrombocytopenia • Hepatotoxicity • Dose-dependent increase in serum creatinine (without change in GFR), interstitial nephritis, crystalluria (in patients with inadequate hydration), and hyperkalemia (with high-dose TMP) • Hypoglycemia and hyponatremia • Drug fever • Nausea and vomiting • Aseptic meningitis and pancreatitis (rare)
Valacyclovir	• Neurotoxicity (e.g., agitation, confusion, hallucination, seizure, coma) with high doses, especially in patients with renal impairment • Nephrotoxicity • Nausea, vomiting, abdominal pain, and headache
Valganciclovir	• Bone marrow suppression • Confusion, pyrexia, and tremor • Nephrotoxicity • Carcinogenic and teratogenic potential and impaired fertility • Nausea, vomiting, and diarrhea
Voriconazole	• Visual disturbances (e.g., abnormal vision, color vision change, and/or photophobia) • Optic neuritis (associated with >28 days treatment) • Headache, delirium, hallucination, peripheral neuropathy (rare), and encephalopathy (associated with trough >5.5 mcg/mL) • Hepatotoxicity • QTc prolongation

Table 5. Serious and/or Common Adverse Reactions Associated with Systemically Administered Drugs Used to Treat or Prevent Opportunistic Infections

Drug(s)	Adverse Reactions
	• Photosensitivity • Voriconazole-associated cutaneous squamous cell carcinoma (with long-term use) • Fluorosis and periostitis with high dose and/or prolonged use • Fever, nausea, vomiting, chills, tachycardia, and peripheral edema • Embryo-fetal toxicity • Nail changes and alopecia (with long-term use) • SBECD accumulation with IV formulation and worsening renal function (especially in patients with eGFR <50 mL/min per package labeling, but observational studies suggest that this may not be a concern)

Key: DRESS = drug reaction with eosinophilia and systemic symptoms; eGFR = estimated glomerular filtration rate; EM = erythema multiforme; G6PD = glucose-6-phosphate dehydrogenase; GFR = glomerular filtration rate; GI = gastrointestinal; IM = intramuscular; IV = intravenous; QTc = QT corrected for heart rate; SBECD = sulfobutylether cyclodextrin; SJS = Stevens-Johnson syndrome; TEN = toxic epidermal necrolysis; TMP = trimethoprim

Table 6. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections that Require Dosage Adjustment in Patients with Renal Insufficiency

Updated: September 25, 2023
Reviewed: January 10, 2024

When renally cleared drugs are administered to patients with reduced renal function, drug accumulation leading to supratherapeutic concentrations and drug toxicities is a primary concern. However, clearance is only one of the pharmacokinetic parameters that affect a drug's disposition. The volume of distribution of a drug also can be altered in patients with reduced renal function. Furthermore, some patients with HIV or diabetes mellitus can have reduced oral absorption of certain drugs. Therefore, although a drug may require a dose reduction in renal failure based on reduced clearance (i.e., increased concentrations), other factors—such as an increased volume of distribution or reduced oral absorption—may decrease concentrations.

Therapeutic drug monitoring (TDM), if available and appropriate, may facilitate dose adjustments in these complicated patients. TDM allows the clinician to make informed, individualized decisions about dose adjustments that are more precise than standardized dose adjustments based on estimated creatinine clearance. Drugs that are marked with an asterisk (*) in the table below are known to have assays (for clinical and/or research purposes) available within the United States and typically in Europe as well. When TDM is appropriate, clinicians should contact their clinical laboratory to determine assay availability and turnaround time for their institution.

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		CrCl^ or eGFR# (mL/min)	Dose
Acyclovir*	IV Dose *Serious HSV* • 5 mg/kg IV every 8 hours *VZV Infections or HSV encephalitis* • 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 days of dialysis.
	PO Dose for Herpes Zoster: 800 mg PO five times per 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 days 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

Table 6. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections that Require Dosage Adjustment in Patients with Renal Insufficiency

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		CrCl^ or eGFR# **(mL/min)**	Dose
		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.	15 mg/kg two to three times per week Perform TDM to adjust dose, with target peak concentration 35–45 mcg/mL and trough concentration <4 mcg/mL. Administer dose after HD on days of dialysis.
Amphotericin B*	3–6 mg/kg IV per day (lipid formulation) or 0.7–1.0 mg/kg IV per day (amphotericin B deoxycholate)	N/A	No dosage adjustment necessary; consider alternative antifungals if renal insufficiency occurs during therapy despite adequate hydration.
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 unless benefits outweigh risks. See "Pharmacokinetics of cidofovir in renal insufficiency and in continuous ambulatory peritoneal dialysis or high-flux hemodialysis" for recommendations on renal dose adjustments.
		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.
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

Table 6. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections that Require Dosage Adjustment in Patients with Renal Insufficiency

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency		
		CrCl^ or eGFR# **(mL/min)**	Dose	
			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 days of dialysis.	
Clarithromycin*	500 mg PO every 12 hours	30–60	Usual dose unless 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. Target peak concentration 20–35 mcg/mL	30–80	Usual dose; consider TDM and monitor for toxicities.	
		<30 (not on HD) or HD	250 mg once daily or 500 mg three times per week Perform TDM and adjust dose accordingly. Monitor for toxicities. Use with caution in patients with ESRD who are not on dialysis.	
Emtricitabine*[a] (FTC)	One 200-mg capsule PO once daily *or* 240-mg solution PO once daily	CrCl^ or eGFR# **(mL/min)**	Oral Capsules	Oral Solution
		15–29	200 mg every 72 hours	80 mg every 24 hours
		<15 and not on HD	200 mg every 96 hours	60 mg every 24 hours
		HD (administer dose after HD on days of dialysis)	200 mg every 24 hours	240 mg every 24 hours

Table 6. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections that Require Dosage Adjustment in Patients with Renal Insufficiency

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency		
		CrCl^ or eGFR# **(mL/min)**	Dose	
Emtricitabine*/ Tenofovir* Alafenamide (FTC/TAF) (FDC Trade Name: Descovy) Note: Please refer to product labels for dosing recommendations for other ARV FDC products containing FTC/TAF.	One tablet (FTC 200 mg/TAF 25 mg) PO once daily	<30 and not on HD	Coformulated tablet is not recommended.	
		HD	One tablet daily. Administer dose after HD on days of dialysis.	
Emtricitabine*/ Tenofovir* Disoproxil Fumarate (FTC/TDF) (FDC Trade Name: Truvada) Note: Please refer to product labels for dosing recommendations for other ARV FDC products containing FTC/TDF.	One (FTC 200 mg/TDF 300 mg) tablet PO daily	30–49	One tablet PO every 48 hours (monitor for worsening renal function or consider switching to TAF)	
		<30 or HD	Do not use coformulated tablet. 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	CrCl^ or eGFR# **(mL/min)**	Usual Renal Dose Adjustment	3TC-Refractory or **Decompensated Liver** Disease
		30 to <50	• 0.25 mg PO every 24 hours, *or* • 0.5 mg PO every 48 hours	• 0.5 mg PO every 24 hours, *or* • 1 mg PO every 48 hours
		10 to <30	• 0.15 mg PO every 24 hours, *or* • 0.5 mg PO every 72 hours	• 0.3 mg PO every 24 hours, *or* • 1 mg PO every 72 hours

Table 6. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections that Require Dosage Adjustment in Patients with Renal Insufficiency

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency		
		CrCl^ or eGFR# (mL/min)	Dose	
		<10 or HD or CAPD (administer after HD on days of dialysis)	• 0.05 mg PO every 24 hours, *or* • 0.5 mg PO once every 7 days	• 0.1 mg PO every 24 hours, *or* • 1 mg PO once every 7 days
Ethambutol*	For MAI: 15 mg/kg PO daily For MTB: 15–25 mg/kg PO daily (See the Dosing Recommendations table in the *Mycobacterium tuberculosis* section for additional MTB dosing recommendations.)	<30 or HD	Usual dose PO three times weekly (in patients on HD, give dose after dialysis).	
		PD	Do not use in patients on PD. Consider alternative MAI or MTB treatment (e.g., moxifloxacin). Perform 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 Consider TDM.	
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	
Fluconazole*	200–1,200 mg PO or IV every 24 hours (dose and route of administration depends on type of OI)	≤50	Administer 100% of the indication-specific initial dose, then adjust maintenance doses to 50% of dose every 24 hours.	
		HD	Administer 100% of the indication-specific initial dose, then adjust maintenance doses to full dose three times per week after HD.	
Flucytosine*	25 mg/kg PO every 6 hours TDM is recommended for patients to guide optimal dosing (target peak serum concentration 2 hours after dose: 25-100 mcg/mL). If TDM is not possible,	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.	

Table 6. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections that Require Dosage Adjustment in Patients with Renal Insufficiency

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		CrCl^ or eGFR# **(mL/min)**	Dose
	monitor CBC twice weekly.		
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.
	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.
Lamivudine[b] (3TC)	300 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 days of dialysis.
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	One (3TC 300 mg/TDF 300 mg) tablet PO every 24 hours	<50	Coformulated tablet is not recommended.

Table 6. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections that Require Dosage Adjustment in Patients with Renal Insufficiency

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency		
		CrCl^ or eGFR# **(mL/min)**	Dose	
products containing 3TC/TDF.				
Levofloxacin*	500 mg (low dose) or 750–1,000 mg (high dose) IV or PO daily	CrCl^ or eGFR# **(mL/min)**	**Low Dose**	High Dose
		20–49	500 mg once, then 250 mg every 24 hours, IV or PO	750 mg every 48 hours IV or PO
		<20 or CAPD or HD (administer dose after HD on days of dialysis)	500 mg once, then 250 mg every 48 hours, IV or PO Dose can be adjusted based on serum concentrations.	750 mg once, then 500 mg every 48 hours, IV or PO
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 May reduce to 90 mcg once weekly if severe adverse effects or laboratory abnormalities occur.	
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 4–6 hours, *or* 8 million units as continuous infusion	
Pentamidine	4 mg/kg IV every 24 hours May reduce dose to 3 mg/kg IV daily in the event of toxicities	<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	<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. Perform posaconazole TDM (target trough	

Table 6. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections that Require Dosage Adjustment in Patients with Renal Insufficiency

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		CrCl^ or eGFR# **(mL/min)**	Dose
	Oral Suspension: 400 mg PO twice daily		concentration at least >1.25 mcg/mL for treatment). IV posaconazole is not recommended by the manufacturer because of potential toxicity due to accumulation of SBCD (vehicle of IV product). However, an observational study did not find worsening in renal function in patients with CrCl <50 ml/min given SBCD. Switch patients with CrCl <50 mL/min to oral posaconazole when feasible.
Pyrazinamide*	See the *Mycobacterium tuberculosis* section for weight-based dosing guidelines.	<30 or HD	25–35 mg/kg/dose three times per week; administer dose after HD.
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
Rifabutin*	5 mg/kg PO daily (usually 300 mg PO daily) See the *Mycobacterium tuberculosis* section and Drug–Drug Interactions in the Adult and Adolescent Antiretroviral Guidelines for dosage adjustment based on interactions with ARVs.	<30	If toxicity is suspected, consider 50% of dose once daily and perform rifabutin TDM.
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.	TDM is no longer available. Consider an alternative aminoglycoside, as clinically appropriate. If used: 15 mg/kg two to three times weekly. Administer dose after HD.
Sulfadiazine	1,000–1,500 mg PO every 6 hours (1,500 mg every 6 hours for patients >60 kg)	≤ 50	No data. Use alternative anti-toxoplasma therapy.
Tecovirimat	IV: *35 to <120 kg*: 200 mg	30–89	No dosage adjustment necessary Use with caution due to potential accumulation of

Table 6. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections that Require Dosage Adjustment in Patients with Renal Insufficiency

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		CrCl^ or eGFR# **(mL/min)**	Dose
	every 12 hours ≥*120 kg:* 300 mg every 12 hours		hydroxypropyl-β-cyclodextrin.
		<30	Contraindicated due to potential accumulation of hydroxypropyl-β-cyclodextrin. Note: IV formulation may be considered in patients with CrCl <30 only if drug absorption via enteral administration is expected to be problematic based on an individual risk-benefit assessment in consultation with CDC. In these circumstances, use with caution and monitor renal function continuously. Switch to the oral formulation as soon as possible.
	PO: *40 to <120 kg:* 600 mg every 12 hours ≥*120 kg:* 600 mg every 8 hours	Any eGFR	No dosage adjustment necessary
Tenofovir* Alafenamide (TAF) Note: Please refer to product labels for dosing recommendations for other ARV FDC products containing FTC/TAF.	25 mg PO daily	<15	Not recommended
		<15 on HD	No dosage adjustment required. Administer dose after HD on days of dialysis.
Tenofovir* Disoproxil Fumarate (TDF) Note: Please refer to product labels for dosing recommendations for other ARV FDC products containing 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
Trimethoprim* / Sulfamethoxazole (TMP-SMX)	For PCP Treatment • 5 mg/kg (of TMP component) IV every 6–8 hours, *or*	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)

Table 6. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections that Require Dosage Adjustment in Patients with Renal Insufficiency

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		CrCl^ or eGFR# (mL/min)	Dose
	• Two TMP-SMX DS tablets PO every 8 hours	HD	5 mg/kg/day (TMP) IV, or two TMP-SMX DS tablets PO daily; administer dose after HD on days of dialysis. 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% (e.g., 1 SS tablet PO daily).
		<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
	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; administer dose after HD on days of dialysis.
	For Herpes Simplex Virus Treatment: 1 g PO twice daily	30–49	No dosage adjustment
		10–29	For Treatment: 1 g PO every 24 hours For Suppressive Therapy: 500 mg PO every 24

Table 6. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections that Require Dosage Adjustment in Patients with Renal Insufficiency

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency		
		CrCl^ or eGFR# **(mL/min)**	Dose	
	For Herpes Simplex Chronic Suppressive Therapy: 500 mg PO twice daily		hours	
		<10	500 mg PO every 24 hours	
		HD	500 mg PO every 24 hours; administer dose after HD on days of dialysis.	
Valganciclovir	Induction Therapy: 900 mg PO twice daily Maintenance Therapy: 900 mg PO once daily	CrCl^ or eGFR# **(mL/min)**	Induction	Maintenance
		40–59	450 mg PO twice daily	450 mg PO daily
		26–39	450 mg PO daily	450 mg PO every 48 hours
		10–25	450 mg PO every 48 hours	450 mg PO twice weekly
		<10 and not on dialysis	Not recommended Use IV ganciclovir. May consider: • 200 mg (oral powder for solution) PO three times per week If oral powder formulation is not available, consider: • 450 mg (tablet) PO three times weekly	Not recommended Use IV ganciclovir. May consider: • 100 mg (oral powder for solution) PO three times per week If oral powder formulation is not available, consider: • 450 mg (tablet) PO twice weekly
		HD	Not recommended Use IV ganciclovir. May consider: • 200 mg (oral powder for solution) PO three times per week after HD If oral powder formulation is not available, may consider: • 450 mg (tablet) PO three times per week after HD	Not recommended Use IV ganciclovir. May consider: • 100 mg (oral powder for solution) PO three times per week after HD If oral powder formulation is not available, may consider: • 450 mg (tablet) PO twice per week after HD
Voriconazole*	6 mg/kg IV every 12 hours for two doses, then 4 mg/kg	<50	IV voriconazole is not recommended by the manufacturer because of potential toxicity due to	

Table 6. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections that Require Dosage Adjustment in Patients with Renal Insufficiency

Drug(s)	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		CrCl^ or eGFR[#] **(mL/min)**	Dose
	IV every 12 hours *or* 200–300 mg PO every 12 hours		accumulation of SBCD (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. Perform TDM to adjust dose.

* Drugs marked with asterisk (*) are those known to have assays available (for clinical and/or research purposes) within the United States and typically in Europe. When TDM is appropriate, clinicians should contact their clinical laboratory to determine assay availability and turnaround time for their institution.

[a] The prescribing information for emtricitabine (Emtriva) recommends adjusting doses for patients with CrCl 30-49 and for patients on hemodialysis. However, the prescribing information for several FDC products that contain emtricitabine (including Descovy, Biktaryy, Genvoya, and Odefsey) recommends that the standard dose (emtricitabine 200 mg) can be given once daily in these patients (on days of hemodialysis, give after completion of dialysis). The recommendations in this table incorporate the dosing guidance from the FDC products.

[b] The prescribing information for lamivudine (Epivir) recommends dosage adjustment from 300 mg once daily to 150 mg once daily for patients with CrCl 30–49 mL/min. However, the prescribing information for several FDC products that contain lamivudine (including Epzicom, Dovato, and Triumeq) recommends no dose adjustment for CrCl 30–49 mL/min. The recommendation in this table incorporates the dosing guidance from the FDC products.

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

[#]When estimating kidney function to facilitate drug dosing in patients with renal insufficiency, please refer to the drug's prescribing information and to the National Institute of Diabetes and Digestive and Kidney Diseases' Determining Drug Dosing in Adults with Chronic Kidney Disease page for a discussion on using CrCl based on the Cockcroft-Gault equation versus eGFR.

Key: 3TC = lamivudine; ARV = antiretroviral; CAPD = continuous ambulatory peritoneal dialysis; CBC = complete blood count; CMV = cytomegalovirus; COBI = cobicistat; CrCl = creatinine clearance; DS = double strength; eGFR = estimated glomerular filtration rate; 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; PCP = *Pneumocystis* pneumonia; PD = peritoneal dialysis; PI = protease inhibitor; PO = orally; SCr = serum creatinine; SQ = subcutaneous; SBCD = sulfobutylether cyclodextrin; SS = single strength; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TDM = therapeutic drug monitoring; TMP-SMX = trimethoprim-sulfamethoxazole; VZV = varicella zoster virus

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

Updated: February 11, 2020
Reviewed: January 10, 2024

Update in Progress