



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

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Table 1. Prophylaxis to Prevent First Episode of Opportunistic Disease (page 1 of 5)

(Last updated August 3, 2017; last reviewed August 3, 2017)

Opportunistic Infections	Indication	Preferred	Alternative
<i>Pneumocystis pneumonia (PCP)</i>	<ul style="list-style-type: none"> CD4 count <200 cells/mm³ (AI), <i>or</i> CD4 <14% (BII), <i>or</i> CD4 count >200 but <250 cells/mm³ if monitoring CD4 cell count every 3 months is not possible (BII) <p>Note: Patients who are receiving pyrimethamine/sulfadiazine for treatment or suppression of toxoplasmosis do not require additional PCP prophylaxis (AII).</p>	<ul style="list-style-type: none"> TMP-SMX^a 1 double-strength (DS) PO daily (AI), <i>or</i> TMP-SMX^a 1 single-strength (SS) daily (AI) 	<ul style="list-style-type: none"> TMP-SMX^a 1 DS PO three times weekly (BI), <i>or</i> Dapsone^b 100 mg PO daily or 50 mg PO BID (BI), <i>or</i> Dapsone^b 50 mg PO daily + (pyrimethamine^c 50 mg + leucovorin 25 mg) PO weekly (BI), <i>or</i> (Dapsone^b 200 mg + pyrimethamine^c 75 mg + leucovorin 25 mg) PO weekly (BI); <i>or</i> Aerosolized pentamidine 300 mg via Respigard II™ nebulizer every month (BI), <i>or</i> Atovaquone 1500 mg PO daily (BI), <i>or</i> (Atovaquone 1500 mg + pyrimethamine^c 25 mg + leucovorin 10 mg) PO daily (CIII)
<i>Toxoplasma gondii encephalitis</i>	<ul style="list-style-type: none"> Toxoplasma IgG-positive patients with CD4 count <100 cells/μL (AII) <p>Note: All regimens recommended for primary prophylaxis against toxoplasmosis are also effective as PCP prophylaxis.</p>	TMP-SMX ^a 1 DS PO daily (AII)	<ul style="list-style-type: none"> TMP-SMX^a 1 DS PO three times weekly (BII), <i>or</i> TMP-SMX^a 1 SS PO daily (BIII), <i>or</i> Dapsone^b 50 mg PO daily + (pyrimethamine^c 50 mg + leucovorin 25 mg) PO weekly (BI), <i>or</i> (Dapsone^b 200 mg + pyrimethamine^c 75 mg + leucovorin 25 mg) PO weekly (BI); <i>or</i> Atovaquone 1500 mg PO daily (CIII); <i>or</i> (Atovaquone 1500 mg + pyrimethamine^c 25 mg + leucovorin 10 mg) PO daily (CIII)
<i>Mycobacterium tuberculosis infection (TB)</i> (i.e., treatment of latent TB infection [LTBI])	<ul style="list-style-type: none"> (+) screening test for LTBI^d, with no evidence of active TB, and no prior treatment for active TB or LTBI (AI), <i>or</i> Close contact with a person with infectious TB, with no evidence of active TB, regardless of screening test results (AII). 	<ul style="list-style-type: none"> (INH 300 mg + pyridoxine 25–50 mg) PO daily x 9 months (AII), <i>or</i> NH 900 mg PO BIW (by DOT) + pyridoxine 25–50 mg PO daily x 9 months (BII). 	<ul style="list-style-type: none"> Rifampin 600 mg PO daily x 4 months (BIII), <i>or</i> Rifabutin (dose adjusted based on concomitant ART)^e x 4 months (BIII), <i>or</i> [Rifapentine (see dose below) PO + INH 900 mg PO + pyridoxine 50 mg PO] once weekly x 12 weeks <p><u>rifapentine dose:</u></p> <ul style="list-style-type: none"> 32.1 to 49.9 kg: 750 mg 50 mg: 900 mg <p>Rifapentine only recommended for patients receiving raltegravir or efavirenz-based ART regimen</p> <p>For persons exposed to drug-resistant TB, select anti-TB drugs after consultation with experts or public health authorities (AII).</p>

Table 1. Prophylaxis to Prevent First Episode of Opportunistic Disease (page 2 of 5)

Opportunistic Infections	Indication	Preferred	Alternative
Disseminated <i>Mycobacterium avium</i> complex (MAC) disease	CD4 count <50 cells/μL—after ruling out active disseminated MAC disease based on clinical assessment (AI) .	<ul style="list-style-type: none"> • Azithromycin 1200 mg PO once weekly (AI), <i>or</i> • Clarithromycin 500 mg PO BID (AI), <i>or</i> • Azithromycin 600 mg PO twice weekly (BIII) 	Rifabutin (dose adjusted based on concomitant ART) ^a (BI) ; rule out active TB before starting rifabutin.
<i>Streptococcus pneumoniae</i> infection	For individuals who have not received any pneumococcal vaccine, regardless of CD4 count, followed by: <ul style="list-style-type: none"> • if CD4 count ≥200 cells/μL • if CD4 count <200 cells/μL 	PCV13 0.5 mL IM x 1 (AI) . PPV23 0.5 mL IM at least 8 weeks after the PCV13 vaccine (AII) . PPV23 can be offered at least 8 weeks after receiving PCV13 (CIII) or can wait until CD4 count increased to ≥200 cells/μL (BIII) .	PPV23 0.5 mL IM x 1 (BII)
	For individuals who have previously received PPV23	One dose of PCV13 should be given at least 1 year after the last receipt of PPV23 (AII) .	
	<u>Re-vaccination</u> <ul style="list-style-type: none"> • If age 19–64 years and ≥5 years since the first PPV23 dose • If age ≥65 years, and if ≥5 years since the previous PPV23 dose 	<ul style="list-style-type: none"> • PPV23 0.5 mL IM or SQ x 1 (BIII) • PPV23 0.5 mL IM or SQ x 1 (BIII) 	
Influenza A and B virus infection	All HIV-infected patients (AIII)	Inactivated influenza vaccine annually (per recommendation for the season) (AIII) Live-attenuated influenza vaccine is contraindicated in HIV-infected patients (AIII) .	
Syphilis	<ul style="list-style-type: none"> • For individuals exposed to a sex partner with a diagnosis of primary, secondary, or early latent syphilis within past 90 days (AII), <i>or</i> • For individuals exposed to a sex partner >90 days before syphilis diagnosis in the partner, if serologic test results are not available immediately and the opportunity for follow-up is uncertain (AIII) 	Benzathine penicillin G 2.4 million units IM for 1 dose (AII)	<i>For penicillin-allergic patients:</i> <ul style="list-style-type: none"> • Doxycycline 100 mg PO BID for 14 days (BII), <i>or</i> • Ceftriaxone 1 g IM or IV daily for 8–10 days (BII), <i>or</i> • Azithromycin 2 g PO for 1 dose (BII) – not recommended for MSM or pregnant women (AII)
<i>Histoplasma capsulatum</i> infection	CD4 count ≤150 cells/μL and at high risk because of occupational exposure or live in a community with a hyperendemic rate of histoplasmosis (>10 cases/100 patient-years) (BI)	Itraconazole 200 mg PO daily (BI)	

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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)	
Varicella-zoster virus (VZV) infection	<p><u>Pre-exposure prevention:</u> Patients with CD4 counts ≥200 cells/μL who have not been vaccinated, have no history of varicella or herpes zoster, or who are seronegative for VZV (CIII)</p> <p>Note: Routine VZV serologic testing in HIV-infected adults and adolescents is not recommended.</p> <p><u>Post-exposure prevention: (AIII)</u> Close contact with a person with chickenpox or herpes zoster; and is susceptible (i.e., no history of vaccination or of either condition, or known to be VZV seronegative)</p>	<p><u>Pre-exposure prevention:</u> Primary varicella vaccination (Varivax™), 2 doses (0.5 mL SQ each) administered 3 months apart (CIII).</p> <p>If vaccination results in disease because of vaccine virus, treatment with acyclovir is recommended (AIII).</p> <p><u>Post-exposure prevention:</u> Varicella-zoster immune globulin (VariZIG™) 125 international units per 10 kg (maximum 625 international units) IM, administered as soon as possible and within 10 days after exposure (AIII)</p> <p>Note: VariZIG is exclusively distributed by FFF Enterprises at 800-843-7477.</p> <p>Individuals receiving monthly high-dose IVIG (>400 mg/kg) are likely to be protected if the last dose of IVIG was administered <3 weeks before exposure.</p>	<p><u>Pre-exposure prevention:</u> VZV-susceptible household contacts of susceptible HIV-infected persons should be vaccinated to prevent potential transmission of VZV to their HIV-infected contacts (BIII).</p> <p><u>Alternative post-exposure prevention:</u></p> <ul style="list-style-type: none"> • Acyclovir 800 mg PO 5 x/day for 5–7 days (BIII), <i>or</i> • Valacyclovir 1 g PO TID for 5–7 days (BIII) <p>These alternatives have not been studied in the HIV population.</p> <p>If antiviral therapy is used, varicella vaccines should not be given until at least 72 hours after the last dose of the antiviral drug.</p>
Human Papillomavirus (HPV) infection	Females aged 13–26 years (BIII)	<ul style="list-style-type: none"> • HPV quadrivalent vaccine 0.5 mL IM at months 0, 1–2, and 6 (BIII), <i>or</i> • HPV bivalent vaccine 0.5 mL IM at months 0, 1–2, and 6 (BIII), <i>or</i> • HPV 9-valent vaccine 0.5 mL IM at months 0, 1–2, and 6 (BIII) 	
	Males aged 13–26 years (BIII)	<ul style="list-style-type: none"> • HPV quadrivalent vaccine 0.5 mL IM at months 0, 1–2, and 6 (BIII), <i>or</i> • HPV 9-valent vaccine 0.5 mL IM at months 0, 1–2, and 6 (BIII) 	

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Opportunistic Infections	Indication	Preferred	Alternative
Hepatitis A virus (HAV) infection	HAV-susceptible patients with chronic liver disease, or who are injection-drug users, or MSM (AII) .	Hepatitis A vaccine 1 mL IM x 2 doses at 0 and 6–12 months (AII) . IgG antibody response should be assessed 1 month after vaccination; non-responders should be revaccinated when CD4 count >200 cells/μL. (BIII) .	<u>For patients susceptible to both HAV and hepatitis B virus (HBV) infection (see below):</u> Combined HAV and HBV vaccine (Twinrix®), 1 mL IM as a 3-dose (0, 1, and 6 months) or 4-dose series (days 0, 7, 21 to 30, and 12 months) (AII)
Hepatitis B virus (HBV) infection	<ul style="list-style-type: none"> • Patients without chronic HBV or without immunity to HBV (i.e., with anti-HBs <10 IU/mL) (AII) • Patients with isolated anti-HBc: vaccinate with 1 standard dose of HBV vaccine, check anti-HBs 1–2 months after, if > 100 IU, no further vaccination needed. If titer is < 100IU, vaccinate with full series (BII) • Early vaccination is recommended before CD4 count falls below 350 cells/μL (AII). • However, in patients with low CD4 cell counts, vaccination should not be deferred until CD4 count reaches >350 cells/μL, because some patients with CD4 counts <200 cells/μL do respond to vaccination (AII). 	<ul style="list-style-type: none"> • HBV vaccine IM (Engerix-B 20 μg/mL or Recombivax HB 10 μg/mL), 0, 1, and 6 months (AII), or • HBV vaccine IM (Engerix-B 40 μg/mL or Recombivax HB 20 μg/mL), 0, 1, 2 and 6 months (BI), • Combined HAV and HBV vaccine (Twinrix®), 1 mL IM as a 3-dose (0, 1, and 6 months) or 4-dose series (days 0, 7, 21 to 30, and 12 months) (AII) <p>Anti-HBs should be obtained 1–2 months after completion of the vaccine series. Patients with anti-HBs <10 IU/mL are considered non-responders, and should be revaccinated with another 3-dose series (BIII).</p>	Some experts recommend vaccinating with 4-doses of double dose of either HBV vaccine (BI) .
	<p><u>Vaccine Non-Responders:</u></p> <ul style="list-style-type: none"> • Anti-HBs <10 international units/mL 1 month after vaccination series • For patients with low CD4 counts at time of first vaccine series, some experts might delay revaccination until after a sustained increase in CD4 count with ART (CIII). 	Re-vaccinate with a second vaccine series (BIII)	<ul style="list-style-type: none"> • HBV vaccine IM (Engerix-B 40 μg/mL or Recombivax HB 20 μg/mL), 0, 1, 2 and 6 months (BI),
Malaria	Travel to disease-endemic area	Recommendations are the same for HIV-infected and HIV-uninfected patients. Recommendations are based on region of travel, malaria risks, and drug susceptibility in the region. Refer to the following website for the most recent recommendations based on region and drug susceptibility: http://www.cdc.gov/malaria/ .	

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Opportunistic Infections	Indication	Preferred	Alternative
Penicilliosis	Patients with CD4 cell counts <100 cells/ μ L who live or stay for a long period in rural areas in northern Thailand, Vietnam, or Southern China (BI)	Itraconazole 200 mg once daily (BI)	Fluconazole 400 mg PO once weekly (BII)

Key to Acronyms: anti-HBc = hepatitis B core antibody; anti-HBs = hepatitis B surface antibody; ART = antiretroviral therapy; BID = twice daily; BIW = twice a week; CD4 = CD4 T lymphocyte cell; DOT = directly observed therapy; DS = double strength; HAV = hepatitis A virus; HBV = hepatitis B virus; HPV = human papillomavirus; IgG = immunoglobulin G; IgM = immunoglobulin M; IM = intramuscular; INH = isoniazid; IV = intravenously; IVIG = intravenous immunoglobulin; LTBI = latent tuberculosis infection; MAC = *Mycobacterium avium* complex; PCP = *Pneumocystis* pneumonia; PCV13 = 13-valent pneumococcal conjugate vaccine; PO = orally; PPV23 = 23-valent pneumococcal polysaccharides vaccine; SQ = subcutaneous; SS = single strength; TB = tuberculosis; TMP-SMX = Trimethoprim-sulfamethoxazole; VZV = varicella zoster virus

^a TMP-SMX DS once daily also confers protection against toxoplasmosis and many respiratory bacterial infections; lower dose also likely confers protection

^b Patients should be tested for glucose-6-phosphate dehydrogenase (G6PD) before administration of dapsone or primaquine. Alternative agent should be used in patients found to have G6PD deficiency

^c Screening tests for LTBI include tuberculin skin test (TST) or interferon-gamma release assays (IGRA)

^d Refer to the [Drug Interactions](#) section in the [Adult and Adolescent ARV Guidelines](#) for dosing recommendation

Evidence Rating:

Strength of Recommendation:

A: Strong recommendation for the statement

B: Moderate recommendation for the statement

C: Optional recommendation for the statement

Quality of Evidence for the Recommendation:

I: One or more randomized trials with clinical outcomes and/or validated laboratory endpoints

II: One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes

III: Expert opinion

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

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 1 of 22) (Last updated August 10, 2017; last reviewed August 10, 2017)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
<i>Pneumocystis</i> Pneumonia (PCP)	<p>Patients who develop PCP despite TMP-SMX prophylaxis can usually be treated with standard doses of TMP-SMX (BIII).</p> <p>Duration of PCP treatment: 21 days (AII)</p> <p><u>For Moderate-to-Severe PCP:</u></p> <ul style="list-style-type: none"> • TMP-SMX: [TMP 15–20 mg and SMX 75–100 mg]/kg/day IV given q6h or q8h (AI), may switch to PO after clinical improvement (AI) <p><u>For Mild-to-Moderate PCP:</u></p> <ul style="list-style-type: none"> • TMP-SMX: [TMP 15–20 mg and SMX 75–100 mg]/kg/day, given PO in 3 divided doses (AI), or • TMP-SMX: (160 mg/800 mg or DS) 2 tablets PO TID (AI) <p><u>Secondary Prophylaxis, after completion of PCP treatment:</u></p> <ul style="list-style-type: none"> • TMP-SMX DS: 1 tablet PO daily (AI), or • TMP-SMX (80 mg/400 mg or SS): 1 tablet PO daily (AI) 	<p><u>For Moderate-to-Severe PCP:</u></p> <ul style="list-style-type: none"> • Pentamidine 4 mg/kg IV daily infused over ≥60 minutes (AI); can reduce dose to 3 mg/kg IV daily because of toxicities (BI), or • Primaquine 30 mg (base) PO daily + (clindamycin 600 mg q6h IV or 900 mg IV q8h) or (clindamycin 450 mg PO q6h or 600 mg PO q8h) (AI) <p><u>For Mild-to-Moderate PCP:</u></p> <ul style="list-style-type: none"> • Dapsone 100 mg PO daily + TMP 5 mg/kg PO TID (BI), or • Primaquine 30 mg (base) PO daily + (clindamycin 450 mg PO q6h or 600 mg PO q8h) (BI), or • Atovaquone 750 mg PO BID with food (BI) <p><u>Secondary Prophylaxis, after completion of PCP treatment:</u></p> <ul style="list-style-type: none"> • TMP-SMX DS: 1 tablet PO three times weekly (BI), or • Dapsone 100 mg PO daily (BI), or • Dapsone 50 mg PO daily + (pyrimethamine^a 50 mg + leucovorin 25 mg) PO weekly (BI), or • (Dapsone 200 mg + pyrimethamine^a 75 mg + leucovorin 25 mg) PO weekly (BI), or • Aerosolized pentamidine 300 mg monthly via Respigard II™ nebulizer (BI), or • Atovaquone 1500 mg PO daily (BI), or • (Atovaquone 1500 mg + pyrimethamine^a 25 mg + leucovorin 10 mg) PO daily (CIII) 	<p><u>Indications for Adjunctive Corticosteroids (AI):</u></p> <ul style="list-style-type: none"> • PaO₂ <70 mmHg at room air, or • Alveolar-arterial O₂ gradient >35 mm Hg <p><u>Prednisone Doses (Beginning as Early as Possible and Within 72 Hours of PCP Therapy) (AI):</u></p> <ul style="list-style-type: none"> • Days 1–5: 40 mg PO BID • Days 6–10: 40 mg PO daily • Days 11–21: 20 mg PO daily <p>IV methylprednisolone can be administered as 75% of prednisone dose.</p> <p>Benefit of corticosteroid if started after 72 hours of treatment is unknown, but some clinicians will use it for moderate-to-severe PCP (BIII).</p> <p>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.</p> <p>Patients who are receiving pyrimethamine^a/sulfadiazine for treatment or suppression of toxoplasmosis do not require additional PCP prophylaxis (AII).</p> <p>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).</p> <p>TMP-SMX should be permanently discontinued in patients with possible or definite Stevens-Johnson Syndrome or toxic epidermal necrosis (AII).</p>

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Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
<i>Toxoplasma gondii</i> Encephalitis	<p><u>Treatment of Acute Infection (AI):</u></p> <ul style="list-style-type: none"> Pyrimethamine^a 200 mg PO 1 time, followed by weight-based therapy: <ul style="list-style-type: none"> If <60 kg, pyrimethamine^a 50 mg PO once daily + sulfadiazine 1000 mg PO q6h + leucovorin 10–25 mg PO once daily If ≥60 kg, pyrimethamine^a 75 mg PO once daily + sulfadiazine 1500 mg PO q6h + leucovorin 10–25 mg PO once daily Leucovorin dose can be increased to 50 mg daily or BID. <p><u>Duration for Acute Therapy:</u></p> <ul style="list-style-type: none"> 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 <p><u>Chronic Maintenance Therapy:</u></p> <ul style="list-style-type: none"> Pyrimethamine^a 25–50 mg PO daily + sulfadiazine 2000–4000 mg PO daily (in 2–4 divided doses) + leucovorin 10–25 mg PO daily (AI) 	<p><u>Treatment of Acute Infection:</u></p> <ul style="list-style-type: none"> Pyrimethamine^a (leucovorin)* + clindamycin 600 mg IV or PO q6h (AI), <i>or</i> TMP-SMX (TMP 5 mg/kg and SMX 25 mg/kg) IV or PO BID (BI), <i>or</i> Atovaquone 1500 mg PO BID with food + pyrimethamine^a (leucovorin)* (BII), <i>or</i> Atovaquone 1500 mg PO BID with food + sulfadiazine 1000–1500 mg PO q6h (weight-based dosing, as in preferred therapy) (BII), <i>or</i> Atovaquone 1500 mg PO BID with food (BII) <p><u>Chronic Maintenance Therapy:</u></p> <ul style="list-style-type: none"> Clindamycin 600 mg PO q8h + (pyrimethamine^a 25–50 mg + leucovorin 10–25 mg) PO daily (BI), <i>or</i> TMP-SMX DS 1 tablet BID (BII), <i>or</i> TMP-SMX DS 1 tablet once daily (BII); <i>or</i> Atovaquone 750–1500 mg PO BID + (pyrimethamine^a 25 mg + leucovorin 10 mg) PO daily (BII), <i>or</i> Atovaquone 750–1500 mg PO BID + sulfadiazine 2000–4000 mg PO daily (in 2–4 divided doses (BII)), <i>or</i> Atovaquone 750–1500 mg PO BID with food (BII) <p>* Pyrimethamine^a and leucovorin doses are the same as for preferred therapy.</p>	<p>Refer to http://www.daraprimdirect.com for information regarding how to access pyrimethamine</p> <p>If pyrimethamine is unavailable or there is a delay in obtaining it, TMP-SMX should be utilized in place of pyrimethamine-sulfadiazine (BI).</p> <p>For patients with a history of sulfa allergy, sulfa desensitization should be attempted using one of several published strategies (BI).</p> <p>Atovaquone should be administered until therapeutic doses of TMP-SMX are achieved (CIII).</p> <p>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.</p> <p>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).</p> <p>If clindamycin is used in place of sulfadiazine, additional therapy must be added to prevent PCP (AII).</p>
Cryptosporidiosis	<ul style="list-style-type: none"> Initiate or optimize ART for immune restoration to CD4 count >100 cells/μL (AII), <i>and</i> Aggressive oral or IV rehydration and replacement of electrolyte loss (AIII), <i>and</i> Symptomatic treatment of diarrhea with anti-motility agents (AIII). 	<p>No therapy has been shown to be effective without ART. Trial of these agents may be used in conjunction with, but not instead of, ART:</p> <ul style="list-style-type: none"> Nitazoxanide 500–1000 mg PO BID for 14 days (CIII), <i>or</i> Paromomycin 500 mg PO QID for 14–21 days (CIII) <p>With optimized ART, symptomatic treatment and rehydration and electrolyte replacement</p>	<p>Tincture of opium may be more effective than loperamide in management of diarrhea (CII).</p>

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Microsporidiosis	<p><u>For GI Infections Caused by <i>Enterocytozoon bienuesi</i>:</u></p> <ul style="list-style-type: none"> • Initiate or optimize ART as immune restoration to CD4 count >100 cells/μL (AII); <i>plus</i> • Manage severe dehydration, malnutrition, and wasting by fluid support (AII) and nutritional supplement (AIII) <p><u>For Intestinal and Disseminated (Not Ocular) Infections Caused by Microsporidia Other Than <i>E. bienuesi</i> and <i>Vittaforma corneae</i>:</u></p> <ul style="list-style-type: none"> • Albendazole 400 mg PO BID (AII), continue until CD4 count >200 cells/μL for >6 months after initiation of ART (BIII) <p><u>For Ocular Infection:</u></p> <ul style="list-style-type: none"> • Topical fumagillin bicyclohexylammonium (Fumidil B) eye drops: 3 mg/mL in saline (fumagillin 70 μg/mL)—2 drops q2h for 4 days, then 2 drops QID (investigational use only in United States) (BII) + albendazole 400 mg PO BID, for management of systemic infection (BIII) • Therapy should be continued until resolution of ocular symptoms and CD4 count increase to >200 cells/μL for >6 months in response to ART (CIII). 	<p><u>For GI Infections Caused by <i>E. bienuesi</i>:</u></p> <ul style="list-style-type: none"> • 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 (1000 mg BID) may have some effect but response may be minimal in patients with low CD4 cell counts (CIII). <p><u>For Disseminated Disease Attributed to <i>Trachipleistophora</i> or <i>Anncaliia</i>:</u></p> <ul style="list-style-type: none"> • Itraconazole 400 mg PO daily + albendazole 400 mg PO BID (CIII) 	<p>Anti-motility agents can be used for diarrhea control if required (BIII).</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 4 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
<i>Mycobacterium tuberculosis</i> (TB) Disease	<p>After collecting specimen for culture and molecular diagnostic tests, empiric TB treatment should be started in individuals with clinical and radiographic presentation suggestive of TB (AIII).</p> <p>Refer to Table 3 for dosing recommendations.</p> <p><u>Initial Phase (2 Months, Given Daily, 5–7 Times/Week by DOT) (AI):</u></p> <ul style="list-style-type: none"> • INH + [RIF or RFB] + PZA + EMB (AI), <p><u>Continuation Phase:</u></p> <ul style="list-style-type: none"> • INH + (RIF or RFB) daily (5–7 times/week) (AIII) <p><u>Total Duration of Therapy (For Drug-Susceptible TB):</u></p> <ul style="list-style-type: none"> • Pulmonary drug-susceptible TB: 6 months (BII) • Pulmonary TB and culture-positive after 2 months of TB treatment: 9 months (BII) • Extra-pulmonary TB w/CNS infection: 9–12 months (BII); • Extra-pulmonary TB w/bone or joint involvement: 6 to 9 months (BII); • Extra-pulmonary TB in other sites: 6 months (BII) <p>Total duration of therapy should be based on number of doses received, not on calendar time</p>	<p>Treatment for Drug-Resistant TB</p> <p><u>Resistant to INH:</u></p> <ul style="list-style-type: none"> • (RIF or RFB) + EMB + PZA + (moxifloxacin or levofloxacin) for 2 months (BII); followed by (RIF or RFB) + EMB + (moxifloxacin or levofloxacin) for 7 months (BII) <p><u>Resistant to Rifamycins +/- Other Drugs:</u></p> <ul style="list-style-type: none"> • Regimen and duration of treatment should be individualized based on resistance pattern, clinical and microbiological responses, and in close consultation with experienced specialists (AIII). 	<p>Adjunctive corticosteroid improves survival for TB meningitis and pericarditis (AI). See text for drug, dose, and duration recommendations.</p> <p>All rifamycins may have significant pharmacokinetic interactions with antiretroviral drugs, please refer to the Drug Interactions section in the Adult and Adolescent ARV Guidelines for dosing recommendations.</p> <p>Therapeutic drug monitoring should be considered in patients receiving rifamycin and interacting ART.</p> <p>Paradoxical IRIS that is not severe can be treated with NSAIDs without a change in TB or HIV therapy (BIII).</p> <p>For severe IRIS reaction, consider prednisone and taper over 4 weeks based on clinical symptoms (BIII).</p> <p>For example:</p> <ul style="list-style-type: none"> • <u>If receiving RIF</u>: prednisone 1.5 mg/kg/day for 2 weeks, then 0.75 mg/kg/day for 2 weeks • <u>If receiving RFB</u>: prednisone 1.0 mg/kg/day for 2 weeks, then 0.5 mg/kg/day for 2 weeks <p>A more gradual tapering schedule over a few months may be necessary for some patients.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 5 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Disseminated <i>Mycobacterium avium</i> Complex (MAC) Disease	<p><u>At Least 2 Drugs as Initial Therapy With:</u></p> <ul style="list-style-type: none"> • Clarithromycin 500 mg PO BID (AI) + ethambutol 15 mg/kg PO daily (AI), or • (Azithromycin 500–600 mg + ethambutol 15 mg/kg) PO daily (AII) if drug interaction or intolerance precludes the use of clarithromycin <p><u>Duration:</u></p> <ul style="list-style-type: none"> • At least 12 months of therapy, can discontinue if no signs and symptoms of MAC disease and sustained (>6 months) CD4 count >100 cells/μL in response to ART 	<p>Addition of a third or fourth drug should be considered for patients with advanced immunosuppression (CD4 counts <50 cells/μL), high mycobacterial loads (>2 log CFU/mL of blood), or in the absence of effective ART (CIII).</p> <p><u>Third or Fourth Drug Options May Include:</u></p> <ul style="list-style-type: none"> • RFB 300 mg PO daily (dosage adjustment may be necessary based on drug interactions) (CI), • Amikacin 10–15 mg/kg IV daily (CIII) or Streptomycin 1 g IV or IM daily (CIII)], or • Moxifloxacin 400 mg PO daily (CIII) or Levofloxacin 500 mg PO daily (CIII) 	<p>Testing of susceptibility to clarithromycin and azithromycin is recommended (BIII).</p> <p>NSAIDs can be used for patients who experience moderate to severe symptoms attributed to IRIS (CIII).</p> <p>If IRIS symptoms persist, short-term (4–8 weeks) systemic corticosteroids (equivalent to 20–40 mg prednisone) can be used (CII).</p>
Bacterial Respiratory Diseases (with focus on pneumonia)	<p>Empiric antibiotic therapy should be initiated promptly for patients presenting with clinical and radiographic evidence consistent with bacterial pneumonia. The recommendations listed are suggested empiric therapy. The regimen should be modified as needed once microbiologic results are available (BIII).</p> <p><u>Empiric Outpatient Therapy:</u></p> <ul style="list-style-type: none"> • A PO beta-lactam + a PO macrolide (azithromycin or clarithromycin) (AII) <ul style="list-style-type: none"> • <i>Preferred beta-lactams:</i> high-dose amoxicillin or amoxicillin/clavulanate • <i>Alternative beta-lactams:</i> cefpodoxime or cefuroxime, or • <i>For penicillin-allergic patients:</i> Levofloxacin 750 mg PO once daily (AII), or moxifloxacin 400 mg PO once daily (AII) <p><u>Duration:</u> 7–10 days (a minimum of 5 days). Patients should be afebrile for 48–72 hours and clinically stable before stopping antibiotics.</p> <p><u>Empiric Therapy for Non-ICU Hospitalized Patients:</u></p> <ul style="list-style-type: none"> • An IV beta-lactam + a macrolide (azithromycin or clarithromycin) (AII) <ul style="list-style-type: none"> • <i>Preferred beta-lactams:</i> ceftriaxone, cefotaxime, or ampicillin-sulbactam • <i>For penicillin-allergic patients:</i> Levofloxacin, 750 mg IV once daily (AII), or moxifloxacin, 400 mg IV once daily (AII) 	<p><u>Empiric Outpatient Therapy:</u></p> <ul style="list-style-type: none"> • A PO beta-lactam + PO doxycycline (CIII) <ul style="list-style-type: none"> • <i>Preferred beta-lactams:</i> high-dose amoxicillin or amoxicillin/clavulanate • <i>Alternative beta-lactams:</i> cefpodoxime or cefuroxime <p><u>Empiric Therapy for Non-ICU Hospitalized Patients:</u></p> <ul style="list-style-type: none"> • An IV beta-lactam + doxycycline (CIII) <p><u>Empiric Therapy For ICU Patients:</u></p> <ul style="list-style-type: none"> • <i>For penicillin-allergic patients:</i> Aztreonam IV + (levofloxacin 750 mg IV once daily or moxifloxacin 400 mg IV once daily) (BIII) <p><u>Empiric Therapy for Patients at Risk of <i>Pseudomonas</i> Pneumonia:</u></p> <ul style="list-style-type: none"> • An IV antipneumococcal, antipseudomonal beta-lactam + an aminoglycoside + azithromycin (BIII), or • Above beta-lactam + an aminoglycoside + (levofloxacin 750 mg IV once daily or moxifloxacin 400 mg IV once daily) (BIII), or • <i>For penicillin-allergic patients:</i> Replace the beta-lactam with aztreonam (BIII). 	<p>Fluoroquinolones should be used with caution in patients in whom TB is suspected but is not being treated.</p> <p>Empiric therapy with a macrolide alone is not routinely recommended, because of increasing pneumococcal resistance (BIII).</p> <p>Patients receiving a macrolide for MAC prophylaxis should not receive macrolide monotherapy for empiric treatment of bacterial pneumonia.</p> <p>For patients begun on IV antibiotic therapy, switching to PO should be considered when they are clinically improved and able to tolerate oral medications.</p> <p>Chemoprophylaxis can be considered for patients with frequent recurrences of serious bacterial pneumonia (CIII).</p> <p>Clinicians should be cautious about using antibiotics to prevent recurrences because of the potential for developing drug resistance and drug toxicities.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 6 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Bacterial Respiratory Diseases <i>(with focus on pneumonia),</i> continued	<p><u>Empiric Therapy for ICU Patients:</u></p> <ul style="list-style-type: none"> • An IV beta-lactam + IV azithromycin (AII), <i>or</i> • An IV beta-lactam + (levofloxacin 750 mg IV once daily or moxifloxacin 400 mg IV once daily) (AII) <ul style="list-style-type: none"> • Preferred beta-lactams: ceftriaxone, cefotaxime, or ampicillin-sulbactam <p><u>Empiric Therapy for Patients at Risk of <i>Pseudomonas</i> Pneumonia:</u></p> <ul style="list-style-type: none"> • An IV antipneumococcal, antipseudomonal beta-lactam + (ciprofloxacin 400 mg IV q8–12h or levofloxacin 750 mg IV once daily) (BIII) <ul style="list-style-type: none"> • Preferred beta-lactams: piperacillin-tazobactam, cefepime, imipenem, or meropenem <p><u>Empiric Therapy for Patients at Risk for Methicillin-Resistant <i>Staphylococcus aureus</i> Pneumonia:</u></p> <ul style="list-style-type: none"> • Add vancomycin IV or linezolid (IV or PO) to the baseline regimen (BIII). • Addition of clindamycin to vancomycin (but not to linezolid) can be considered for severe necrotizing pneumonia to minimize bacterial toxin production (CIII). 		

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 7 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Bacterial Enteric Infections: <i>Empiric Therapy pending definitive diagnosis.</i>	<p>Diagnostic fecal specimens should be obtained before initiation of empiric antibiotic therapy. If culture is positive, antibiotic susceptibilities should be performed to inform antibiotic choices given increased reports of antibiotic resistance. If a culture independent diagnostic test is positive, reflex cultures for antibiotic susceptibilities should also be done.</p> <p>Empiric antibiotic therapy is indicated for advanced HIV patients (CD4 count <200 cells/μL or concomitant AIDS-defining illnesses), with clinically severe diarrhea (\geq6 stools/day or bloody stool) and/or accompanying fever or chills.</p> <p><u>Empiric Therapy:</u></p> <ul style="list-style-type: none"> • Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (AIII) <p>Therapy should be adjusted based on the results of diagnostic work-up.</p> <p>For patients with chronic diarrhea (>14 days) without severe clinical signs, empiric antibiotics therapy is not necessary, can withhold treatment until a diagnosis is made.</p>	<p><u>Empiric Therapy:</u></p> <ul style="list-style-type: none"> • Ceftriaxone 1 g IV q24h (BIII), <i>or</i> • Cefotaxime 1 g IV q8h (BIII) 	<p>Oral or IV rehydration (if indicated) should be given to patients with diarrhea (AIII).</p> <p>Antimotility agents should be avoided if there is concern about inflammatory diarrhea, including <i>Clostridium-difficile</i>-associated diarrhea (BIII).</p> <p>If no clinical response after 3–4 days, consider follow-up stool culture with antibiotic susceptibility testing or alternative diagnostic tests (e.g., toxin assays, molecular testing) to evaluate alternative diagnosis, antibiotic resistance, or drug-drug interactions.</p> <p>IV antibiotics and hospitalization should be considered in patients with marked nausea, vomiting, diarrhea, electrolyte abnormalities, acidosis, and blood pressure instability.</p>
Salmonellosis	<p>All HIV-infected patients with salmonellosis should receive antimicrobial treatment due to an increase of bacteremia (by 20–100 fold) and mortality (by up to 7-fold) compared to HIV-negative individuals (AIII).</p> <ul style="list-style-type: none"> • Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h, if susceptible (AIII) <p><u>Duration of Therapy:</u></p> <p><i>For gastroenteritis without bacteremia:</i></p> <ul style="list-style-type: none"> • If CD4 count \geq200 cells/μL: 7–14 days (BIII) • If CD4 count <200 cells/μL: 2–6 weeks (BIII) <p><i>For gastroenteritis with bacteremia:</i></p> <ul style="list-style-type: none"> • If CD4 count \geq200/μL: 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/μL: 2–6 weeks (BIII) 	<ul style="list-style-type: none"> • Levofloxacin 750 mg (PO or IV) q24h (BIII), <i>or</i> • Moxifloxacin 400 mg (PO or IV) q24h (BIII), <i>or</i> • TMP 160 mg-SMX 800 mg (PO or IV) q12h (BIII), <i>or</i> • Ceftriaxone 1 g IV q24h (BIII), <i>or</i> • Cefotaxime 1 g IV q8h (BIII) 	<p>Oral or IV rehydration if indicated (AIII).</p> <p>Antimotility agents should be avoided (BIII).</p> <p>The role of long-term secondary prophylaxis in patients with recurrent <i>Salmonella</i> bacteremia is not well established. Must weigh benefit against risks of long-term antibiotic exposure (BIII).</p> <p>Effective ART may reduce the frequency, severity, and recurrence of salmonella infections.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 8 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Salmonellosis , continued	<p><u>Secondary Prophylaxis Should Be Considered For:</u></p> <ul style="list-style-type: none"> • Patients with recurrent <i>Salmonella</i> gastroenteritis +/- bacteremia (CIII), or • Patients with CD4 <200 cells/μL with severe diarrhea (CIII) 		
Shigellosis	<ul style="list-style-type: none"> • Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (AIII) <p><u>Duration of Therapy:</u></p> <ul style="list-style-type: none"> • <i>Gastroenteritis</i>: 7–10 days (AIII) (if azithromycin is used, treat for 5 days) • <i>Bacteremia</i>: \geq14 days (BIII) • <i>Recurrent Infections</i>: up to 6 weeks (BIII) <p>Note: Increased resistance of <i>Shigella</i> to fluoroquinolones is occurring in the United States. Avoid fluoroquinolones if ciprofloxacin MIC is \geq0.12 ug/ml even if the laboratory identifies the isolate as sensitive. Many <i>Shigella</i> strains resistant to fluoroquinolones exhibit resistance to other commonly used antibiotics. Thus, antibiotic sensitivity testing of <i>Shigella</i> isolates from HIV-infected individuals should be performed routinely.</p>	<ul style="list-style-type: none"> • Levofloxacin 750 mg (PO or IV) q24h (BIII), or • Moxifloxacin 400 mg (PO or IV) q24h (BIII), or • TMP 160 mg-SMX 800 mg (PO or IV) q12h (BIII) (Note: <i>Shigella</i> 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: azithromycin is not recommended for patients with bacteremia (AIII)) <p>Note: Azithromycin-resistant <i>Shigella</i> spp has been reported in HIV-infected MSM.</p>	<p>Therapy is indicated both to shorten duration of illness and prevent spread of infection (AIII).</p> <p>Given increasing antimicrobial resistance and limited data showing that antibiotic therapy limits transmission, antibiotic treatment may be withheld in patients with CD4 >500 cells/mm³ whose diarrhea resolves prior to culture confirmation of <i>Shigella</i> infection (CIII).</p> <p>Oral or IV rehydration if indicated (AIII).</p> <p>Antimotility agents should be avoided (BIII).</p> <p>If no clinical response after 5–7 days, consider follow-up stool culture, alternative diagnosis, or antibiotic resistance.</p> <p>Effective ART may decrease the risk of recurrence of <i>Shigella</i> infections.</p>
Campylobacteriosis	<p><u>For Mild Disease and If CD4 Count >200 cells/μL:</u></p> <ul style="list-style-type: none"> • No therapy unless symptoms persist for more than several days (CIII) <p><u>For Mild-to-Moderate Disease (If Susceptible):</u></p> <ul style="list-style-type: none"> • Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (BIII), or • Azithromycin 500 mg PO daily (BIII) (Note: Not for patients with bacteremia (AIII)) <p><u>For <i>Campylobacter</i> Bacteremia:</u></p> <ul style="list-style-type: none"> • Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (BIII) + an aminoglycoside (BIII) 	<p><u>For Mild-to-Moderate Disease (If Susceptible):</u></p> <ul style="list-style-type: none"> • Levofloxacin 750 mg (PO or IV) q24h (BIII), or • Moxifloxacin 400 mg (PO or IV) q24h (BIII) <p>Add an aminoglycoside to fluoroquinolone in bacteremic patients (BIII).</p>	<p>Oral or IV rehydration if indicated (AIII).</p> <p>Antimotility agents should be avoided (BIII).</p> <p>If no clinical response after 5–7 days, consider follow-up stool culture, alternative diagnosis, or antibiotic resistance.</p> <p>There is an increasing rate of fluoroquinolone resistance in the United States (24% resistance in 2011).</p> <p>The rationale of addition of an aminoglycoside to a fluoroquinolone in bacteremic patients is to prevent emergence of quinolone resistance.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 9 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Campylobacteriosis , continued	<p><u>Duration of Therapy:</u></p> <ul style="list-style-type: none"> • <i>Gastroenteritis</i>: 7–10 days (AIII) (5 days with azithromycin) • <i>Bacteremia</i>: ≥ 14 days (BIII) • <i>Recurrent bacteremia</i>: 2–6 weeks (BIII) 		Effective ART may reduce the frequency, severity, and recurrence of campylobacter infections.
<i>Clostridium difficile</i> infection (CDI)	<p>Vancomycin 125 mg (PO) QID for 10–14 days (AI)</p> <p>For severe, life-threatening CDI, see text and references for additional information.</p>	For mild, outpatient disease: metronidazole 500 mg (PO) TID for 10–14 days (CII).	<p><i>Recurrent CDI:</i></p> <p>Treatment is the same as in patients without HIV infection. Fecal microbiota therapy may be successful and safe to treat recurrent CDI in HIV-infected patients (CIII). See text and references for additional information.</p>
Bartonellosis	<p><u>For Bacillary Angiomatosis, Peliosis Hepatis, Bacteremia, and Osteomyelitis:</u></p> <ul style="list-style-type: none"> • Doxycycline 100 mg PO or IV q12h (AII), or • Erythromycin 500 mg PO or IV q6h (AII) <p><u>CNS Infections:</u></p> <ul style="list-style-type: none"> • (Doxycycline 100 mg +/- RIF 300 mg) PO or IV q12h (AIII) <p><u>Confirmed <i>Bartonella</i> Endocarditis:</u></p> <ul style="list-style-type: none"> • (Doxycycline 100 mg IV q12h + gentamicin 1 mg/kg IV q8h) for 2 weeks, then continue with doxycycline 100 mg IV or PO q12h (BII) <p><u>Other Severe Infections:</u></p> <ul style="list-style-type: none"> • (Doxycycline 100 mg PO or IV +/- RIF 300 mg PO or IV) q12h (BIII), or • (Erythromycin 500 mg PO or IV q6h) +/- RIF 300 mg PO or IV q12h (BIII) <p><u>Duration of Therapy:</u></p> <ul style="list-style-type: none"> • At least 3 months (AII) 	<p><u>For Bacillary Angiomatosis, Peliosis Hepatis, Bacteremia, And Osteomyelitis:</u></p> <ul style="list-style-type: none"> • Azithromycin 500 mg PO daily (BIII) • Clarithromycin 500 mg PO BID (BIII) <p><u>Confirmed <i>Bartonella</i> Endocarditis but with Renal Insufficiency:</u></p> <ul style="list-style-type: none"> • (Doxycycline 100 mg IV + RIF 300 mg PO or IV) q12h for 2 weeks, then continue with doxycycline 100 mg IV or PI q12h (BII) 	<p>When RIF is used, take into consideration the potential for significant interaction with ARV drugs and other medications (see Table 5 for dosing recommendations).</p> <p>If relapse occurs after initial (>3 month) course of therapy, long-term suppression with doxycycline or a macrolide is recommended as long as CD4 count <200 cells/μL (AIII).</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 10 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Syphilis (<i>Treponema pallidum</i> Infection)	<p><u>Early Stage (Primary, Secondary, and Early-Latent Syphilis):</u></p> <ul style="list-style-type: none"> • Benzathine penicillin G 2.4 million units IM for 1 dose (AII) <p><u>Late-Latent Disease (>1 year or of Unknown Duration, and No Signs of Neurosyphilis):</u></p> <ul style="list-style-type: none"> • Benzathine penicillin G 2.4 million units IM weekly for 3 doses (AII) <p><u>Late-Stage (Tertiary–Cardiovascular or Gummatous Disease):</u></p> <ul style="list-style-type: none"> • Benzathine penicillin G 2.4 million units IM weekly for 3 doses (AII) (Note: rule out neurosyphilis before initiation of benzathine penicillin, and obtain infectious diseases consultation to guide management) <p><u>Neurosyphilis (Including Otic or Ocular Disease):</u></p> <ul style="list-style-type: none"> • Aqueous crystalline penicillin G 18–24 million units per day (administered as 3–4 million units IV q4h or by continuous IV infusion) for 10–14 days (AII) +/- benzathine penicillin G 2.4 million units IM weekly for 3 doses after completion of IV therapy (CIII) 	<p><u>Early Stage (Primary, Secondary, and Early-Latent Syphilis):</u></p> <p><i>For penicillin-allergic patients</i></p> <ul style="list-style-type: none"> • Doxycycline 100 mg PO BID for 14 days (BII), <i>or</i> • Ceftriaxone 1 g IM or IV daily for 10–14 days (BII), <i>or</i> • Azithromycin 2 g PO for 1 dose (BII) (Note: azithromycin is not recommended for men who have sex with men or pregnant women (AII)) <p><u>Late-Latent Disease (>1 year or of Unknown Duration, and No Signs of Neurosyphilis):</u></p> <p><i>For penicillin-allergic patients</i></p> <ul style="list-style-type: none"> • Doxycycline 100 mg PO BID for 28 days (BIII) <p><u>Neurosyphilis:</u></p> <ul style="list-style-type: none"> • Procaine penicillin 2.4 million units IM daily plus probenecid 500 mg PO QID for 10–14 days (BII) +/- benzathine penicillin G 2.4 million units IM weekly for 3 doses after completion of above (CIII), <i>or</i> • <i>For penicillin-allergic patients:</i> Desensitization to penicillin is the preferred approach (BIII); if not feasible, ceftriaxone, 2 g IV daily for 10–14 days (BII) 	<p>The efficacy of non-penicillin alternatives has not been evaluated in HIV-infected patients and they should be used only with close clinical and serologic monitoring.</p> <p>Combination of procaine penicillin and probenecid is not recommended for patients who are allergic to sulfa-containing medications (AIII).</p> <p>The Jarisch-Herxheimer reaction is an acute febrile reaction accompanied by headache and myalgia that can occur within the first 24 hours after therapy for syphilis. This reaction occurs most frequently in patients with early syphilis, high non-treponemal titers, and prior penicillin treatment.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 11 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Mucocutaneous candidiasis	<p><u>For Oropharyngeal Candidiasis: Initial Episodes (For 7–14 Days):</u></p> <p><i>Oral Therapy</i></p> <ul style="list-style-type: none"> Fluconazole 100 mg PO daily (AI), <i>or</i> <p><i>Topical Therapy</i></p> <ul style="list-style-type: none"> Clotrimazole troches, 10 mg PO 5 times daily (BI), <i>or</i> Miconazole mucoadhesive buccal 50-mg tablet—apply to mucosal surface over the canine fossa once daily (do not swallow, chew, or crush) (BI) <p><u>For Esophageal Candidiasis (For 14–21 Days):</u></p> <ul style="list-style-type: none"> Fluconazole 100 mg (up to 400 mg) PO or IV daily (AI), <i>or</i> Itraconazole oral solution 200 mg PO daily (AI) <p><u>For Uncomplicated Vulvo-Vaginal Candidiasis:</u></p> <ul style="list-style-type: none"> Oral fluconazole 150 mg for 1 dose (AII), <i>or</i> Topical azoles (clotrimazole, butoconazole, miconazole, tioconazole, or terconazole) for 3–7 days (AII) <p><u>For Severe or Recurrent Vulvo-Vaginal Candidiasis:</u></p> <ul style="list-style-type: none"> Fluconazole 100–200 mg PO daily for ≥7 days (AII), <i>or</i> Topical antifungal ≥7 days (AII) 	<p><u>For Oropharyngeal Candidiasis: Initial Episodes (For 7–14 Days):</u></p> <p><i>Oral Therapy</i></p> <ul style="list-style-type: none"> Itraconazole oral solution 200 mg PO daily (BI), <i>or</i> Posaconazole oral suspension 400 mg PO BID for 1 day, then 400 mg daily (BI) <p><i>Topical Therapy</i></p> <ul style="list-style-type: none"> Nystatin suspension 4–6 mL QID or 1–2 flavored pastilles 4–5 times daily (BII) <p><u>For Esophageal Candidiasis (For 14–21 Days):</u></p> <ul style="list-style-type: none"> Voriconazole 200 mg PO or IV BID (BI), <i>or</i> Anidulafungin 100 mg IV 1 time, then 50 mg IV daily (BI), <i>or</i> Caspofungin 50 mg IV daily (BI), <i>or</i> Micafungin 150 mg IV daily (BI), <i>or</i> Amphotericin B deoxycholate 0.6 mg/kg IV daily (BI), <i>or</i> Lipid formulation of amphotericin B 3–4 mg/kg IV daily (BIII) <p><u>For Uncomplicated Vulvo-Vaginal Candidiasis:</u></p> <ul style="list-style-type: none"> Itraconazole oral solution 200 mg PO daily for 3–7 days (BII) 	<p>Chronic or prolonged use of azoles may promote development of resistance.</p> <p>Higher relapse rate for esophageal candidiasis seen with echinocandins than with fluconazole use.</p> <p>Suppressive therapy usually not recommended (BIII) unless patients have frequent or severe recurrences.</p> <p><u>If Decision Is to Use Suppressive Therapy:</u></p> <p><i>Oropharyngeal candidiasis:</i></p> <ul style="list-style-type: none"> Fluconazole 100 mg PO daily or three times weekly (BI), <i>or</i> Itraconazole oral solution 200 mg PO daily (CI) <p><i>Esophageal candidiasis:</i></p> <ul style="list-style-type: none"> Fluconazole 100–200 mg PO daily (BI), <i>or</i> Posaconazole 400 mg PO BID (BII) <p><i>Vulvo-vaginal candidiasis:</i></p> <ul style="list-style-type: none"> Fluconazole 150 mg PO once weekly (CII)

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 12 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Cryptococcosis	<p><u>Cryptococcal Meningitis</u></p> <p><i>Induction Therapy (for at least 2 weeks, followed by consolidation therapy):</i></p> <ul style="list-style-type: none"> Liposomal amphotericin B 3–4 mg/kg IV daily + flucytosine 25 mg/kg PO QID (AI) (Note: Flucytosine dose should be adjusted in patients with renal dysfunction.) <p><i>Consolidation Therapy (for at least 8 weeks (AI), followed by maintenance therapy):</i></p> <ul style="list-style-type: none"> Fluconazole 400 mg PO (or IV) daily (AI) <p><i>Maintenance Therapy:</i></p> <ul style="list-style-type: none"> Fluconazole 200 mg PO daily for at least 12 months (AI) <p><u>For Non-CNS, Extrapulmonary Cryptococcosis and Diffuse Pulmonary Disease:</u></p> <ul style="list-style-type: none"> Treatment same as for cryptococcal meningitis (BIII) <p><u>Non-CNS Cryptococcosis with Mild-to-Moderate Symptoms and Focal Pulmonary Infiltrates:</u></p> <ul style="list-style-type: none"> Fluconazole, 400 mg PO daily for 12 months (BIII) 	<p><u>Cryptococcal meningitis</u></p> <p><i>Induction Therapy (for at least 2 weeks, followed by consolidation therapy):</i></p> <ul style="list-style-type: none"> Amphotericin B deoxycholate 0.7 mg/kg IV daily + flucytosine 25 mg/kg PO QID (AI), or Amphotericin B lipid complex 5 mg/kg IV daily + flucytosine 25 mg/kg PO QID (BII), or Liposomal amphotericin B 3–4 mg/kg IV daily + fluconazole 800 mg PO or IV daily (BIII), or Amphotericin B deoxycholate 0.7 mg/kg IV daily + fluconazole 800 mg PO or IV daily (BI), or Fluconazole 400–800 mg PO or IV daily + flucytosine 25 mg/kg PO QID (BII), or Fluconazole 1200 mg PO or IV daily (CII) <p><i>Consolidation Therapy (for at least 8 weeks (AI), followed by maintenance therapy):</i></p> <ul style="list-style-type: none"> Itraconazole 200 mg PO BID for 8 weeks—less effective than fluconazole (CI) <p><i>Maintenance Therapy:</i></p> <ul style="list-style-type: none"> No alternative therapy recommendation 	<p>Addition of flucytosine to amphotericin B has been associated with more rapid sterilization of CSF and decreased risk for subsequent relapse.</p> <p>Patients receiving flucytosine should have either blood levels monitored (peak level 2 hours after dose should be 30–80 mcg/mL) or close monitoring of blood counts for development of cytopenia. Dosage should be adjusted in patients with renal insufficiency (BII).</p> <p>Opening pressure should always be measured when an LP is performed (AII). Repeated LPs or CSF shunting are essential to effectively manage increased intracranial pressure (BIII).</p> <p>Corticosteroids and mannitol are ineffective in reducing ICP and are NOT recommended (BII).</p> <p>Corticosteroid should not be routinely used during induction therapy unless it is used for management of IRIS (AI).</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 13 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Histoplasmosis	<p><u>Moderately Severe to Severe Disseminated Disease</u></p> <p><i>Induction Therapy (for at least 2 weeks or until clinically improved):</i></p> <ul style="list-style-type: none"> Liposomal amphotericin B 3 mg/kg IV daily (AI) <p><i>Maintenance Therapy</i></p> <ul style="list-style-type: none"> Itraconazole 200 mg PO TID for 3 days, then 200 mg PO BID (AII) <p><u>Less Severe Disseminated Disease</u></p> <p><i>Induction and Maintenance Therapy:</i></p> <ul style="list-style-type: none"> Itraconazole 200 mg PO TID for 3 days, then 200 mg PO BID (AII) <p><i>Duration of Therapy:</i></p> <ul style="list-style-type: none"> At least 12 months <p><u>Meningitis</u></p> <p><i>Induction Therapy (4–6 weeks):</i></p> <ul style="list-style-type: none"> Liposomal amphotericin B 5 mg/kg/day (AIII) <p><i>Maintenance Therapy:</i></p> <ul style="list-style-type: none"> Itraconazole 200 mg PO BID to TID for ≥1 year and until resolution of abnormal CSF findings (AII) <p><u>Long-Term Suppression Therapy:</u></p> <p><i>For patients with severe disseminated or CNS infection (AIII) after completion of at least 12 months of therapy; and those who relapse despite appropriate therapy (BIII):</i></p> <ul style="list-style-type: none"> Itraconazole 200 mg PO daily (AIII) 	<p><u>Moderately Severe to Severe Disseminated Disease</u></p> <p><i>Induction Therapy (for at least 2 weeks or until clinically improved):</i></p> <ul style="list-style-type: none"> Amphotericin B lipid complex 3 mg/kg IV daily (AIII), or Amphotericin B cholesteryl sulfate complex 3 mg/kg IV daily (AIII) <p><u>Alternatives to Itraconazole for Maintenance Therapy or Treatment of Less Severe Disease:</u></p> <ul style="list-style-type: none"> Voriconazole 400 mg PO BID for 1 day, then 200 mg BID (BIII), or Posaconazole 400 mg PO BID (BIII) Fluconazole 800 mg PO daily (CII) <p><u>Meningitis:</u></p> <ul style="list-style-type: none"> No alternative therapy recommendation <p><u>Long-Term Suppression Therapy:</u></p> <ul style="list-style-type: none"> Fluconazole 400 mg PO daily (BIII) 	<p>Itraconazole, posaconazole, and voriconazole may have significant interactions with certain ARV agents. These interactions are complex and can be bi-directional. Refer to Table 5 for dosage recommendations.</p> <p>Therapeutic drug monitoring and dosage adjustment may be necessary to ensure triazole antifungal and ARV efficacy and reduce concentration-related toxicities.</p> <p>Random serum concentration of itraconazole + hydroitraconazole should be >1 µg/mL.</p> <p>Clinical experience with voriconazole or posaconazole in the treatment of histoplasmosis is limited.</p> <p>Acute pulmonary histoplasmosis in HIV-infected patients with CD4 counts >300 cells/µL should be managed as non-immunocompromised host (AIII).</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 14 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Coccidioidomycosis	<p><u>Clinically Mild Infections (e.g., Focal Pneumonia):</u></p> <ul style="list-style-type: none"> Fluconazole 400 mg* PO daily (AII), <i>or</i> Itraconazole 200 mg* PO BID (BII) <p><u>Bone or Joint Infections:</u></p> <ul style="list-style-type: none"> Itraconazole 200 mg* PO BID (AI) <p><u>Severe, Non-Meningeal Infection (Diffuse Pulmonary Infection or Severely Ill Patients with Extrathoracic, Disseminated Disease):</u></p> <ul style="list-style-type: none"> Lipid formulation amphotericin B 3–5 mg/kg IV daily (AIII), <i>or</i> Amphotericin B deoxycholate 0.7–1.0 mg/kg IV daily (AII) Duration of therapy: continue until clinical improvement, then switch to a triazole (BIII) <p><u>Meningeal Infections:</u></p> <ul style="list-style-type: none"> Fluconazole 400–800 mg* IV or PO daily (AII) 	<p><u>Mild Infections (Focal Pneumonia) For Patients Who Failed to Respond to Fluconazole or Itraconazole:</u></p> <ul style="list-style-type: none"> Posaconazole 300mg delayed-release tablet* PO BID x 1 day, then once daily (BIII), <i>or</i> Posaconazole 400 mg oral suspension* PO BID (BII), <i>or</i> Voriconazole 200 mg* PO BID (BIII) <p><u>Bone or Joint Infection:</u></p> <ul style="list-style-type: none"> Fluconazole 400 mg* PO daily (BI) <p><u>Severe, Non-Meningeal Infection (Diffuse Pulmonary Infection or Severely Ill Patients with Extrathoracic, Disseminated Disease):</u></p> <ul style="list-style-type: none"> Some specialists will add a triazole (fluconazole* or itraconazole*) 400 mg per day to amphotericin B therapy and continue triazole once amphotericin B is stopped (BIII). <p><u>Meningeal Infections:</u></p> <ul style="list-style-type: none"> Itraconazole 200 mg* PO TID for 3 days, then 200 mg PO BID (BII), <i>or</i> Voriconazole 200–400 mg* PO BID (BIII), <i>or</i> Posaconazole 300 mg delayed-release tablet* PO BID x 1 day, then once daily (CIII), <i>or</i> Posaconazole 400 mg oral suspension* PO BID (CIII), <i>or</i> Intrathecal amphotericin B deoxycholate, when triazole antifungals are ineffective (AIII) 	<p>Relapse can occur in 25%–33% of HIV-negative patients with diffuse pulmonary or disseminated diseases. Therapy should be given for at least 12 months and usually much longer; discontinuation is dependent on clinical and serological response and should be made in consultation with experts (BIII).</p> <p>Therapy should be lifelong in patients with meningeal infections because relapse occurs in 80% of HIV-infected patients after discontinuation of triazole therapy (AII).</p> <p>*Fluconazole, itraconazole, posaconazole, and voriconazole may have significant interactions with other medications including ARV drugs. These interactions are complex and can be bi-directional. Refer to Table 5 or 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.</p> <p>Intrathecal amphotericin B should only be given in consultation with a specialist and administered by an individual with experience with the technique.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 15 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Cytomegalovirus (CMV) Disease	<p><u>CMV Retinitis Induction Therapy (followed by Chronic Maintenance Therapy):</u></p> <p><i>For Immediate Sight-Threatening Lesions (within 1500 microns of the fovea):</i></p> <ul style="list-style-type: none"> Intravitreal injections of ganciclovir (2 mg) or foscarnet (2.4 mg) for 1-4 doses over a period of 7-10 days to achieve high intraocular concentration faster (AIII); plus Valganciclovir 900 mg PO BID for 14–21 days, then 900mg once daily (AI): <p><u>For Peripheral Lesions:</u></p> <ul style="list-style-type: none"> Valganciclovir 900 mg PO BID for 14–21 days, then 900 mg once daily (AI) <p><u>Chronic Maintenance:</u></p> <ul style="list-style-type: none"> Valganciclovir 900 mg PO daily (AI) for 3-6 months until ART induced immune recovery (see Table 4) <p><u>CMV Esophagitis or Colitis:</u></p> <ul style="list-style-type: none"> Ganciclovir 5 mg/kg IV q12h; may switch to valganciclovir 900 mg PO q12h once the patient can tolerate oral therapy (BI) Duration: 21–42 days or until symptoms have resolved (CII) Maintenance therapy is usually not necessary, but should be considered after relapses (BII). <p><u>Well-Documented, Histologically Confirmed CMV Pneumonia:</u></p> <ul style="list-style-type: none"> 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. <p><u>CMV Neurological Disease</u></p> <p>Note: Treatment should be initiated promptly.</p> <ul style="list-style-type: none"> Ganciclovir 5 mg/kg IV q12h + (foscarnet 90 mg/kg IV q12h or 60 mg/kg IV q8h) to stabilize disease and maximize response, continue until symptomatic improvement and resolution of neurologic symptoms (CIII) 	<p><u>CMV Retinitis</u></p> <p><i>For Immediate Sight-Threatening Lesions (within 1500 microns of the fovea): Intravitreal therapy as listed in the Preferred section, plus one of the following:</i></p> <p><u>Alternative Systemic Induction Therapy (followed by Chronic Maintenance Therapy):</u></p> <ul style="list-style-type: none"> Ganciclovir 5 mg/kg IV q12h for 14–21 days (AI), or Foscarnet 90 mg/kg IV q12h or 60 mg/kg q8h for 14–21 days (AI), 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) (BI). (Note: This regimen should be avoided in patients with sulfa allergy because of cross hypersensitivity with probenecid.) <p><u>Chronic Maintenance (for 3-6 months until ART induced immune recovery (see Table 4):</u></p> <ul style="list-style-type: none"> Ganciclovir 5 mg/kg IV 5–7 times weekly (AI), or 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) <p><u>CMV Esophagitis or Colitis:</u></p> <ul style="list-style-type: none"> Foscarnet 90 mg/kg IV q12h or 60 mg/kg q8h (BI) for patients with treatment-limiting toxicities to ganciclovir or with ganciclovir resistance, or Valganciclovir 900 mg PO q12h 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). 	<p>The choice of therapy for CMV retinitis should be individualized, based on location and severity of the lesions, level of immunosuppression, and other factors (e.g., concomitant medications and ability to adhere to treatment) (AIII).</p> <p>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.</p> <p>The ganciclovir ocular implant, which is effective for treatment of CMV retinitis is no longer available. For sight threatening retinitis, intravitreal injections of ganciclovir or foscarnet can be given to achieve higher ocular concentration faster.</p> <p>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).</p> <p>IRU may develop in the setting of immune reconstitution.</p> <p><u>Treatment of IRU</u></p> <ul style="list-style-type: none"> Periocular corticosteroid or short courses of systemic steroid (BIII). <p>Initial therapy in patients with CMV retinitis, esophagitis, colitis, and pneumonitis should include initiation or optimization of ART (BIII).</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 16 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Cytomegalovirus (CMV) Disease, continued	<ul style="list-style-type: none"> The optimal duration of therapy and the role of oral valganciclovir have not been established. Optimize ART to achieve viral suppression and immune reconstitution (BIII). 		
Herpes Simplex Virus (HSV) Disease	<p><u>Orolabial Lesions (For 5–10 Days):</u></p> <ul style="list-style-type: none"> Valacyclovir 1 g PO BID (AIII), <i>or</i> Famciclovir 500 mg PO BID (AIII), <i>or</i> Acyclovir 400 mg PO TID (AIII) <p><u>Initial or Recurrent Genital HSV (For 5–14 Days):</u></p> <ul style="list-style-type: none"> Valacyclovir 1 g PO BID (AI), <i>or</i> Famciclovir 500 mg PO BID (AI), <i>or</i> Acyclovir 400 mg PO TID (AI) <p><u>Severe Mucocutaneous HSV:</u></p> <ul style="list-style-type: none"> Initial therapy acyclovir 5 mg/kg IV q8h (AIII) After lesions begin to regress, change to PO therapy as above. Continue until lesions are completely healed. <p><u>Chronic Suppressive Therapy</u></p> <p><i>For patients with severe recurrences of genital herpes (AI) or patients who want to minimize frequency of recurrences (AI):</i></p> <ul style="list-style-type: none"> Valacyclovir 500 mg PO BID (AI) Famciclovir 500 mg PO BID (AI) Acyclovir 400 mg PO BID (AI) Continue indefinitely regardless of CD4 cell count. 	<p><u>For Acyclovir-Resistant HSV</u></p> <p><i>Preferred Therapy:</i></p> <ul style="list-style-type: none"> Foscarnet 80–120 mg/kg/day IV in 2–3 divided doses until clinical response (AI) <p><i>Alternative Therapy (CIII):</i></p> <ul style="list-style-type: none"> IV cidofovir (dosage as in CMV retinitis), <i>or</i> Topical trifluridine, <i>or</i> Topical cidofovir, <i>or</i> Topical imiquimod <p><u>Duration of Therapy:</u></p> <ul style="list-style-type: none"> 21–28 days or longer 	<p>Patients with HSV infections can be treated with episodic therapy when symptomatic lesions occur, or with daily suppressive therapy to prevent recurrences.</p> <p>Topical formulations of trifluridine and cidofovir are not commercially available.</p> <p>Extemporaneous compounding of topical products can be prepared using trifluridine ophthalmic solution and the IV formulation of cidofovir.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 17 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Varicella Zoster Virus (VZV) Disease	<p><u>Primary Varicella Infection (Chickenpox)</u></p> <p><i>Uncomplicated Cases (For 5–7 Days):</i></p> <ul style="list-style-type: none"> • Valacyclovir 1 g PO TID (AII), or • Famciclovir 500 mg PO TID (AII) <p><i>Severe or Complicated Cases:</i></p> <ul style="list-style-type: none"> • Acyclovir 10–15 mg/kg IV q8h for 7–10 days (AIII) • May switch to oral valacyclovir, famciclovir, or acyclovir after defervescence if no evidence of visceral involvement (BIII). <p><u>Herpes Zoster (Shingles)</u></p> <p><i>Acute Localized Dermatomal:</i></p> <ul style="list-style-type: none"> • For 7–10 days; consider longer duration if lesions are slow to resolve • Valacyclovir 1 g PO TID (AII), or • Famciclovir 500 mg TID (AII) <p><i>Extensive Cutaneous Lesion or Visceral Involvement:</i></p> <ul style="list-style-type: none"> • Acyclovir 10–15 mg/kg IV q8h until clinical improvement is evident (AII) • May switch to PO therapy (valacyclovir, famciclovir, or acyclovir) after clinical improvement (i.e., when no new vesicle formation or improvement of signs and symptoms of visceral VZV), to complete a 10–14 day course (BIII). <p><u>Progressive Outer Retinal Necrosis (PORN):</u></p> <ul style="list-style-type: none"> • (Ganciclovir 5 mg/kg +/- foscarnet 90 mg/kg) IV q12h + (ganciclovir 2 mg/0.05mL +/- foscarnet 1.2 mg/0.05 ml) intravitreal injection BIW (AIII) • Initiate or optimize ART (AIII) <p><u>Acute Retinal Necrosis (ARN):</u></p> <ul style="list-style-type: none"> • (Acyclovir 10–15 mg/kg IV q8h) + (ganciclovir 2 mg/0.05mL intravitreal injection BIW X 1–2 doses) for 10–14 days, followed by valacyclovir 1g PO TID for 6 weeks (AIII) 	<p><u>Primary Varicella Infection (Chickenpox)</u></p> <p><i>Uncomplicated Cases (For 5–7 Days):</i></p> <ul style="list-style-type: none"> • Acyclovir 800 mg PO 5 times/day (BII) <p><u>Herpes Zoster (Shingles)</u></p> <p><i>Acute Localized Dermatomal:</i></p> <ul style="list-style-type: none"> • For 7–10 days; consider longer duration if lesions are slow to resolve • Acyclovir 800 mg PO 5 times/day (BII) 	<p>In managing VZV retinitis - Consultation with an ophthalmologist experienced in management of VZV retinitis is strongly recommended (AIII).</p> <p>Duration of therapy for VZV retinitis is not well defined, and should be determined based on clinical, virologic, and immunologic responses and ophthalmologic responses.</p> <p>Optimization of ART is recommended for serious and difficult-to-treat VZV infections (e.g., retinitis, encephalitis) (AIII).</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 18 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments		
HHV-8 Diseases <i>(Kaposi Sarcoma [KS], Primary Effusion Lymphoma [PEL], Multicentric Castleman's Disease [MCD])</i>	<p><u>Mild To Moderate KS (ACTG Stage T0):</u></p> <ul style="list-style-type: none">Initiate or optimize ART (AII) <p><u>Advanced KS [ACTG Stage T1, Including Disseminated Cutaneous (AI) Or Visceral KS (BIII)]:</u></p> <ul style="list-style-type: none">Chemotherapy (per oncology consult) + ART <p><u>Primary Effusion Lymphoma:</u></p> <ul style="list-style-type: none">Chemotherapy (per oncology consult) + ART (AI)PO valganciclovir or IV ganciclovir can be used as adjunctive therapy (CIII). <p><u>MCD:</u></p> <ul style="list-style-type: none">Valganciclovir 900 mg PO BID for 3 weeks (CII), orGanciclovir 5 mg/kg IV q12h for 3 weeks (CII), orValganciclovir 900 mg PO BID + zidovudine 600 mg PO q6h for 7–21 days (CII)	<p><u>MCD</u></p> <ul style="list-style-type: none">Rituximab (375 mg/m² given weekly for 4–8 weeks) may be an alternative to or used adjunctively with antiviral therapy (CII).	<ul style="list-style-type: none">Patients who received rituximab for MCD may experience subsequent exacerbation or emergence of KS		
Human Papillomavirus (HPV) Disease	<p>Treatment of Condyloma Acuminata (Genital Warts)</p> <table><tr><td><p><u>Patient-Applied Therapy for Uncomplicated External Warts That Can Be Easily Identified by Patients:</u></p><ul style="list-style-type: none">Podophyllotoxin (e.g., podofilox 0.5% solution or 0.5% gel): Apply to all lesions BID 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), orImiquimod 5% cream: Apply to lesion at bedtime and remove in the morning on 3 non-consecutive nights weekly for up to 16 weeks, until lesions are no longer visible. Each treatment should be washed with soap and water 6–10 hours after application (BII), orSinecatechins 15% ointment: Apply to affected areas TID for up to 16 weeks, until warts are completely cleared and not visible (BIII).</td><td><p><u>Provider-Applied Therapy for Complex or Multicentric Lesions, or Lesions Inaccessible to Patient</u></p><p><i>Applied Therapy:</i></p><ul style="list-style-type: none">Cryotherapy (liquid nitrogen or cryoprobe): Apply until each lesion is thoroughly frozen. Repeat every 1–2 weeks for up to 4 weeks, until lesions are no longer visible (BIII). Some providers allow the lesion to thaw, then freeze a second time in each session (BIII), orTrichloroacetic 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), orSurgical excision (BIII) or laser surgery (CIII) to external or anal warts, orPodophyllin resin 10%–25% in tincture of benzoin: Apply to all lesions (up to 10 cm²), then wash off a few hours later, repeat weekly for up to 6 weeks until lesions are no longer visible (CIII).</td></tr></table>		<p><u>Patient-Applied Therapy for Uncomplicated External Warts That Can Be Easily Identified by Patients:</u></p> <ul style="list-style-type: none">Podophyllotoxin (e.g., podofilox 0.5% solution or 0.5% gel): Apply to all lesions BID 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), orImiquimod 5% cream: Apply to lesion at bedtime and remove in the morning on 3 non-consecutive nights weekly for up to 16 weeks, until lesions are no longer visible. Each treatment should be washed with soap and water 6–10 hours after application (BII), orSinecatechins 15% ointment: Apply to affected areas TID for up to 16 weeks, until warts are completely cleared and not visible (BIII).	<p><u>Provider-Applied Therapy for Complex or Multicentric Lesions, or Lesions Inaccessible to Patient</u></p> <p><i>Applied Therapy:</i></p> <ul style="list-style-type: none">Cryotherapy (liquid nitrogen or cryoprobe): Apply until each lesion is thoroughly frozen. Repeat every 1–2 weeks for up to 4 weeks, until lesions are no longer visible (BIII). Some providers allow the lesion to thaw, then freeze a second time in each session (BIII), orTrichloroacetic 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), orSurgical excision (BIII) or laser surgery (CIII) to external or anal warts, orPodophyllin resin 10%–25% in tincture of benzoin: Apply to all lesions (up to 10 cm²), then wash off a few hours later, repeat weekly for up to 6 weeks until lesions are no longer visible (CIII).	<p>HIV-infected patients may have larger or more numerous warts and may not respond as well to therapy for genital warts when compared to HIV-uninfected individuals.</p> <p>Topical cidofovir has activity against genital warts, but the product is not commercially available (CIII).</p> <p>Intralesional interferon-alpha is usually not recommended because of high cost, difficult administration, and potential for systemic side effects (CIII).</p> <p>The rate of recurrence of genital warts is high despite treatment in HIV-infected patients.</p> <p>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.</p>
<p><u>Patient-Applied Therapy for Uncomplicated External Warts That Can Be Easily Identified by Patients:</u></p> <ul style="list-style-type: none">Podophyllotoxin (e.g., podofilox 0.5% solution or 0.5% gel): Apply to all lesions BID 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), orImiquimod 5% cream: Apply to lesion at bedtime and remove in the morning on 3 non-consecutive nights weekly for up to 16 weeks, until lesions are no longer visible. Each treatment should be washed with soap and water 6–10 hours after application (BII), orSinecatechins 15% ointment: Apply to affected areas TID for up to 16 weeks, until warts are completely cleared and not visible (BIII).	<p><u>Provider-Applied Therapy for Complex or Multicentric Lesions, or Lesions Inaccessible to Patient</u></p> <p><i>Applied Therapy:</i></p> <ul style="list-style-type: none">Cryotherapy (liquid nitrogen or cryoprobe): Apply until each lesion is thoroughly frozen. Repeat every 1–2 weeks for up to 4 weeks, until lesions are no longer visible (BIII). Some providers allow the lesion to thaw, then freeze a second time in each session (BIII), orTrichloroacetic 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), orSurgical excision (BIII) or laser surgery (CIII) to external or anal warts, orPodophyllin resin 10%–25% in tincture of benzoin: Apply to all lesions (up to 10 cm²), then wash off a few hours later, repeat weekly for up to 6 weeks until lesions are no longer visible (CIII).				

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 19 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Hepatitis B Virus (HBV) Disease	<p>ART regimen which includes 2 drugs that are active against both HBV and HIV is recommended for all HIV/HBV-co-infected patients regardless of CD4 cell count and HBV DNA level (AII).</p> <p>Tenofovir alafenamide (TAF)/emtricitabine or tenofovir disoproxil fumarate (TDF)/emtricitabine PO once daily (+ additional drug (s) for HIV) (AIII).</p> <p>The choice of TAF vs. TDF should be based on renal function and risk of renal or bone toxicities.</p> <p><u>CrCl >60 mL/min</u> TDF 300 mg plus (FTC 200 mg or 3TC 300 mg)] or [TAF (10 or 25 mg)^a plus FTC 200 mg] PO once daily (AIII).</p> <p><u>CrCl 30-59 mL/min</u> TAF (10 or 25 mg)^a + FTC 200 mg PO once daily (AII)</p> <p><u>CrCl <30 mL/min</u> A fully suppressive ART regimen without tenofovir should be used, with the addition of renally dosed entecavir to the regimen</p> <p><u>Duration:</u> Continue treatment indefinitely (AIII)</p>	<p><u>If TAF or TDF Cannot Be Used as Part of HIV/HBV Therapy:</u> Use entecavir (dose adjustment according to renal function) plus a fully suppressive ART regimen without TAF or TDF (BIII).</p> <p><u>CrCl < 30 mL/min</u> ART with renally dose adjusted TDF and FTC can be used (BIII) if recovery of renal function is unlikely (See Table 7 for dosage recommendation)</p> <p><u>If patient is not receiving ART:</u></p> <ul style="list-style-type: none"> • HBV treatment is indicated for elevated ALT, HBV DNA >2000mIU/mL, significant liver fibrosies, advanced liver disease or cirrhosis (AI) • Peginterferon alfa-2a 180 µg SQ once weekly for 48 weeks (CIII), or • Peginterferon alfa 2b 1.5 µg/kg SQ once weekly for 48 weeks (CIII) 	<p>Chronic administration of lamivudine or emtricitabine as the only active drug against HBV should be avoided because of high rate of selection of HBV resistance (AI).</p> <p>Directly acting HBV drugs such as adefovir, emtricitabine, entecavir, lamivudine, telbivudine, or tenofovir must not be given in the absence of a fully suppressive ART regimen to avoid selection of drug resistance HIV (AI).</p> <p>When changing ART regimens, continue agents with anti-HBV activity (BIII).</p> <p>If anti-HBV therapy is discontinued and a flare occurs, therapy should be re-instituted because it can be potentially life-saving (AIII).</p> <p>As HBV reactivation can occur during treatment for HCV with directly active agents (DAAs) in the absence of HBV-active drugs, all HIV-HBV-coinfected patients who will be treated for HCV should be on HBV-active ART at the time of HCV treatment initiation (AII)</p>
Hepatitis C Virus (HCV) Disease	The field of HCV drug development is evolving rapidly. The armamenarium of approved drugs is likely to expand considerably in the next few years. Clinicians should refer to the most recent HCV treatment guidelines (http://www.hcvguidelines.org) for the most updated recommendations.		
Progressive Multifocal Leukoencephalopathy (PML) (JC Virus Infections)	<p>There is no specific antiviral therapy for JC virus infection. The main treatment approach is to reverse the immunosuppression caused by HIV.</p> <p>Initiate ART immediately in ART-naïve patients (AII).</p> <p>Optimize ART in patients who develop PML in phase of HIV viremia on ART (AIII)</p>	None.	Corticosteroids may be used for PML-IRIS characterized by contrast enhancement, edema or mass effect, and with clinical deterioration (BIII) (see text for further discussion).

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 20 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Malaria	<p>Because <i>Plasmodium falciparum</i> malaria can progress within hours from mild symptoms or low-grade fever to severe disease or death, all HIV-infected patients with confirmed or suspected <i>P. falciparum</i> infection should be hospitalized for evaluation, initiation of treatment, and observation (AIII).</p> <p>Treatment recommendations for HIV-infected patients are the same as HIV-uninfected patients (AIII).</p> <p>Choice of therapy is guided by the degree of parasitemia, the species of <i>Plasmodium</i>, the patient's clinical status, region of infection, and the likely drug susceptibility of the infected species, and can be found at http://www.cdc.gov/malaria.</p>	<p>When suspicion for malaria is low, antimalarial treatment should not be initiated until the diagnosis is confirmed.</p>	<p>For treatment recommendations for specific regions, clinicians should refer to the following web link: http://www.cdc.gov/malaria/ or call the CDC Malaria Hotline: (770) 488-7788: M–F 8 AM–4:30 PM ET, or (770) 488-7100 after hours</p>
Leishmaniasis, visceral	<p><u>For Initial Infection:</u></p> <ul style="list-style-type: none"> • Liposomal amphotericin B 2–4 mg/kg IV daily (AII), <i>or</i> • 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) <p><u>Chronic Maintenance Therapy (Secondary Prophylaxis); Especially in Patients with CD4 Count <200 cells/μL:</u></p> <ul style="list-style-type: none"> • Liposomal amphotericin B 4 mg/kg every 2–4 weeks (AII), <i>or</i> • Amphotericin B lipid complex (AII) 3 mg/kg every 21 days (AII) 	<p><u>For Initial Infection:</u></p> <ul style="list-style-type: none"> • Other lipid formulation of amphotericin B, dose and schedule as in Preferred Therapy, <i>or</i> • Amphotericin B deoxycholate 0.5–1.0 mg/kg IV daily for total dose of 1.5–2.0 g (BII), <i>or</i> • Sodium stibogluconate (pentavalent antimony) (BII) 20 mg/kg IV or IM daily for 28 days. <p><u>Another Option:</u></p> <ul style="list-style-type: none"> • Miltefosine 100 mg PO daily for 4 weeks (available in the United States under a treatment IND) (CIII) <p><u>Chronic Maintenance Therapy (Secondary Prophylaxis):</u></p> <ul style="list-style-type: none"> • Sodium stibogluconate 20 mg/kg IV or IM every 4 weeks (BII) 	<p>ART should be initiated or optimized (AIII).</p> <p>For sodium stibogluconate, contact the CDC Drug Service at (404) 639-3670 or drugservice@cdc.gov.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 21 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Leishmaniasis, cutaneous	<ul style="list-style-type: none"> • Liposomal amphotericin B 2–4 mg/kg IV daily for 10 days (BIII), <i>or</i> • 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), <i>or</i> • Sodium stibogluconate 20 mg/kg IV or IM daily for 3–4 weeks (BIII) <p><u>Chronic Maintenance Therapy:</u> May be indicated in immunocompromised patients with multiple relapses (CIII)</p>	<p><u>Possible Options Include:</u></p> <ul style="list-style-type: none"> • Oral miltefosine (can be obtained via a treatment IND), <i>or</i> • Topical paromomycin, <i>or</i> • Intralesional sodium stibogluconate, <i>or</i> • Local heat therapy <p>No data exist for any of these agents in HIV-infected patients; choice and efficacy dependent on species of <i>Leishmania</i>.</p>	None.
Chagas Disease (American Trypanosomiasis)	<p><u>For Acute, Early Chronic, and Re-Activated Disease:</u></p> <ul style="list-style-type: none"> • Benznidazole 5–8 mg/kg/day PO in 2 divided doses for 30–60 days (BIII) (not commercially available in the United States; contact the CDC Drug Service at drugservice@cdc.gov or (404) 639-3670, or the CDC emergency operations center at (770) 488-7100) 	<p><u>For Acute, Early Chronic, and Reactivated Disease</u></p> <p>Nifurtimox 8–10 mg/kg/day PO for 90–120 days (CIII) (not commercially available in the U.S., contact the CDC Drug Service at drugservice@cdc.gov or (404) 639-3670, or the CDC emergency operations center at (770) 488-7100)</p>	<p>Treatment is effective in reducing parasitemia and preventing clinical symptoms or slowing disease progression. It is ineffective in achieving parasitological cure.</p> <p>Duration of therapy has not been studied in HIV-infected patients.</p> <p>Initiate or optimize ART in patients undergoing treatment for Chagas disease, once they are clinically stable (AIII).</p>
Penicilliosis marneffei	<p><u>For Acute Infection in Severely Ill Patients:</u></p> <ul style="list-style-type: none"> • Liposomal amphotericin B 3–5 mg/kg/day IV for 2 weeks, followed by itraconazole 200 mg PO BID for 10 weeks (AII), followed by chronic maintenance therapy (as below) <p><u>For Mild Disease:</u></p> <ul style="list-style-type: none"> • Itraconazole 200 mg PO BID for 8 weeks (BII); followed by chronic maintenance therapy (as below) <p><u>Chronic Maintenance Therapy (Secondary Prophylaxis):</u></p> <ul style="list-style-type: none"> • Itraconazole 200 mg PO daily (AI) 	<p><u>For Acute Infection in Severely Ill Patients:</u></p> <ul style="list-style-type: none"> • Voriconazole 6 mg/kg IV q12h for 1 day, then 4 mg/kg IV q12h for at least 3 days, followed by 200 mg PO BID for a maximum of 12 weeks (BII), followed by maintenance therapy <p><u>For Mild Disease:</u></p> <ul style="list-style-type: none"> • Voriconazole 400 mg PO BID for 1 day, then 200 mg BID for a maximum of 12 weeks (BII), followed by chronic maintenance therapy 	<p>ART should be initiated simultaneously with treatment for penicilliosis to improve treatment outcome (CIII).</p> <p>Itraconazole and voriconazole may have significant interactions with certain ARV agents. These interactions are complex and can be bi-directional. Refer to Table 5 for dosage recommendations.</p> <p>Therapeutic drug monitoring and dosage adjustment may be necessary to ensure triazole antifungal and ARV efficacy and reduce concentration-related toxicities.</p>

Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 22 of 22)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
Isosporiasis	<p>For Acute Infection:</p> <ul style="list-style-type: none"> • TMP-SMX (160 mg/800 mg) PO (or IV) QID for 10 days (AII), <i>or</i> • TMP-SMX (160 mg/800 mg) PO (or IV) BID for 7–10 days (BI) • Can start with BID 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 mal-absorption. <p><u>Chronic Maintenance Therapy (Secondary Prophylaxis):</u></p> <ul style="list-style-type: none"> • In patients with CD4 count <200/μL, TMP-SMX (160 mg/800 mg) PO TIW (AI) 	<p>For Acute Infection:</p> <ul style="list-style-type: none"> • Pyrimethamine 50–75 mg PO daily + leucovorin 10–25 mg PO daily (BIII), <i>or</i> • Ciprofloxacin 500 mg PO BID for 7 days (CI) as a second line alternative <p><u>Chronic Maintenance Therapy (Secondary Prophylaxis):</u></p> <ul style="list-style-type: none"> • TMP-SMX (160 mg/800 mg) PO daily or (320 mg/1600 mg) three times weekly (BIII) • Pyrimethamine 25 mg PO daily + leucovorin 5–10 mg PO daily (BIII) • Ciprofloxacin 500 mg three times weekly (CI) as a second-line alternative 	<p>Fluid and electrolyte management in patients with dehydration (AIII).</p> <p>Nutritional supplementation for malnourished patients (AIII).</p> <p>Immune reconstitution with ART may result in fewer relapses (AIII).</p>

Key to Acronyms: ACTG = AIDS Clinical Trials Group; ART = antiretroviral therapy; ARV = antiretroviral; ATV/r = ritonavir-boosted atazanavir; BID = twice a day; BIW = twice weekly; BOC = boceprevir; CD4 = CD4 T lymphocyte cell; CDC = The Centers for Disease Control and Prevention; CFU = colony-forming unit; CNS = central nervous system; CSF = cerebrospinal fluid; CYP3A4 = Cytochrome P450 3A4; ddl = didanosine; DOT = directly-observed therapy; DS = double strength; EFV = efavirenz; EMB = ethambutol; g = gram; G6PD = Glucose-6-phosphate dehydrogenase; GI = gastrointestinal; ICP = intracranial pressure; ICU = intensive care unit; IM = intramuscular; IND = investigational new drug; INH = isoniazid; IRIS = immune reconstitution inflammatory syndrome; IV = intravenous; LP = lumbar puncture; mg = milligram; mmHg = millimeters of mercury; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NSAID = non-steroidal anti-inflammatory drugs; PegIFN = Pegylated interferon; PI = protease inhibitor; PO = oral; PORN = Progressive Outer Retinal Necrosis; PZA = pyrazinamide; qAM = every morning; QID = four times a day; q(n)h = every “n” hours; qPM = every evening; RBV = ribavirin; RFB = rifabutin; RIF = rifampin; SQ = subcutaneous; SS = single strength; TID = three times daily; TVR = telaprevir; TMP-SMX = trimethoprim-sulfamethoxazole; ZDV = zidovudine

^a Refer to <http://www.daraprimdirect.com> for information regarding how to access pyrimethamine

Evidence Rating:

Strength of Recommendation:

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

Quality of Evidence for the Recommendation:

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

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

Table 3. Recommended Doses of First-Line Drugs for Treatment of Tuberculosis in Adults and Adolescents (Last updated May 18, 2017; last reviewed May 18, 2017)

Drug	Daily
Isoniazid	5 mg/kg (usual dose 300 mg)
Rifampin^a	10 mg/kg (usual dose 600 mg)
Note: Rifampin is not recommended in patients receiving HIV PIs, ETR, RPV, EVG/COBI, or TAF	
Rifabutin^a	5 mg/kg (usual dose 300 mg)
without HIV PIs, EFV, RPV	
with HIV PIs	150 mg ^b
with EFV	450–600 mg
with TAF or EVG/COBI containing regimens	not recommended
Pyrazinamide (weight-based dosing)	1000 mg (18.2–25.0 mg/kg)
40–55 kg	
56–75 kg	1500 mg (20.0–26.8 mg/kg)
76–90 kg	2000 mg (22.2–26.3 mg/kg)
>90 kg	2000 mg ^c
Ethambutol	800 mg (14.5–20.0 mg/kg)
40–55 kg	
56–75 kg	1200 mg (16.0–21.4 mg/kg)
76–90 kg	1600 mg (17.8–21.1 mg/kg)
>90 kg	1600 mg ^c

^a For more detailed guidelines on use of different antiretroviral drugs with rifamycin, clinicians should refer to the [Drug Interactions](#) section of the [Adult and Adolescent ARV Guidelines](#)

^b Acquired rifamycin resistance has been reported in patients with inadequate rifabutin levels while on 150 mg twice weekly dosing together with ritonavir-boosted PIs. May consider therapeutic drug monitoring when rifabutin is used with a ritonavir-boosted PI and adjust dose accordingly.

^c Monitor for therapeutic response and consider therapeutic drug monitoring to assure dosage adequacy in patients who weigh >90 kg.

Key to Acronyms: COBI = cobicistat; EFV = efavirenz; EVG = elvitegravir; FTC = emtricitabine; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; TAF = tenofovir alafenamide

Table 4. Indications for Discontinuing and Restarting Opportunistic Infection Secondary Prophylaxis or Chronic Maintenance in HIV-Infected Adults and Adolescents (page 1 of 3) (Last updated July 25, 2017; last reviewed July 25, 2017)

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
<i>Pneumocystis</i> Pneumonia	CD4 count increased from <200 to >200 cells/μL for >3 months in response to ART (AI) Can consider when CD4 count 100-200 cells/μL if HIV RNA remain below limits of detection for at least 3-6 months (BII)	CD4 count <100 cells/mm ³ (AIII) CD4 count 100-200 cells/μL and with HIV RNA above detection limit of the assay (AIII).	CD4 count increased from <200 cells/μL to >200 cells/μL for >3 months in response to ART (BII) Can consider when CD4 count 100-200 cells/μL if HIV RNA remain below limits of detection for at least 3-6 months (BII) If PCP occurs at a CD4 count >200 cells/μL while not on ART, discontinuation of prophylaxis can be considered once HIV RNA levels are suppressed to below limits of detection for at least 3 to 6 months (CIII). Note: If PCP occurs at a CD4 count >200 cells/μL while on ART, continue PCP prophylaxis for life, regardless of how high the CD4 cell count rises as a consequence of ART (BIII).	<ul style="list-style-type: none"> • CD4 count <100 cells/μL (AIII) • CD4 count 100-200 cells/μL and with HIV RNA above detection limit of the assay (AIII).
<i>Toxoplasma gondii</i> Encephalitis	CD4 count increased to >200 cells/μL for >3 months in response to ART (AI) Can consider when CD4 count 100-200 cells/μL if HIV RNA remain below limits of detection for at least 3-6 months (BII)	CD4 count <100 cells/μL, (AIII) CD4 count 100-200 cells/μL and with HIV RNA above detection limit of the assay (AIII).	Successfully completed initial therapy, remain free of signs and symptoms of TE, and CD4 count >200 cells/μL for >6 months in response to ART (BI).	CD4 count <200 cells/μL (AIII)
Microsporidiosis	Not applicable	Not applicable	No signs and symptoms of non-ocular (BIII) or ocular (CIII) microsporidiosis and CD4 count >200 cells/μL for >6 months in response to ART.	No recommendation
Disseminated <i>Mycobacterium avium</i> Complex Disease	CD4 count >100 cells/μL for ≥3 months in response to ART (AI)	CD4 count <50 cells/μL (AIII)	<u>If the following criteria are fulfilled (AI):</u> <ul style="list-style-type: none"> • Completed ≥12 months of therapy, and • No signs and symptoms of MAC disease, and • Have sustained (>6 months) CD4 count >100 cells/μL in response to ART. 	CD4 count <100 cells/μL (AIII)
Salmonellosis	Not applicable	Not applicable	Resolution of <i>Salmonella</i> infection and after response to ART with sustained viral suppression and CD4 counts >200 cells/μL (CII)	No recommendation

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

Opportunistic Infection	Indication for Discontinuing Primary Prophylaxis	Indication for Restarting Primary Prophylaxis	Indication for Discontinuing Secondary Prophylaxis/Chronic Maintenance Therapy	Indication for Restarting Secondary Prophylaxis/Chronic Maintenance
Bartonellosis	Not applicable	Not applicable	<ul style="list-style-type: none"> Received at least 3–4 months of treatment, <i>and</i> CD4 count >200 cells/μL for ≥6 months (CIII) Some specialists would only discontinue therapy if <i>Bartonella</i> titers have also decreased by four-fold (CIII). 	No recommendation
Mucosal Candidiasis	Not applicable	Not applicable	If used, reasonable to discontinue when CD4 count >200 cells/μL (AIII) .	No recommendation
Cryptococcal Meningitis	Not applicable	Not applicable	<p><u>If the following criteria are fulfilled (BII):</u></p> <ul style="list-style-type: none"> Completed initial (induction and consolidation) therapy, <i>and</i> Received at least 1 year of maintenance therapy, <i>and</i> Remain asymptomatic of cryptococcal infection, <i>and</i> CD4 count ≥100 cells/μL for >3 months, and with suppressed plasma HIV RNA in response to ART 	CD4 count <100 cells/μL (AIII)
<i>Histoplasma capsulatum</i> Infection	CD4 count >150 cells/μL for 6 months while on ART (BIII)	For patients at high risk of acquiring histoplasmosis, restart at CD4 count <150 cells/μL (CIII)	<p><u>If the following criteria (AI) are fulfilled:</u></p> <ul style="list-style-type: none"> Received itraconazole for >1 year, <i>and</i> Negative fungal blood cultures, <i>and</i> CD4 count ≥150 cells/μL for ≥6 months in response to ART, <i>and</i> Serum <i>Histoplasma</i> antigen <2 ng/mL 	CD4 count <150 cells/mm ³ (BIII)
Coccidioidomycosis	CD4 count ≥250 cells/μL and with viral suppression while on ART (CIII)	Restart at CD4 count <250 cells/μL (BIII)	<p><u>Only for patients with focal coccidioidal pneumonia (AII):</u></p> <ul style="list-style-type: none"> Clinically responded to ≥ 6 months antifungal therapy, with CD4 count ≥250 cells/mm³, and with viral suppression while on ART. Should continue monitoring for recurrence with serial chest radiographs and coccidioidal serology every 6-12 months. <p><u>For patients with diffuse pulmonary (BIII), disseminated non-meningeal (BIII):</u></p> <ul style="list-style-type: none"> Therapy is at least 12 months and usually much longer; discontinuation is dependent on clinical and serological response and should be made in consultation with experts <p><u>For meningeal diseases (AII):</u></p> <p>Suppressive therapy should be continued indefinitely, even with increase in CD4 count on ART.</p>	No recommendation

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

Opportunistic Infection	Indication for Discontinuing Primary Prophylaxis	Indication for Restarting Primary Prophylaxis	Indication for Discontinuing Secondary Prophylaxis/Chronic Maintenance Therapy	Indication for Restarting Secondary Prophylaxis/Chronic Maintenance
Cytomegalovirus Retinitis	Not applicable	Not applicable	<ul style="list-style-type: none"> • CMV treatment for at least 3 to 6 months; and with CD4 count >100 cells/μL for >3 to 6 months in response to ART (AII). • Therapy should be discontinued only after consultation with an ophthalmologist, taking into account anatomic location of lesions, vision in the contralateral eye, and feasibility of regular ophthalmologic monitoring. • Routine (i.e., every 3 months) ophthalmologic follow-up is recommended after stopping therapy for early detection of relapse or immune restoration uveitis, and then periodically after sustained immune reconstitution (AIII). 	CD4 count <100 cells/μL (AIII)
<i>Penicillium marneffei</i> Infection	CD4 count >100 cells/μL for >6 months in response to ART (BII)	CD4 count <100 cells/μL (BIII)	CD4 count >100 cells/μL for ≥6 months in response to ART (BII)	<ul style="list-style-type: none"> • CD4 count <100 cells/μL (AIII), or • If penicilliosis recurs at CD4 count >100 cells/μL (CIII)
Visceral Leishmaniasis (and possibly cutaneous leishmaniasis in immunocompromised patients with multiple relapses)	Not applicable	Not applicable	There is no consensus regarding when to stop secondary prophylaxis. Some investigators suggest that therapy can be stopped if CD4 count increases to >200 to 350 cells/μL for 3–6 months in response to ART, but others suggest that therapy should be continued indefinitely.	No recommendation
<i>Isospora belli</i> Infection	Not applicable	Not applicable	Sustained increase in CD4 count to >200 cells/μL for >6 months in response to ART and without evidence of <i>I. belli</i> infection (BIII)	No recommendation

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

Evidence Rating:

Strength of Recommendation:

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

Quality of Evidence for the Recommendation:

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

Table 5. Significant Pharmacokinetic Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 1 of 15) (Last updated March 13, 2017; last reviewed March 13, 2017)

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

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

“Do not co-administer”

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

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

“Co-administration should be avoided, if possible”

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

“Use with caution”

Drug combinations are recommended to be used with caution when:

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

Rifamycin-Related Interactions

Rifamycins are potent inducers of Phase I and Phase II drug metabolizing reactions. Daily doses of rifampin are well studied, and induction increases over a week or more. Based on limited data, larger doses of rifampin (e.g., 1200 mg) appear to produce the same maximum induction, but more rapidly. Single doses of rifampin may not produce significant induction. In general, rifabutin is about 40% as potent a CYP3A4 inducer as rifampin, but this can vary by substrate and enzymatic reaction. In general, daily rifapentine (for active tuberculosis [TB] disease) is at least as potent an inducer as rifampin. However, the potential of drug interactions with once weekly rifapentine (prescribed with isoniazid for latent TB infection) is not well studied, but may result in reduction of exposure of drugs that are CYP3A4 substrates. When a rifamycin is used with a potential interacting drug, close monitoring for clinical efficacy of the other agent is advised.

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

Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Artemether/ Lumefantrine	Clarithromycin	↑ Lumefantrine expected	Co-administration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
	Dasabuvir Ombitasvir Paritaprevir Ritonavir	↑ Artemether and lumefantrine possible	Use with caution. Monitor for artemether- and lumefantrine-associated toxicities.
	Erythromycin	↑ Lumefantrine possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Fluconazole	↑ Lumefantrine possible	Co-administration should be avoided, if possible. If co-administered, monitor for lumefantrine toxicities (e.g., QT prolongation).
	Itraconazole	↑ Lumefantrine expected	Co-administration should be avoided, if possible. If co-administered, monitor for lumefantrine toxicities (e.g., QT prolongation).
	Posaconazole	↑ Lumefantrine expected	Co-administration should be avoided, if possible. If co-administered, monitor for lumefantrine toxicities (e.g., QT prolongation).
	Rifabutin ^a	↓ Artemether, DHA, and lumefantrine expected	Use with caution. Monitor for antimalarial efficacy.
	Rifampin ^a	↓ Artemether, DHA, and lumefantrine AUC by 89%, 85%, and 68%, respectively	Do not co-administer.
	Rifapentine ^a	↓ Artemether, DHA, and lumefantrine expected	Do not co-administer.
	Voriconazole	↑ Lumefantrine expected	Co-administration should be avoided, if possible. If co-administered, monitor for lumefantrine toxicities (e.g., QT prolongation).
Atovaquone	Dasabuvir Ombitasvir Paritaprevir Ritonavir	↔ Atovaquone (based on data from atovaquone and atazanavir/ritonavir interaction)	No dosage adjustment necessary.
	Doxycycline	Atovaquone conc. ↓ by approximately 40% with tetracycline. No interaction study with doxycycline.	Dose adjustment not established; if co-administered, take atovaquone with fatty meal and monitor for decreased atovaquone efficacy.
	Rifabutin ^a	Atovaquone C _{SS} ↓ 34%; rifabutin C _{SS} ↓ 19%	Dose adjustment not established; if co-administered, take atovaquone with fatty meal and monitor for decreased atovaquone efficacy.
	Rifampin ^a	Atovaquone C _{SS} ↓ 52%; rifampin C _{SS} ↑ 37%	Do not co-administer.
	Rifapentine ^a	↓ Atovaquone expected	Do not co-administer.
Bedaquiline	Clarithromycin	↑ Bedaquiline expected	Co-administration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
	Dasabuvir Ombitasvir Paritaprevir Ritonavir	↑ Bedaquiline expected	Co-administration should be avoided, if possible. Consider alternative HCV regimen.

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

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

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

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

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

Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	Rifabutin ^a	↓ Daclatasvir expected	Dose not established. Consider increasing daclatasvir dose to 90 mg once daily and monitor for therapeutic efficacy.
	Rifampin ^a	Daclatasvir AUC ↓ 79%	Do not co-administer.
	Rifapentine ^a	↓ Daclatasvir expected	Dose not established. Consider increasing daclatasvir dose to 90 mg once daily and monitor for therapeutic efficacy.
	Simeprevir	Simeprevir AUC ↑ 44%; daclatasvir AUC ↑ 96%	No dosage adjustment. Monitor for simeprevir and daclatasvir-associated toxicities.
	Voriconazole	↑ Daclatasvir expected	Reduce daclatasvir dose to 30 mg once daily.
Dapsone	Rifabutin ^a	Dapsone AUC ↓ 27% to 40%	Co-administration should be avoided if possible. Consider alternatives for dapsone.
	Rifampin ^a	Dapsone conc. ↓ 7- to 10-fold and t _{1/2} ↓ from 24 to 11 hours	Co-administration should be avoided, if possible. Consider alternatives for dapsone.
	Rifapentine ^a	↓ Dapsone expected	Co-administration should be avoided, if possible. Consider alternatives for dapsone.
Dasabuvir Ombitasvir Paritaprevir Ritonavir	Artemether/ Lumefantrine	↑ Artemether and lumefantrine possible	Use with caution. Monitor for artemether- and lumefantrine-associated toxicities.
	Atovaquone	↔ Atovaquone (based on data from atovaquone and ritonavir/atazanavir interaction)	No dosage adjustment necessary.
	Bedaquiline	↑ Bedaquiline expected	Co-administration should be avoided, if possible. Consider alternative HCV regimen.
	Clarithromycin	↑ Clarithromycin and paritaprevir expected; ↑ ombitasvir and dasabuvir possible	Co-administration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
	Erythromycin	↑ Erythromycin expected and paritaprevir expected; ↑ ombitasvir and dasabuvir possible	Co-administration should be avoided, if possible. Consider azithromycin in place of erythromycin.
	Itraconazole	↑ Itraconazole and paritaprevir expected; ↑ ombitasvir and dasabuvir possible	Itraconazole doses >200 mg/day are not recommended unless dosing is guided by itraconazole levels. Monitor for itraconazole and HCV regimen-associated toxicities.
	Posaconazole	↑ Posaconazole and paritaprevir expected; ↑ ombitasvir and dasabuvir possible	Monitor for posaconazole and HCV regimen-associated toxicities. Monitor posaconazole conc. and adjust dose if necessary.
	Rifabutin ^a	↑ Rifabutin expected; ↓ paritaprevir possible	Co-administration should be avoided if possible. With co-administration, decrease rifabutin dose to 150 mg/day and monitor rifabutin conc. Monitor HCV regimen for efficacy.
	Rifampin ^a	↓ Paritaprevir, ritonavir, ombitasvir, and dasabuvir expected	Do not co-administer.
	Rifapentine ^a	↓ Paritaprevir, ritonavir, ombitasvir, and dasabuvir expected	Do not co-administer.
	Voriconazole	Voriconazole AUC ↓ 39% (with ritonavir); ↑ paritaprevir expected	Co-administer only if the benefits outweigh the risk. Monitor voriconazole conc. to guide dosage adjustments.

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

Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
Doxycycline	Atovaquone	Atovaquone concentration ↓ by approximately 40% with tetracycline. No interaction study with doxycycline.	Dose adjustment not established; if co-administered, take atovaquone with fatty meal and monitor for decreased atovaquone efficacy.
	Rifabutin ^a	No data. ↓ Doxycycline possible.	Monitor closely for doxycycline efficacy or consider alternative therapy.
	Rifampin ^a	Doxycycline AUC ↓ by 59%	Use with caution. Monitor closely for doxycycline efficacy or consider alternative therapy.
	Rifapentine ^a	No data. ↓ Doxycycline possible.	Monitor closely for doxycycline efficacy or consider alternative therapy.
Elbasvir/ Grazoprevir	Clarithromycin	↑ Elbasvir and grazoprevir expected	Co-administration should be avoided, if possible. If co-administered, monitor closely for hepatotoxicity. Consider azithromycin in place of clarithromycin.
	Itraconazole	↑ Elbasvir and grazoprevir expected	Co-administration should be avoided, if possible. If co-administered, monitor closely for hepatotoxicity.
	Posaconazole	↑ Elbasvir and grazoprevir expected	Co-administration should be avoided, if possible. If co-administered, monitor closely for hepatotoxicity.
	Rifabutin ^a	↓ Elbasvir and grazoprevir possible	Co-administration should be avoided if possible. Consider alternative HCV regimen.
	Rifampin ^a	Grazoprevir AUC ↓ 7%, C ₂₄ ↓ 90%; ↓ elbasvir expected	Do not co-administer.
	Rifapentine ^a	↓ Elbasvir and grazoprevir possible	Do not co-administer.
	Voriconazole	↑ Elbasvir and grazoprevir expected	Co-administration should be avoided if possible. If co-administered, monitor closely for hepatotoxicity.
Erythromycin	Artemether/ Lumefantrine	↑ Lumefantrine possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Bedaquiline	↑ Bedaquiline possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Chloroquine	↑ Chloroquine possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Daclatasvir	↑ Daclatasvir possible	No dosage adjustment. Monitor for daclatasvir-associated toxicities.
	Dasabuvir Ombitasvir Paritaprevir Ritonavir	↑ Erythromycin and paritaprevir expected; ↑ ombitasvir and dasabuvir possible	Co-administration should be avoided, if possible. Consider azithromycin in place of erythromycin.
	Fluconazole	↑ Erythromycin possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Itraconazole	Itraconazole AUC ↑ 36%; ↑ erythromycin possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Mefloquine	↑ Mefloquine possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Posaconazole	↑ Erythromycin expected	Do not co-administer. Consider azithromycin in place of erythromycin.

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

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

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

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

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

Drug	Interacting Agent	Effect on Primary and/or Concomitant Drug Concentrations	Recommendations
	TDF	TDF AUC ↑ 98% (when given with EFV/FTC) TDF AUC ↑ 40% (when given with RPV/FTC) When used with EVG/c/TDF/FTC, ↑ TDF and ledipasvir expected	Monitor for TDF-associated toxicities when coadministered with PI/r, PI/c, or EFV. Consider an alternative to PI/r plus TDF/FTC or alternative HCV therapy if possible. Do not co-administer with EVG/c/TDF/FTC. Consider TAF in place of TDF.
Linezolid	Rifabutin ^a	No data. ↓ Linezolid possible.	Monitor for linezolid efficacy.
	Rifampin ^a	Linezolid AUC ↓ 32%	Monitor for linezolid efficacy.
	Rifapentine ^a	No data. ↓ Linezolid possible.	Monitor for linezolid efficacy.
Mefloquine	Clarithromycin	↑ Mefloquine expected	Use with caution. Consider azithromycin in place of clarithromycin. If co-administered, monitor for mefloquine toxicity (e.g., QT prolongation).
	Erythromycin	↑ Mefloquine possible	Do not co-administer. Consider azithromycin in place of erythromycin.
	Fluconazole	↑ Mefloquine possible	Co-administration should be avoided, if possible. If co-administered, monitor for mefloquine toxicities (e.g., QT prolongation).
	Itraconazole	↑ Mefloquine expected	Co-administration should be avoided, if possible. If co-administered, monitor for mefloquine toxicities (e.g., QT prolongation).
	Posaconazole	↑ Mefloquine expected	Co-administration should be avoided, if possible. If co-administered, monitor for mefloquine toxicities (e.g., QT prolongation).
	Rifabutin ^a	↓ Mefloquine possible	Monitor for mefloquine efficacy.
	Rifampin ^a	Mefloquine AUC ↓ 68%	Do not co-administer. Use alternative antimalarial drug or rifabutin.
	Rifapentine ^a	↓ Mefloquine expected	Do not co-administer. Use alternative antimalarial drug or rifabutin.
	Voriconazole	↑ Mefloquine expected	Co-administration should be avoided, if possible. If co-administered, monitor for mefloquine toxicities (e.g., QT prolongation).
Posaconazole	Artemether/Lumefantrine	↑ Lumefantrine expected	Co-administration should be avoided, if possible. If co-administered, monitor for lumefantrine toxicities (e.g., QT prolongation).
	Bedaquiline	↑ Bedaquiline expected	Co-administration should be avoided, if possible. If co-administered, monitor for bedaquiline toxicities (e.g., QT prolongation).
	Chloroquine	↑ Chloroquine expected	Co-administration should be avoided, if possible. If co-administered, monitor for chloroquine toxicities (e.g., QT prolongation).
	Clarithromycin	↑ Clarithromycin expected	Co-administration should be avoided, if possible. Consider azithromycin in place of clarithromycin.
	Daclatasvir	↑ Daclatasvir expected	Reduce daclatasvir dose to 30 mg once daily.

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

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

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

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

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

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

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

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

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

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

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

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

Key to Acronyms: 14-OH = active metabolite of clarithromycin; AUC = area under the curve; C₂₄ = concentration at 24h post dose; C_{min} = minimum concentration; C_{ss} = concentration at steady state; CYP3A4 = Cytochrome P450 3A4; des-Rbt = desacetyl rifabutin; DHA = dihydroartemisinin; EFV = efavirenz; EVG = elvitegravir; FTC = emtricitabine; HCV = hepatitis C virus; PI/c = cobicistat-boosted protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; RPV = rilpivirine; T_{1/2} = half-life; TAF = tenofovir alafenamide; TB = tuberculosis; TDF = tenofovir disoproxil fumarate

^a Rifamycins are potent inducers of Phase I and Phase II drug-metabolizing reactions. Daily doses of rifampin are well studied, and induction increases over a week or more. Based on limited data, larger doses of rifampin (for example, 1200 mg) appear to produce the same maximum induction, but more rapidly. Single doses of rifampin may not produce significant induction. In general, rifabutin is about 40% as potent a CYP3A4 inducer as rifampin, but this can vary by substrate and enzymatic reaction. In general, daily rifapentine (for active TB disease) is at least as potent an inducer as rifampin. However, the potential of drug interactions with once weekly rifapentine (for latent TB infection, along with isoniazid) is not well studied, but may result in reduction of exposure of drugs that are CYP3A4 substrates. When a rifamycin is used with a potential interacting drug, close monitoring for clinical efficacy of the other agent is advised.

Table 6. Common or Serious Adverse Reactions Associated With Drugs Used for Preventing or Treating Opportunistic Infections (page 1 of 6) (Last updated March 13, 2017; last reviewed March 13, 2017)

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

Table 6. Common or Serious Adverse Reactions Associated With Drugs Used for Preventing or Treating Opportunistic Infections (page 2 of 6)

Drugs	Common or Serious Adverse Reactions
Cephalosporins (for Ceftriaxone, see above)	Hypersensitivity reaction, rash, nausea, vomiting, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, bone marrow suppression, CNS toxicities such as seizure and confusion (rare, mostly seen with high doses used in patients with renal insufficiency or elderly patients without dosage adjustment), hemolytic anemia
Chloroquine and Hydroxychloroquine	Headache, pruritus, skin pigmentation, nausea, vomiting, abdominal pain, diarrhea, anorexia, photosensitivity, visual disturbances including blurry vision and retinal toxicity, auditory disturbances, QTc prolongation, cardiomyopathy, neuromyopathy (rare, but may occur with long-term use), bone marrow suppression, hemolysis (associated with G6PD deficiency), hypersensitivity reaction (including TEN, SJS, and EM), hepatitis, neuropsychiatric changes (including extrapyramidal reactions and suicidal behavior), convulsive seizures, severe hypoglycemia (may require adjustment of antidiabetic medications)
Cidofovir	Nephrotoxicity, proteinuria, ocular hypotony, anterior uveitis/iritis, neutropenia, metabolic acidosis (including Fanconi's syndrome), diarrhea, asthenia, fever, headache, alopecia, anemia Side effects most likely related to co-administration of probenecid: rash, nausea, vomiting, anorexia
Ciprofloxacin	Nausea, vomiting, abdominal pain, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, headache, dizziness, sleep disturbances, tendonitis and tendon rupture (associated with age >60 and concomitant steroid use), photosensitivity, hypoglycemia, hepatotoxicity, QTc prolongation, neurotoxicity (especially with high doses, use in elderly patients, or use in patients with renal dysfunction), seizures, peripheral neuropathy
Clarithromycin	Hepatotoxicity, ototoxicity (with high doses or prolonged use), headache, nausea, vomiting, abdominal cramps, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, rash, QTc prolongation, dysgeusia
Clindamycin	Nausea, vomiting, abdominal pain, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, rash, arrhythmia associated with rapid IV infusion, metallic taste (with IV infusion), thrombophlebitis, abnormal liver function tests
Clotrimazole (Troche)	Generally well-tolerated. Nausea, vomiting, anorexia, metallic taste, increase in serum transaminases (rare)
Cycloserine	Neuropsychiatric toxicities (headache, somnolence, lethargy, vertigo, tremor, dysarthria, irritability, confusion, paranoia, psychosis), seizures (particularly in patients with history of chronic alcoholism), allergic dermatitis, rash, elevated transaminases, congestive heart failure (in patients receiving cycloserine 1-1.5 g daily)
Dapsone	Methemoglobinemia, hemolytic anemia (especially in patients with G6PD deficiency), neutropenia, dermatologic reactions (including rash), sulfone syndrome (fever, exfoliative dermatitis, lymphadenopathy, hepatic necrosis, hemolysis), peripheral neuropathy, hepatotoxicity, drug-induced lupus erythematosus, nephrotic syndrome, phototoxicity
Daclatasvir	Fatigue, headache, nausea, anemia, bradycardia (when co-administered with sofosbuvir and amiodarone)
Dasabuvir, Ombitasvir, Paritaprevir, and Ritonavir	Hepatotoxicity, nausea, pruritus, rash, insomnia, fatigue, asthenia, dyspnea (associated with ribavirin co-administration)
Doxycycline	Photosensitivity reaction, nausea, vomiting, diarrhea, esophageal ulceration, thrombophlebitis (with IV infusion), hepatotoxicity (rare), intracranial hypertension, <i>C. difficile</i> -associated diarrhea and colitis, tissue hyperpigmentation
Elbasvir/Grazoprevir	Fatigue, headache, nausea, ALT elevations, anemia (when given with ribavirin)
Emtricitabine	Generally well-tolerated. Headache, nausea, skin hyperpigmentation, diarrhea, rash
Entecavir	Generally well-tolerated. Headache, fatigue, dizziness, nausea
Erythromycin	Nausea, vomiting, abdominal pain, anorexia, rash, hepatotoxicity, cholestatic jaundice, ototoxicity (hearing loss, tinnitus), rash, QTc prolongation and cardiac arrhythmia, <i>C. difficile</i> -associated diarrhea and colitis, thrombophlebitis (with IV infusion)

Table 6. Common or Serious Adverse Reactions Associated With Drugs Used for Preventing or Treating Opportunistic Infections (page 3 of 6)

Drugs	Common or Serious Adverse Reactions
Ethambutol	Optic neuritis (dose dependent), peripheral neuropathy, headache, nausea, vomiting, anorexia, hepatotoxicity, hyperuricemia, hypersensitivity reaction, disorientation, hallucinations
Ethionamide	Dose-dependent gastrointestinal side effects (nausea, vomiting, diarrhea, abdominal pain, metallic taste, anorexia), dizziness, drowsiness, depression, postural hypotension, hepatotoxicity, hypothyroidism (with or without goiter), gynecomastia, impotence, hypoglycemia
Famciclovir	Generally well-tolerated. Headache, nausea, vomiting, diarrhea, nephrotoxicity (in patients with underlying renal disease)
Flucytosine	Concentration-dependent bone marrow suppression (anemia, neutropenia, thrombocytopenia), diarrhea, nausea, vomiting, rash, hepatotoxicity
Fluconazole	Hepatotoxicity, rash, nausea, vomiting, diarrhea, abdominal discomfort, reversible alopecia (with doses ≥ 400 mg/d for >2 months), QTc prolongation
Foscarnet	Nephrotoxicity, electrolyte imbalances (hypocalcemia, hypomagnesemia, hypophosphatemia, hyperphosphatemia, hypokalemia), penile ulceration, nausea, vomiting, anorexia, headache, seizure (associated with electrolyte imbalances), anemia, injection-site associated thrombophlebitis
Fumagillin (Investigational)	Oral therapy: Neutropenia, thrombocytopenia, vertigo, nausea, vomiting, diarrhea, anorexia, abdominal cramps Ocular therapy: Minimal systemic effect or local effect
Ganciclovir	Neutropenia, thrombocytopenia, anemia, injection-site-associated thrombophlebitis, increased serum creatinine, carcinogenic and teratogenic potential, impaired fertility, neuropathy
Imipenem/Cilastatin	Hypersensitivity reaction (immediate or delayed), nausea, vomiting, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, thrombophlebitis, headache, bone marrow suppression, drug fever, CNS effects such as seizure, myoclonus, and confusion (especially with higher doses, in patients with underlying CNS disorders, or with renal insufficiency)
Interferon-Alfa and Peginterferon-Alfa	Flu-like syndrome (fever, headache, fatigue, and myalgia), neuropsychiatric disorders (depression and suicidal ideation), neutropenia, anemia, thrombocytopenia, thyroid dysfunction, injection-site reactions, alopecia, nausea, anorexia, diarrhea, weight loss, development or exacerbation of autoimmune disorders, ocular effects (retinal hemorrhage, retinal artery or vein obstructions, and cotton wool spots)
Isoniazid	Hepatotoxicity, peripheral neuropathy, optic neuritis, psychosis (rare), diarrhea, nausea
Itraconazole	Hepatotoxicity, congestive heart failure, edema, hypokalemia, nausea, vomiting, diarrhea, abdominal pain, rash, QTc prolongation, neuropathy
Lamivudine	Generally well-tolerated. Nausea, vomiting
Ledipasvir/Sofosbuvir	Fatigue, headache, asthenia (most common), nausea, diarrhea, insomnia, mild transient asymptomatic lipase elevation, mild bilirubin elevation
Levofloxacin	Nausea, vomiting, abdominal pain, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, headache, dizziness, sleep disturbances, tendonitis and tendon rupture (associated with >60 years of age and concomitant steroid use), photosensitivity, hypoglycemia, hepatotoxicity, QTc prolongation, neurotoxicity (especially with high doses, use in elderly patients, or use in patients with renal dysfunction), seizures (rare), peripheral neuropathy
Linezolid	Anemia, neutropenia, thrombocytopenia (especially with treatment lasting for longer than 2- to 4-weeks), peripheral neuropathy, optic neuritis with long-term therapy, serotonin syndrome (especially in patients receiving concomitant serotonergic agents), seizure (in patients with a history of seizure or with risk factors for seizure), lactic acidosis (rare), diarrhea, headache, nausea, vomiting
Mefloquine	Depression, psychosis, anxiety, rash (reports of TEN and SJS), nausea, vomiting, diarrhea, epigastric pain, agitation, dizziness, headache, insomnia, abnormal dreams, QTc prolongation, arrhythmias (extrasystole, sinus bradycardia), agranulocytosis/aplastic anemia

Table 6. Common or Serious Adverse Reactions Associated With Drugs Used for Preventing or Treating Opportunistic Infections (page 4 of 6)

Drugs	Common or Serious Adverse Reactions
Meropenem	Generally well-tolerated. Hypersensitivity reaction (immediate or delayed), nausea, vomiting, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, thrombophlebitis, headache, bone marrow suppression, drug fever
Micafungin	Generally well-tolerated. Histamine-related infusion reactions (such as flushing, rash, pruritus, hypotension, dyspnea) may occur, but these are rare if infusion lasts over 1 hour; anaphylaxis and anaphylactoid reaction, hepatotoxicity, thrombophlebitis, nausea, vomiting, diarrhea, hypokalemia, hemolysis (rare)
Miconazole Buccal Tablets	Dysgeusia, diarrhea, nausea, vomiting, upper abdominal pain, headache, local reactions (oral discomfort, burning, pain, tongue/mouth ulceration, gingival pruritus, swelling, dry mouth), hypersensitivity reaction (rare—may occur in patients with known hypersensitivity reaction to milk product concentrate)
Miltefosine	Nausea, vomiting, diarrhea, headache, motion sickness, leukocytosis, thrombocytosis, nephrotoxicity, retinal degeneration, elevated transaminases and bilirubin, teratogenic potential, impaired fertility
Moxifloxacin	Nausea, vomiting, abdominal pain, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, headache, dizziness, sleep disturbances, tendonitis and tendon rupture (associated with >60 years of age and concomitant steroid use), photosensitivity, hypoglycemia, hepatotoxicity, QTc prolongation, neurotoxicity (especially with high doses, use in elderly patients, or use in patients with renal dysfunction), seizures (rare), peripheral neuropathy
Nifurtimox	Anorexia, weight loss, nausea, vomiting, abdominal pain, headache, dizziness, mood changes, insomnia, myalgia, peripheral neuropathy, rash, pruritus, memory loss
Nitazoxanide	Generally well-tolerated. Nausea, vomiting, diarrhea, abdominal pain, headache
Nystatin (Oral Preparations)	Unpleasant taste, nausea, vomiting, anorexia, diarrhea, hypersensitivity reaction (rare)
Penicillin G	All Penicillin G Preparations: Hypersensitivity reactions (immediate or delayed reactions, including anaphylaxis), bone marrow suppression, nausea, vomiting, diarrhea, <i>C. difficile</i> -associated diarrhea and colitis, drug fever <u>Benzathine Penicillin G and Procaine Penicillin G</u> : IM injection-site reactions (pain and erythema), procaine neuropsychiatric reactions (high dose), neurovascular damage (as a result of inadvertent intravascular instead of IM injection) <u>Aqueous Crystalline Penicillin G (IV)</u> : Thrombophlebitis, neurotoxicity at high doses (especially in patients with renal dysfunction)
Pentamidine	<u>IV Infusion</u> : Nephrotoxicity, infusion-related hypotension, thrombophlebitis, QTc prolongation, arrhythmias (including torsades de pointes), pancreatitis, hypoglycemia, hyperglycemia, diabetes mellitus, hepatotoxicity, electrolyte abnormalities, leucopenia, thrombocytopenia <u>Aerosolized Therapy</u> : Bronchospasm, cough, dyspnea, tachypnea, metallic taste, pancreatitis (rare)
Pentavalent Antimony (Sodium Stibogluconate)	Nausea, vomiting, abdominal pain, anorexia, pancreatitis (rare), headache, hepatotoxicity, arthralgia, myalgia, cardiac toxicity with higher than 20 mg/kg dose, rash, thrombophlebitis, leukopenia, anemia, thrombocytopenia
Posaconazole	Nausea, vomiting, diarrhea, abdominal pain, headache, hepatotoxicity, hypokalemia, QTc prolongation, rash <u>IV Infusion</u> : Thrombophlebitis, cyclodextrin accumulation (especially in patients with eGFR <50 mL/min, which may lead to renal toxicities)
Piperacillin-Tazobactam	Generally well-tolerated. Hypersensitivity reaction, rash, diarrhea, nausea, vomiting, <i>C. difficile</i> -associated diarrhea and colitis, thrombophlebitis, thrombocytopenia (rare), impaired platelet aggregation, seizure (with high doses used in patients with renal insufficiency)
Primaquine	Methemoglobinemia, hemolytic anemia (especially in patients with G6PD deficiency), leukopenia, neutropenia, abdominal cramps, nausea, vomiting, QTc prolongation, pruritus, rash, dizziness

Table 6. Common or Serious Adverse Reactions Associated With Drugs Used for Preventing or Treating Opportunistic Infections (page 5 of 6)

Drugs	Common or Serious Adverse Reactions
Pyrimethamine	Neutropenia, thrombocytopenia, megaloblastic anemia, rash
Quinidine Glucuronate	QTc prolongation, lightheadedness, nausea, vomiting, diarrhea, abdominal pain, drug-induced SLE, headache, rash, hemolysis (with G6PD deficiency), hepatotoxicity, heartburn/esophagitis, cinchonism (tinnitus, vertigo, blurred vision)
Quinine	Headache, nausea, vomiting, diarrhea, cinchonism (tinnitus, vertigo, blurred vision), hypersensitivity reaction, hypoglycemia, thrombocytopenia, QTc prolongation
Ribavirin	Hemolytic anemia, dyspnea, hyperbilirubinemia, fatigue, myalgia, headache, nausea, vomiting, anorexia, dyspepsia, rash, dry cough, teratogenicity, hypersensitivity reaction, hepatotoxicity
Rifabutin	Hepatotoxicity, uveitis (dose dependent), red-orange discoloration of body fluids, rash, arthralgia, neutropenia, nausea, vomiting, abdominal pain, diarrhea, anorexia
Rifampin	Hepatotoxicity (cholestatic hepatitis), red-orange discoloration of body fluids, thrombocytopenia, hemolytic anemia, rash, hypersensitivity reactions with flu-like syndrome, nausea, vomiting, anorexia, abdominal pain, flatulence, diarrhea, renal failure, headache, confusion
Rifapentine	Hypersensitivity reaction, hepatotoxicity, anemia, lymphopenia, neutropenia, arthralgia, conjunctivitis, headache, vomiting, nausea, diarrhea, rash, pruritus, anorexia and lymphadenopathy, red-orange discoloration of body fluids, <i>C. difficile</i> -associated diarrhea and colitis
Simeprevir	Rash and pruritus (generally mild in severity, but severe rashes have been reported), photosensitivity reaction, direct and indirect asymptomatic hyperbilirubinemia without elevation in AST/ALT, mild dyspnea, headache, fatigue, insomnia, dizziness, nausea
Sofosbuvir	Generally well-tolerated. Fatigue, headache, nausea, insomnia, anemia, bilirubin elevation (associated with ribavirin co-administration), asymptomatic CK elevation and lipase elevation, pancytopenia, depression (associated with Peg-IFN co-administration)
Streptomycin	Nephrotoxicity, ototoxicity (both hearing loss and vestibular toxicity are possible), other severe neurotoxic reactions (mostly in patients with impaired renal function), pain upon IM injection, eosinophilia, <i>C. difficile</i> -associated diarrhea and colitis
Sulfadiazine	Rash (including SJS, EM, TEN), anemia, neutropenia, thrombocytopenia, crystalluria (with or without urolithiasis), renal insufficiency, nausea, vomiting, drug fever, hepatotoxicity, headache, peripheral neuritis, tinnitus, vertigo, insomnia
Telbivudine	Generally well-tolerated. Nausea, vomiting, abdominal pain, increase in creatine kinase, headache, dizziness, fatigue, diarrhea, myopathy, myalgia, cough, fever, dyspepsia, abdominal pain
Tenofovir DF	Renal insufficiency, proximal renal tubulopathy (with hypophosphatemia, hypouricemia, normoglycemic glycosuria), decrease in bone mineral density, nausea
Tenofovir Alafenamide	Less renal or bone toxicities compared to tenofovir DF
Tetracycline	Photosensitivity, tooth discoloration if taken by infants and children, reduced skeletal development, pruritus, esophageal ulceration, nausea, vomiting, diarrhea, hepatotoxicity, rash, increased BUN, intracranial hypertension
Trimethoprim-Sulfamethoxazole	Rash (including SJS, EM, and TEN), photosensitivity, anemia, neutropenia, thrombocytopenia, hepatotoxicity, increase in serum creatinine (without change in GFR), interstitial nephritis, nausea, vomiting, crystalluria (in patients with inadequate hydration), hyperkalemia (more common with high-dose TMP), drug fever
Valacyclovir	Generally well-tolerated. Nausea, vomiting, headache, crystalluria (with high dose or renal impairment), neurotoxicity (with high doses, especially in patients with renal impairment; agitation, confusion, hallucination, seizure, coma), abdominal pain
Valganciclovir	Neutropenia, thrombocytopenia, anemia, nausea, vomiting, diarrhea, confusion, pyrexia, tremor, acute renal failure, carcinogenic and teratogenic potential, impaired fertility
Vancomycin	Infusion-related reactions (associated with infusion rate and can include flushing, hypotension, and rash), thrombophlebitis, rash, neutropenia, thrombocytopenia (rare), ototoxicity (associated with excessive concentration), nephrotoxicity (associated with high daily dose and high trough concentrations)

Table 6. Common or Serious Adverse Reactions Associated With Drugs Used for Preventing or Treating Opportunistic Infections (page 6 of 6)

Drugs	Common or Serious Adverse Reactions
Velpatasvir/Sofosbuvir	Headache, fatigue
Voriconazole	Visual disturbances (associated with initial dosing), optic neuritis (associated with >28 days treatment), skin photosensitivity, hepatotoxicity, fever, nausea, rash, vomiting, chills, tachycardia, QTc prolongation, peripheral edema, headache, delirium, hallucination, encephalopathy (associated with trough >5.5 mcg/mL), peripheral neuropathy (rare), fluorosis and perioritis with high dose and/or prolonged use, cyclodextrin accumulation (associated with use of IV formulation in patients with CrCl <50 mL/min, which may lead to renal toxicities)

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

Table 7. Dosing Recommendations for Drugs Used in Treating or Preventing Opportunistic Infections Where Dosage Adjustment is Needed in Patients with Renal Insufficiency (page 1 of 7)
(Last updated May 7, 2013; last reviewed September 13, 2017) NOTE: Update in Progress

Drugs	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		Creatinine Clearance (mL/min)*	Dose
Acyclovir	<u>IV dose for:</u> • serious HSV - 5 mg/kg IV q8h, <i>or</i> • VZV infections - 10 mg/kg IV q8h	25–50	100% of dose IV q12h
		10–25	100% of dose IV q24h
		<10	50% of dose IV q24h
		hemodialysis	50% of dose q24h; administer after dialysis on day of dialysis
	<u>PO Dose for Herpes Zoster:</u> 800 mg PO 5 times/day	10–25	800 mg PO q8h
		<10	800 mg PO q12h
		hemodialysis	800 mg PO q12h; administer dose after dialysis
Adefovir	10 mg PO q24h	30–49	10 mg PO q48h
		10–29	10 mg PO q72h
		hemodialysis	10 mg PO weekly (dose after dialysis)
Amikacin (for mycobacterial infections)	IV 15 mg/kg/day or 25 mg/kg TIW	Use with caution in patients with renal insufficiency.	Adjust dose based on serum concentrations with target peak concentration 35–45 mcg/mL and trough concentration <4 mcg/mL.
Amphotericin B	• 0.7–1.0 mg/kg/day IV (amphotericin B deoxycholate), <i>or</i> • 3–6 mg/kg/day IV (lipid formulation)		No dosage adjustment necessary; alternative antifungals should be considered if renal insufficiency occurs during therapy despite adequate hydration.
Capreomycin	15 mg/kg (maximum dose 1000 mg) IV or IM per day	Use with caution in patients with renal insufficiency.	Refer to product label for dosing guidelines based on creatinine clearance. Consider monitoring capreomycin serum concentrations.
Chloroquine (base)	<u>For Treatment of Acute Malaria:</u> • 600 mg PO for 1 dose, followed by 300 mg PO at 6, 24, and 48 hours (for a total dose of 1500 mg)	<10	50% of dose
Cidofovir	• 5 mg/kg IV on days 0, repeat 5 mg/kg IV dose at day 7, then 5 mg/kg IV every 2 weeks (days 21, 35, 49, 63, etc.) Each dose should be given with probenecid and saline hydration (see Table 2).	• Pretreatment SCr >1.5 mg/dL, <i>or</i> • CrCl < 55 mL/min, <i>or</i> • >100 mg/dL (>2+) protein in urinalysis	Cidofovir is not recommended
		If SCr increases by 0.3–0.4 mg/dL from baseline	3 mg/kg IV per dose
		• If SCr increases >0.5 mg/dL >baseline, <i>or</i> • ≥3+ proteinuria	Discontinue therapy

Table 7. Dosing Recommendations for Drugs Used in Treating or Preventing Opportunistic Infections Where Dosage Adjustment is Needed in Patients with Renal Insufficiency (page 2 of 7)

Drugs	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		Creatinine Clearance (mL/min)*	Dose
Ciprofloxacin	<ul style="list-style-type: none"> • 500–750 mg PO q12h, <i>or</i> • 400 mg IV q8–12h 	<30	250–500 mg PO q24h <i>or</i> 400 mg IV q24h
		hemodialysis or peritoneal dialysis	250–500 mg PO q24hr <i>or</i> 200–400 mg IV q24h (administered after dialysis)
Clarithromycin	500 mg PO BID	<30	250 mg PO BID <i>or</i> 500 mg PO once daily
Cycloserine	10 mg/kg/day PO in 2 divided doses (maximum 1000 mg/day)	50–80	Normal dose, consider monitoring serum concentration and toxicities
		<50 (not on hemodialysis)	Not recommended because of accumulation and toxicities.
		hemodialysis	250 mg PO once daily <i>or</i> 500 mg PO TIW—consider monitoring serum cycloserine concentration
Emtricitabine	<ul style="list-style-type: none"> • 200-mg tablet PO once daily, <i>or</i> • 240-mg solution PO once daily 		<u>Oral Tablets</u> <u>Oral Solution</u>
		30–49	200 mg q48h 120 mg q24h
		15–29	200 mg q72h 80 mg q24h
		<15 or hemodialysis (dose after dialysis)	200 mg q96h 60 mg q24h
Emtricitabine/Tenofovir (co-formulation as Truvada) Please refer to product information for dosing recommendations for other ARV fixed dose combination product containing tenofovir/emtricitabine.	200 mg/300 mg - 1 tablet PO daily	30–49	1 tablet PO q48h (monitor for worsening renal function; consider alternative to TDF)
		<30 or hemodialysis	Co-formulated tablet should not be used for CrCl <30 mL/min. Use individual formulation and adjust dose according to recommendations for individual drugs.

Table 7. Dosing Recommendations for Drugs Used in Treating or Preventing Opportunistic Infections Where Dosage Adjustment is Needed in Patients with Renal Insufficiency (page 3 of 7)

Drugs	Usual Dose	Dosage Adjustment in Renal Insufficiency		
		Creatinine Clearance (mL/min)*	Dose	
Entecavir	<u>Usual Dose:</u> • 0.5 mg PO once daily <u>For Treatment of 3TC-Refractory HBV or for Patients with Decompensated Liver Disease:</u> • 1 mg PO once daily		<u>Usual Dose</u>	<u>3TC-Refractory or Decompensated Liver Disease</u>
		30 to <50	• 0.25 mg q24h, <i>or</i> • 0.5 mg q48h	• 0.5 mg q24h, <i>or</i> • 1 mg q48h
		10 to <30	• 0.15 mg q24h, <i>or</i> • 0.5 mg q72h	• 0.3 mg q24h, <i>or</i> • 1 mg q72h
		<10 or hemodialysis or CAPD (administer after dialysis on dialysis day)	• 0.05 mg q24h, <i>or</i> • 0.5 mg q7 days	• 0.1 mg q24h, <i>or</i> • 1 mg q7 days
Ethambutol	• 15–25 mg/kg PO daily • (15 mg/kg PO daily for MAI; 15–25 mg/kg PO daily for MTB)	10–50	15–25 mg/kg q24–36h	
		<10	15–25 mg/kg q48h	
		hemodialysis	15–25 mg/kg TIW after hemodialysis Can consider TDM to guide optimal dosing	
Famciclovir	<u>For Herpes Zoster:</u> • 500 mg PO q8h	40–59	500 mg PO q12h	
		20–39	500 mg PO q24h	
		<20	250 mg PO q24h	
		hemodialysis	250 mg PO after each dialysis	
Fluconazole	200–1200 mg PO or IV q24h	≤50	50% of dose q24h	
		hemodialysis	Full dose after each dialysis	
Flucytosine	25 mg/kg PO q6h If available, TDM is recommended for all patients to guide optimal dosing (goal peak 30–80 mcg/mL 2 hour post dose)	20–40	25 mg/kg q12h	
		10–20	25 mg/kg q24h	
		<10	25 mg/kg q48h	
		hemodialysis	25–50 mg/kg q48–72h (after hemodialysis)	
Foscarnet	180 mg/kg/day IV in 2 divided doses for induction therapy for CMV infection 90–120 mg/kg IV once daily for maintenance therapy for CMV infection or for treatment of HSV infections	Dosage adjustment needed according to calculated CrCl/kg; consult product label for dosing table.		

Table 7. Dosing Recommendations for Drugs Used in Treating or Preventing Opportunistic Infections Where Dosage Adjustment is Needed in Patients with Renal Insufficiency (page 4 of 7)

Drugs	Usual Dose	Dosage Adjustment in Renal Insufficiency		
		Creatinine Clearance (mL/min)*	Dose	
Ganciclovir	<u>Induction Therapy:</u> • 5 mg/kg IV q12h	50–69	2.5 mg/kg IV q12h	
		25–49	2.5 mg/kg IV q24h	
		10–24	1.25 mg/kg IV q24h	
		<10 or on hemodialysis	1.25 mg/kg IV TIW after dialysis	
	<u>Maintenance Therapy:</u> • 5 mg/kg IV q24h	50–69	2.5 mg/kg IV q24h	
		25–49	1.25 mg/kg IV q24h	
		10–24	0.625 mg/kg IV q24h	
		<10 or on hemodialysis	0.625 mg/kg IV TIW after dialysis	
Lamivudine	300 mg PO q24h	30–49	150 mg PO q24h	
		15–29	150 mg PO once, then 100 mg PO q24h	
		5–14	150 mg PO once, then 50 mg PO q24h	
		<5 or on hemodialysis	50 mg PO once, then 25 PO mg q24h (give the dose after dialysis on dialysis day)	
Levofloxacin	500 mg (low dose) or 750 mg (high dose) IV or PO daily <u>Nosocomial Pneumonia/ Osteomyelitis:</u> • 750 mg daily	20–49	<u>Lower Dose</u> 500 mg once, then 250 mg q24h	<u>High Dose</u> 750 mg q48h
		<19 or on CAPD or hemodialysis (dose after dialysis)	500 mg once, then 250 mg q48h	750 mg once, then 500 mg q48h
Peginterferon Alfa-2a	180 mcg SQ once weekly	<30	135 mcg SQ once weekly	
		hemodialysis		
Peginterferon Alfa-2b	1.5 mcg/kg SQ once weekly	30–50	Reduce dose by 25%	
		10–29 and hemodialysis	Reduce dose by 50%	
Penicillin G Potassium (or sodium)	<u>Neurosyphilis or Ocular/Otic Syphilis:</u> • 3–4 million units IV q4h, <i>or</i> • 18–24 million units IV daily as continuous infusion	10–50	2–3 million units q4h or 12–18 million units as continuous infusion	
		<10	2 million units q4–6h or 8–12 million units as continuous infusion	
		hemodialysis or CAPD	2 million units q6h or 8 million units as continuous infusion	
Pentamidine	4 mg/kg IV q24h	10–50	3 mg/kg IV q24h	
		<10	4 mg/kg IV q48h	

Table 7. Dosing Recommendations for Drugs Used in Treating or Preventing Opportunistic Infections Where Dosage Adjustment is Needed in Patients with Renal Insufficiency (page 5 of 7)

Drugs	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		Creatinine Clearance (mL/min)*	Dose
Pyrazinamide	See Table 3 for weight-based dosing guidelines	<10	50% of usual dose
		hemodialysis	Usual dose given after dialysis
Quinidine Gluconate (salt) (10 mg quinidine gluconate salt = 6.25 mg quinidine base)	<u>Loading Dose:</u> • 10 mg/kg (salt) IV over 1–2 hours, then 0.02 mg/kg/min (salt) IV for up to 72 hours or until able to take PO meds Consider TDM for all patients to optimize dosing.	<10	75% of normal dose
		hemodialysis	75% of normal dose; some clinicians recommend supplementation with 100 mg–200 mg after dialysis.
Quinine Sulfate	650 mg salt (524 mg base) PO q8h	<10 or hemodialysis	650 mg once, then 325 mg PO q12h
Ribavirin	For genotypes 1 and 4: • 1000–1200 mg PO per day in 2 divided doses (based on weight, see Table 2 for full dosing recommendation) For genotype 2 and 3: • 400 mg PO BID for genotypes 2 and 3	30–50	Alternate dosing 200 mg PO and 400 mg PO every other day
		<30 or hemodialysis	200 mg PO daily
Rifabutin	300 mg PO daily (see Table 5 for dosage adjustment based on drug-drug interaction)	<30	50% of dose once daily. Consider TDM
Streptomycin	• 15 mg/kg IM or IV q24h, <i>or</i> • 25 mg/kg IM or IV TIW	Use with caution in patients with renal insufficiency.	Adjust dose based on serum concentrations.
Sulfadiazine	1000–1500 mg PO q6h (1500 mg q6h for >60kg)	10–50	1000–1500 mg PO q12h (ensure adequate hydration)
		<10 or hemodialysis	1000–1500 mg PO q24h (dose after HD on days of dialysis)
Telbivudine	600 mg PO daily	30–49	Oral tablets: 600 mg PO q48h Oral solution: 400 mg PO q24h
		<30	Oral tablets: 600 mg PO q72h Oral solution: 200 mg PO q24h
		hemodialysis	Oral tablets: 600 mg PO q96h (dose after dialysis) Oral solution: 120 mg PO q24h (dose after dialysis on dialysis day)

Table 7. Dosing Recommendations for Drugs Used in Treating or Preventing Opportunistic Infections Where Dosage Adjustment is Needed in Patients with Renal Insufficiency (page 6 of 7)

Drugs	Usual Dose	Dosage Adjustment in Renal Insufficiency		
		Creatinine Clearance (mL/min)*	Dose	
Tenofovir	300 mg PO daily	30–49	300 mg PO q48h	
		10–29	300 mg PO q72–96h	
		<10 and not on dialysis	Not recommended	
		hemodialysis	300 mg PO once weekly (dose after dialysis) Can consider alternative agent for treatment of HBV and/or HIV if TDF-associated renal toxicity occurs.	
Tetracycline	250 mg PO q6h Consider using doxycycline in patients with renal dysfunction.	10–49	250 mg PO q12–24h	
		<10	250 mg PO q24h	
		hemodialysis	250 mg PO q24h; dose after dialysis	
Trimethoprim/ Sulfamethoxazole	<u>For PCP Treatment:</u> • 5 mg/kg (of TMP component) IV q8h, <i>or</i> • 2 DS tablets PO q8h	10–30	5 mg/kg (TMP) IV q12h or TMP-SMX 2 DS tablets PO q12h	
		<10	5 mg/kg (TMP) IV q24h, or TMP-SMX DS tablet PO q12h (or 2 TMP-SMX DS tablets q24h)	
		hemodialysis	5 mg/kg/day (TMP) IV or 2 TMP-SMX DS tablets PO; dose after dialysis on dialysis day Can consider TDM to optimize therapy (target TMP concentrations: 5–8 mcg/mL)	
Valacyclovir	<u>For Herpes Zoster:</u> • 1 g PO TID	30–49	1 g PO q12h	
		10–29	1 g PO q24h	
		<10	500 mg PO q24h	
		hemodialysis	500 mg PO q24h; dose after dialysis on dialysis days	
Valganciclovir	<u>Induction Therapy:</u> • 900 mg PO BID <u>Maintenance Therapy:</u> • 900 mg PO daily	40–59	<u>Induction</u> 450 mg PO BID	<u>Maintenance</u> 450 mg PO daily
		25–39	450 mg PO daily	450 mg PO q48h
		10–25	450 mg PO q48h	450 mg PO BIW
		<10 not on dialysis	not recommended	not recommended
		hemodialysis (clinical efficacy of this dosage has not been established)	200 mg PO TIW after dialysis (oral powder formulation)	100 mg PO TIW after dialysis (oral powder formulation)

Table 7. Dosing Recommendations for Drugs Used in Treating or Preventing Opportunistic Infections Where Dosage Adjustment is Needed in Patients with Renal Insufficiency (page 7 of 7)

Drugs	Usual Dose	Dosage Adjustment in Renal Insufficiency	
		Creatinine Clearance (mL/min)*	Dose
Voriconazole	<ul style="list-style-type: none"> • 6 mg/kg IV q12h 2 times, then 4 mg/kg q12h, <i>or</i> • 200–300 mg PO q12h 	<50	<p>IV voriconazole is not recommended because of potential toxicity due to accumulation of sulfobutylether cyclodextrin (vehicle of IV product).</p> <p>Should switch to PO voriconazole in these patients. No need for dosage adjustment when PO dose is used.</p>

Key to Acronyms: 3TC = lamivudine; BID = twice daily; BIW = twice weekly; CAPD = continuous ambulatory peritoneal dialysis; CMV = cytomegalovirus; CrCl = creatinine clearance; DS = double strength; HBV = hepatitis B virus; HSV = herpes simplex virus; IM = intramuscular; IV = intravenous; MAI = *Mycobacterium avium intracellulare*; MTB = *Mycobacterium tuberculosis*; PCP = *Pneumocystis pneumonia*; PO = orally; q(n)h = every “n” hours; SQ = subcutaneous; SCr = ; TDF = tenofovir disoproxil fumarate; TDM = therapeutic drug monitoring; TID = three times daily; TIW = three times weekly; TMP = trimethoprim; SMX = sulfamethoxazole; VZV = varicella zoster virus

Creatinine Clearance Calculation	
<p>Male:</p> $\frac{(140 - \text{age in years}) \times \text{weight (kg)}}{72 \times \text{Serum Creatinine}}$	<p>Female:</p> $\frac{(140 - \text{age in years}) \times \text{weight (kg)} \times 0.85}{72 \times \text{Serum Creatinine}}$

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 1 of 9) (Last updated October 28, 2014; last reviewed July 25, 2017)

NOTE: Update in Progress

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

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 2 of 9)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Boceprevir	B	Not teratogenic in rats, rabbits. No human pregnancy data.	Treatment of HCV currently generally not indicated in pregnancy.
Capreomycin	C	Increase in skeletal variants in rats. Limited experience in human pregnancy; theoretical risk of fetal ototoxicity.	Drug-resistant TB
Caspofungin	C	Embryotoxic, skeletal defects in rats, rabbits No experience with human use.	Invasive <i>Candida</i> or <i>Aspergillus</i> infections refractory to amphotericin and azoles
Cephalosporins	B	Not teratogenic in animals. Large experience in human pregnancy has not suggested increase in adverse outcomes.	Bacterial infections; alternate treatment for MAC
Chloroquine	C	Associated with anophthalmia, microphthalmia at fetotoxic doses in animals. Not associated with increased risk in human pregnancy at doses used for malaria.	Drug of choice for malaria prophylaxis and treatment of sensitive species in pregnancy.
Cidofovir	C	Embryotoxic and teratogenic (meningocele, skeletal abnormalities) in rats and rabbits. No experience in human pregnancy.	Not recommended
Ciprofloxacin, other quinolones	C	Arthropathy in immature animals; not embryotoxic or teratogenic in mice, rats, rabbits, or monkeys. More than 1100 cases of quinolone use in human pregnancy have not been associated with arthropathy or birth defects.	Severe MAC infections; multidrug resistant TB, anthrax, bacterial infections
Clarithromycin	C	Cardiovascular defects noted in one strain of rats and cleft palate in mice at high doses, not teratogenic in rabbits or monkeys. Two human studies, each with >100 first-trimester exposures, did not show increase in defects but one study found an increase in spontaneous abortion.	Treatment or secondary MAC prophylaxis, if other choices exhausted
Clindamycin	B	No concerns specific to pregnancy in animal or human studies.	Treatment of anaerobic bacterial infections and used with quinine for chloroquineresistant malaria; alternate agent for secondary prophylaxis of <i>Toxoplasma</i> encephalitis
Clofazimine	C	Not teratogenic in mice, rats, or rabbits. Limited experience reported (19 cases); no anomalies noted but red-brown skin discoloration reported in several infants exposed throughout pregnancy.	No indications.
Clotrimazole troches	C	Not teratogenic in animals at exposures expected from treatment of oral or vaginal <i>Candida</i> . No increase in adverse pregnancy outcomes with vaginal use.	Oral or vaginal <i>Candida</i> infections and prophylaxis
Cycloserine	C	Not teratogenic in rats. No data available from human studies.	Drug-resistant TB

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 3 of 9)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Dapsone	C	No animal data. Limited human experience does not suggest teratogenicity; might displace bound bilirubin in the neonate, increasing the risk of kernicterus. Case reports of hemolytic anemia in fetus/infant with maternal treatment.	Alternate choice for primary or secondary PCP prophylaxis
Diphenoxylate	C	Limited animal and human data do not indicate teratogenicity.	Symptomatic treatment of diarrhea
Doxycycline, other tetracyclines	D	Risk of hepatic toxicity increased with tetracyclines in pregnancy; staining of fetal bones and teeth contraindicates use in pregnancy.	No indications
Emtricitabine	B	No concerns in pregnancy from limited animal and human data.	As part of fully suppressive combination antiretroviral regimen for treatment of HIV, HBV. Report exposures during pregnancy to Antiretroviral Pregnancy Registry: http://www.APRegistry.com .
Entecavir	C	Animal data do not suggest teratogenicity at human doses; limited experience in human pregnancy.	Not recommended because of limited data in pregnancy. Use as part of fully suppressive ARV regimen with ARV agents active against both HIV and HBV. Report exposures during pregnancy to Antiretroviral Pregnancy Registry: http://www.APRegistry.com
Erythromycin	B	Hepatotoxicity with erythromycin estolate in pregnancy; other forms acceptable; no evidence of teratogenicity	Bacterial and chlamydial infections
Ethambutol	B	Teratogenic, at high doses, in mice, rats, rabbits. No evidence of teratogenicity in 320 cases of human use for treatment of TB.	Active TB and MAC treatment; avoid in first trimester if possible
Ethionamide	C	Increased rate of defects (omphalocele, exencephaly, cleft palate) in rats, mice, and rabbits with high doses; not seen with usual human doses. Limited human data; case reports of CNS defects.	Active TB; avoid in first trimester if possible
Famciclovir	B	No evidence of teratogenicity in rats or rabbits, limited human experience.	Recurrent genital herpes and primary varicella infection. Report exposures during pregnancy to the Famvir Pregnancy Registry (1-888-669-6682).
Fluconazole	C	Abnormal ossification, structural defects in rats, mice at high doses. Case reports of rare pattern of craniofacial, skeletal and other abnormalities in five infants born to four women with prolonged exposure during pregnancy; no increase in defects seen in several series after single dose treatment.	Single dose may be used for treatment of vaginal Candida though topical therapy preferred. Not recommended for prophylaxis during early pregnancy. Can be used for invasive fungal infections after first trimester; amphotericin B preferred in first trimester if similar efficacy expected.

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 4 of 9)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Flucytosine	C	Facial clefts and skeletal defects in rats; cleft palate in mice, no defects in rabbits. No reports of use in first trimester of human pregnancy; may be metabolized to 5-fluorouracil, which is teratogenic in animals and possibly in humans.	Use after first trimester if indicated for lifethreatening fungal infections.
Foscarnet	C	Skeletal variants in rats, rabbits and hypoplastic dental enamel in rats. Single case report of use in human pregnancy in third trimester.	Interim agent for treatment or secondary prophylaxis of life-threatening or sight-threatening CMV infection.
Fumagillin	Not FDA approved	Caused complete litter destruction or growth retardation in rats, depending on when administered. No data in human pregnancy.	Topical solution can be used for ocular microsporidial infections.
Ganciclovir, valganciclovir	C	Embryotoxic in rabbits and mice; teratogenic in rabbits (cleft palate, anophthalmia, aplastic kidney and pancreas, hydrocephalus). Case reports of safe use in human pregnancy after transplants, treatment of fetal CMV.	Treatment or secondary prophylaxis of lifethreatening or sight-threatening CMV infection. Preferred agent for therapy in children.
Imipenem, meropenem	C/B	Not teratogenic in animals; limited human experience.	Serious bacterial infections
Imiquimod	B	Not teratogenic in rats and rabbits; 8 case reports of human use, only 2 in first trimester.	Because of limited experience, other treatment modalities such as cryotherapy or trichloroacetic acid recommended for wart treatment during pregnancy.
Influenza vaccine	C	Not teratogenic. Live vaccines, including intranasal influenza vaccine, are contraindicated in pregnancy.	All pregnant women should receive injectable influenza vaccine because of the increased risk of complications of influenza during pregnancy. Ideally, HIV-infected women should be on ART before vaccination to limit potential increases in HIV RNA levels with immunization.
Interferons (alfa, beta, gamma)	C	Abortifacient at high doses in monkeys, mice; not teratogenic in monkeys, mice, rats, or rabbits. Approximately 30 cases of use of interferon-alfa in pregnancy reported; 14 in first trimester without increase in anomalies; possible increased risk of intrauterine growth retardation.	Not indicated. Treatment of HCV currently generally not recommended in pregnancy.
Isoniazid	C	Not teratogenic in animals. Possible increased risk of hepatotoxicity during pregnancy; prophylactic pyridoxine, 50 mg/day, should be given to prevent maternal and fetal neurotoxicity.	Active TB; prophylaxis for exposure or skin test conversion

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 5 of 9)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Itraconazole	C	Teratogenic in rats and mice at high doses. Case reports of craniofacial, skeletal abnormalities in humans with prolonged fluconazole exposure during pregnancy; no increase in defect rate noted among over 300 infants born after first-trimester itraconazole exposure.	Only for documented systemic fungal disease, not prophylaxis. Consider using amphotericin B in first trimester if similar efficacy expected.
Kanamycin	D	Associated with club feet in mice, inner ear changes in multiple species. Hearing loss in 2.3% of 391 children after long-term <i>in utero</i> therapy.	Drug-resistant TB
Ketoconazole	C	Teratogenic in rats, increased fetal death in mice, rabbits. Inhibits androgen and corticosteroid synthesis; may impact fetal male genital development; case reports of craniofacial, skeletal abnormalities in humans with prolonged fluconazole exposure during pregnancy.	None
Lamivudine	C	Not teratogenic in animals. No evidence of teratogenicity with >3700 first-trimester exposures reported to Antiretroviral Pregnancy Registry.	HIV and HBV therapy, only as part of a fully suppressive combination ARV regimen. Report exposures to Antiretroviral Pregnancy Registry: http://www.APRegistry.com .
Ledipasvir/sofosbuvir	B	No evidence of teratogenicity in rats or rabbits. No experience in human pregnancy	Treatment of hepatitis C generally not indicated in pregnancy.
Leucovorin (folinic acid)	C	Prevents birth defects of valproic acid, methotrexate, phenytoin, aminopterin in animal models. No evidence of harm in human pregnancies.	Use with pyrimethamine if use of pyrimethamine cannot be avoided.
Linezolid	C	Not teratogenic in animals. Decreased fetal weight and neonatal survival at ~ human exposures, possibly related to maternal toxicity. Limited human experience.	Serious bacterial infections
Loperamide	B	Not teratogenic in animals. No increase in birth defects among infants born to 89 women with first-trimester exposure in one study; another study suggests a possible increased risk of hypospadias with first-trimester exposure, but confirmation required.	Symptomatic treatment of diarrhea after the first trimester
Mefloquine	C	Animal data and human data do not suggest an increased risk of birth defects, but miscarriage and stillbirth may be increased.	Second-line therapy of chloroquine-resistant malaria in pregnancy, if quinine/clindamycin not available or not tolerated. Weekly as prophylaxis in areas with chloroquine-resistant malaria.
Meglumine	Not FDA approved	See Antimonials, pentavalent	
Metronidazole	B	Multiple studies do not indicate teratogenicity. Studies on several hundred women with firsttrimester exposure found no increase in birth defects.	Anaerobic bacterial infections, bacterial vaginosis, trichomoniasis, giardiasis, amebiasis
Micafungin	C	Teratogenic in rabbits; no human experience.	Not recommended

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 6 of 9)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Miltefosine	Not FDA approved	Embryotoxic in rats, rabbits; teratogenic in rats. No experience with human use.	Not recommended
Nifurtimox	Not FDA approved	Not teratogenic in mice and rats. Increased chromosomal aberrations in children receiving treatment; uncertain significance. No experience in human pregnancy.	Not indicated in chronic infection; seek expert consultation if acute infection or symptomatic reactivation of <i>T. cruzi</i> in pregnancy.
Nitazoxanide	B	Not teratogenic in animals; no human data	Severely symptomatic cryptosporidiosis after the first trimester
Para-amino salicylic acid (PAS)	C	Occipital bone defects in one study in rats; not teratogenic in rabbits. Possible increase in limb, ear anomalies in one study with 143 first-trimester exposures; no specific pattern of defects noted, several studies did not find increased risk.	Drug-resistant TB
Paromomycin	C	Not teratogenic in mice and rabbits. Limited human experience, but poor oral absorption makes toxicity, teratogenicity unlikely.	Amebic intestinal infections, possibly cryptosporidiosis
Penicillin	B	Not teratogenic in multiple animal species. Vast experience with use in human pregnancy does not suggest teratogenicity, other adverse outcomes.	Syphilis, other susceptible bacterial infections
Pentamidine	C	Embryocidal but not teratogenic in rats, rabbits with systemic use. Limited experience with systemic use in pregnancy.	Alternate therapy for PCP and leishmaniasis.
Piperacillin-tazobactam	B	Not teratogenic in limited animal studies. Limited experience in pregnancy but penicillins generally considered safe.	Bacterial infections
Pneumococcal vaccine	C	No studies in animal pregnancy. Polysaccharide vaccines generally considered safe in pregnancy. Well-tolerated in third-trimester studies.	Initial or booster dose for prevention of invasive pneumococcal infections. HIV-infected pregnant women should be on ART before vaccination to limit potential increases in HIV RNA levels with immunization.
Podophyllin, podofilox	C	Increased embryonic and fetal deaths in rats, mice but not teratogenic. Case reports of maternal, fetal deaths after use of podophyllin resin in pregnancy; no clear increase in birth defects with first-trimester exposure.	Because alternative treatments for genital warts in pregnancy are available, use not recommended; inadvertent use in early pregnancy is not indication for abortion.
Posaconazole	C	Embryotoxic in rabbits; teratogenic in rats at similar to human exposures. No experience in human pregnancy.	Not recommended
Prednisone	B	Dose-dependent increased risk of cleft palate in mice, rabbits, hamsters; dose-dependent increase in genital anomalies in mice. Human data inconsistent regarding increased risk of cleft palate. Risk of growth retardation, low birth weight may be increased with chronic use; monitor for hyperglycemia with use in third trimester.	Adjunctive therapy for severe PCP; multiple other non-HIV-related indications

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 7 of 9)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Primaquine	C	No animal data. Limited experience with use in human pregnancy; theoretical risk for hemolytic anemia if fetus has G6PD deficiency.	Alternate therapy for PCP, chloroquine-resistant malaria
Proguanil	C	Not teratogenic in animals. Widely used in malaria-endemic areas with no clear increase in adverse outcomes.	Alternate therapy and prophylaxis of <i>P. falciparum</i> malaria
Pyrazinamide	C	Not teratogenic in rats, mice. Limited experience with use in human pregnancy.	Active TB
Pyrimethamine	C	Teratogenic in mice, rats, hamsters (cleft palate, neural tube defects, and limb anomalies). Limited human data have not suggested an increased risk of birth defects; because folate antagonist, use with leucovorin.	Treatment and secondary prophylaxis of toxoplasmic encephalitis; alternate treatment of PCP
Quinidine gluconate	C	Generally considered safe in pregnancy; high doses associated with preterm labor. One case of fetal 8th nerve damage reported.	Alternate treatment of malaria, control of fetal arrhythmias
Quinine sulfate	C	High doses, often taken as an abortifacient, have been associated with birth defects, especially deafness, in humans and animals. Therapeutic doses have not been associated with an increased risk of defects in humans or animals. Monitor for hypoglycemia.	Treatment of chloroquine-resistant malaria
Ribavirin	X	Dose-dependent risk of multiple defects (craniofacial, central nervous system, skeletal, anophthalmia) in rats, mice, hamsters starting at below human doses. Reports of treatment during second half of pregnancy in nine women without incident; first 49 cases in registry did not suggest increased risk, but limited data.	Contraindicated in early pregnancy; no clear indications in pregnancy. Report exposures during pregnancy to Ribavirin Pregnancy Registry at (800) 593-2214 or www.ribavirinpregnancyregistry.com
Rifabutin	B	Not teratogenic in rats and rabbits; no specific concerns for human pregnancy.	Treatment or prophylaxis of MAC, active TB
Rifampin	C	Teratogenic at high doses in mice (cleft palate) and rats (spina bifida) but not in rabbits. No clear teratogenicity in humans.	Active TB
Simeprevir	C	Decreased fetal weights and increased skeletal variants in mice at 4x human exposure. Increased deaths and decreased fetal and neonatal growth and developmental delay after in utero exposure in rats. No experience in human pregnancy.	Treatment of HCV currently generally not recommended in pregnancy.
Sinecatechin ointment	C	No evidence of teratogenicity in rats and rabbits after oral or intravaginal dosing. No experience in human pregnancy.	Not recommended based on lack of data.
Sofobusvir	B	No evidence of teratogenicity in rats or rabbits. No experience in human pregnancy.	Treatment of HCV generally not indicated in pregnancy. Regimens including ribavirin and interferon are contraindicated in pregnancy.

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 8 of 9)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Streptomycin	D	No teratogenicity in mice, rats, guinea pigs. Possible increased risk of deafness and VIII nerve damage; no evidence of other defects.	Alternate therapy for active TB
Sulfadiazine	B	Sulfonamides teratogenic in some animal studies. No clear teratogenicity in humans; potential for increased jaundice, kernicterus if used near delivery.	Secondary prophylaxis of toxoplasmic encephalitis
Telaprevir	B	Not teratogenic in mice, rats. No human pregnancy data.	Treatment of HCV currently generally not indicated in pregnancy.
Telbivudine	B	Not teratogenic in rats, rabbits. Limited experience in human pregnancy.	Not recommended because of limited data in pregnancy. Use as part of fully suppressive antiretroviral regimen with antiretroviral agents active against both HIV and hepatitis B. Report exposures during pregnancy to Antiretroviral Pregnancy Registry: http://www.APRegistry.com .
Tenofovir	B	No evidence of birth defects in rats, rabbits, or monkeys at high doses; chronic administration in immature animals of multiple species at 6–50 times human doses has led to dose-specific bone changes ranging from decreased mineral density to severe osteomalacia and fractures. Clinical studies in humans (particularly children) show bone demineralization with chronic use; clinical significance unknown. No evidence of increased birth defects in nearly 2000 first-trimester exposures in women.	Component of fully suppressive antiretroviral regimen in pregnant women. Report exposures during pregnancy to Antiretroviral Pregnancy Registry: http://www.APRegistry.com .
Trichloroacetic acid, bichloroacetic acid	Not rated	No studies. Used topically so no systemic absorption expected.	Topical therapy of non-cervical genital warts
Trifluridine	C	Not teratogenic in rats, rabbits. Minimal systemic absorption expected with topical ocular use.	Topical agent for treatment of ocular herpes infections
Trimethoprim-sulfamethoxazole	C	Teratogenic in rats and mice. Possible increase in congenital cardiac defects, facial clefts, neural tube and urinary defects with first-trimester use. Unclear if higher levels of folate supplementation lower risk. Theoretical risk of elevated bilirubin in the neonate if used near delivery.	Therapy of PCP during pregnancy. Primary and secondary PCP prophylaxis in the second/third trimester; consider aerosolized pentamidine in first trimester. Recommend fetal ultrasound at 18–20 weeks after firsttrimester exposure.
Valacyclovir	B	Not teratogenic in mice, rats, and rabbits. Experience with valacyclovir in pregnancy limited; prodrug of acyclovir, which is considered safe for use in pregnancy.	Treatment of HSV and varicella infections in pregnancy
Vancomycin	C	Not teratogenic in rats, rabbits. Limited human experience.	Serious bacterial infections

Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 9 of 9)

Drug	FDA Category	Pertinent Animal Reproductive and Human Pregnancy Data	Recommended Use During Pregnancy
Voriconazole	D	Embryotoxic in rats, rabbits. Teratogenic in rats (cleft palate, hydronephrosis, and ossification defects). No experience with human use.	Not recommended

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