<table>
<thead>
<tr>
<th>Opportunistic Infections</th>
<th>Indication</th>
<th>Preferred</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coccidioidomycosis</td>
<td>A new positive IgM or IgG serologic test in patients who live in a disease-endemic area and with CD4 count &lt;250 cells/µL (&lt;BIII&gt;)</td>
<td>Fluconazole 400 mg PO daily (&lt;BIII&gt;)</td>
<td></td>
</tr>
<tr>
<td>Hepatitis A Virus (HAV) Infection</td>
<td>HAV-susceptible patients with chronic liver disease, or who are injection-drug users, or MSM (&lt;AII&gt;).</td>
<td>Hepatitis A vaccine 1 mL IM x 2 doses at 0 and 6–12 months (&lt;AII&gt;). IgG antibody response should be assessed 1 month after vaccination; non-responders should be revaccinated when CD4 count &gt;200 cells/µL. (&lt;BIII&gt;).</td>
<td>For patients susceptible to both HAV and hepatitis B virus (HBV) infection (see below): Combined HAV and HBV vaccine (Twinrix&lt;sup&gt;®&lt;/sup&gt;), 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) (&lt;AII&gt;)</td>
</tr>
</tbody>
</table>
### Table 1. Prophylaxis to Prevent First Episode of Opportunistic Disease (page 2 of 7)

<table>
<thead>
<tr>
<th>Opportunistic Infections</th>
<th>Indication</th>
<th>Preferred</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis B Virus (HBV) Infection</strong></td>
<td>• Patients without chronic HBV or without immunity to HBV (i.e., anti-HBs &lt;10 international units/mL) (AII) &lt;br&gt; • Vaccination is recommended before CD4 count falls below 350 cells/µL (AII) &lt;br&gt; • In patients with CD4 counts 350 cells/µL, vaccination should not be deferred until CD4 count reaches &gt;350 cells/µL, because some patients with CD4 counts &lt;200 cells/µL do respond to vaccination (AII).</td>
<td>• HBV vaccine IM (Engerix-B 20 µg/mL or Recombivax HB 10 µg/mL, 0, 1, and 6 months (AII), or &lt;br&gt; • HBV vaccine IM (Engerix-B 40 µg/mL or Recombivax HB 20 µg/mL, 0, 1, 2 and 6 months (BI), &lt;br&gt; • Vaccine conjugated to CpG (Heplisav-B®) IM at 0 and 1 months (CIII) – a 2-dose series can only be used when both doses given are Heplisav-B®. &lt;br&gt; • 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)</td>
<td>Some experts recommend vaccinating with 40-µg doses of either HBV vaccine (CIII).</td>
</tr>
<tr>
<td><strong>Vaccine Non-Responders:</strong></td>
<td>• Anti-HBs &lt;10 international units/mL 1 month after vaccination series &lt;br&gt; • 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).</td>
<td>Re-vaccinate with a second vaccine series (BIII)</td>
<td>• HBV vaccine IM (Engerix-B 40 µg/mL or Recombivax HB 20 µg/mL, 0, 1, 2 and 6 months (BI).</td>
</tr>
</tbody>
</table>
Table 1. Prophylaxis to Prevent First Episode of Opportunistic Disease (page 3 of 7)

<table>
<thead>
<tr>
<th>Opportunistic Infections</th>
<th>Indication</th>
<th>Preferred</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histoplasmosis</td>
<td>CD4 count ≤150 cells/µL and at high risk because of occupational exposure or live in a community with a hyperendemic rate of histoplasmosis (&gt;10 cases/100 patient-years) (BI)</td>
<td>Itraconazole 200 mg PO daily (BI)</td>
<td></td>
</tr>
<tr>
<td>Human Papillomavirus (HPV) Infection</td>
<td>Females and males aged 13–26 years (AIII)</td>
<td>• HPV recombinant vaccine 9 valent (Types 6, 11, 16, 18, 31, 33, 45, 52, 58) 0.5 mL IM at 0, 1–2, and 6 months (AIII)</td>
<td>For patients who have completed a vaccination series with the recombinant bivalent or quadrivalent vaccine, many experts would give an additional full series of recombinant 9-valent vaccine, but there are no data to define who might benefit or how cost effective this approach might be (CIII).</td>
</tr>
<tr>
<td>Influenza A and B Virus Infection</td>
<td>All persons with HIV (AIII)</td>
<td>Inactivated influenza vaccine annually (per recommendation for the season) (AIII)</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High-dose inactivated influenza vaccine may be given to individuals aged ≥65 years (CIII).</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Live-attenuated influenza vaccine is contraindicated in patients with HIV (AIII).</td>
<td></td>
</tr>
<tr>
<td>Malaria</td>
<td>Travel to disease-endemic area</td>
<td>Recommendations are the same for HIV-infected and HIV-uninfected patients.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recommendations are based on region of travel, malaria risks, and drug susceptibility in the region.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Refer to the following website for the most recent recommendations based on region and drug susceptibility: <a href="http://www.cdc.gov/malaria/">http://www.cdc.gov/malaria/</a>.</td>
<td></td>
</tr>
</tbody>
</table>
| Mycobacterium avium Complex (MAC) Disease | For CD4 Count <50 cells/mm³  
• Not recommended for those who immediately initiate ART (AII).  
• Recommended for those who are not on fully suppressive ART, after ruling out active disseminated MAC disease (AI). | • Azithromycin 1200 mg PO once weekly (AI), or  
• Clarithromycin 500 mg PO BID (AI), or  
• Azithromycin 600 mg PO twice weekly (BIII) | Rifabutin (dose adjusted based on concomitant ART) (BI); rule out active TB before starting rifabutin. |
### Table 1. Prophylaxis to Prevent First Episode of Opportunistic Disease

<table>
<thead>
<tr>
<th>Opportunistic Infections</th>
<th>Indication</th>
<th>Preferred</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mycobacterium tuberculosis infection (TB)</strong> (i.e., treatment of latent TB infection [LTBI])</td>
<td>Positive screening test for LTBI, with no evidence of active TB, and no prior treatment for active TB or LTBI (AI) or Close contact with a person with infectious TB, with no evidence of active TB, regardless of screening test results (AI).</td>
<td>(INH 300 mg plus pyridoxine 25-50 mg) PO daily for 9 months (AII) or LTBI treatment and ART act independently to decrease the risk of TB disease. Thus, ART is recommended for all persons with HIV and LTBI (AI).</td>
<td>Rifapentine (see dose below) PO plus INH 900 mg PO plus pyridoxine 50 mg PO once weekly for 12 weeks (AII) Note: Rifapentine only recommended for persons receiving RAL or EFV-based ART regimen Rifapentine Weekly Dose Weighing 32.1 to 49.9 kg: • 750 mg Weighing &gt;50 kg: • 900 mg or Rifampin 600 mg PO daily for 4 months (BII) or For persons exposed to drug-resistant TB, select anti-TB drugs after consultation with experts or public health authorities (AII).</td>
</tr>
<tr>
<td><strong>Pneumocystis Pneumonia (PCP)</strong></td>
<td>• CD4 count &lt;200 cells/mm³ (AI), or • CD4 &lt;14% (BII), or • If ART initiation must be delayed, CD4 count ≥200, but &lt;250 cells/mm³ and if monitoring of CD4 cell count every 3 months is not possible (BII) Note: Patients who are receiving pyrimethamine/sulfadiazine for treatment or suppression of toxoplasmosis do not require additional PCP prophylaxis (AII).</td>
<td>• TMP-SMX® 1 DS tablet PO daily (AI), or • TMP-SMX® 1 SS tablet daily (AI)</td>
<td>• TMP-SMX® 1 DS PO three times weekly (BII), or • Dapsone® 100 mg PO daily or 50 mg PO BID (BII), or • Dapsone® 50 mg PO daily with (pyrimethamine® 50 mg plus leucovorin 25 mg) PO weekly (BII), or • (Dapsone® 200 mg plus pyrimethamine® 75 mg plus leucovorin 25 mg) PO weekly (BII); or • Aerosolized pentamidine 300 mg via Respigard™ nebulizer every month (BII), or • Atovaquone 1500 mg PO daily (BII), or • (Atovaquone 1500 mg plus pyrimethamine® 25 mg plus leucovorin 10 mg) PO daily (CIII)</td>
</tr>
<tr>
<td>Opportunistic Infections</td>
<td>Indication</td>
<td>Preferred</td>
<td>Alternative</td>
</tr>
<tr>
<td>---------------------------</td>
<td>------------</td>
<td>-----------</td>
<td>-------------</td>
</tr>
<tr>
<td>Streptococcus pneumoniae Infection</td>
<td>For individuals who have never received any pneumococcal vaccine, regardless of CD4 count</td>
<td>PCV13 0.5 mL IM one time (AI) followed by: If CD4 Count ≥200 cells/mm³ • PPV23 0.5 mL IM at least 8 weeks after the PCV13 vaccine (AI). If CD4 Count &lt;200 cells/mm³ • PPV23 can be offered at least 8 weeks after receiving PCV13 (CIII), or • Can wait until CD4 count increased to &gt;200 cells/mm³ on ART (BIII).</td>
<td>PPV23 0.5 mL IM one time (BII)</td>
</tr>
<tr>
<td>For individuals who have previously received PPV23</td>
<td>One dose of PCV13 should be given at least 1 year after the last receipt of PPV23 (AII). Adults (aged ≥19 years) should wait at least 1 year, and adolescents (aged &lt;19 years) should wait at least 8 weeks after last receipt of PPV23 (BIII).</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Re-Vaccination</td>
<td>• If aged 19–64 years and ≥5 years since the first PPV23 dose • Final dose to be given at age ≥65 years, and if ≥5 years since the previous PPV23 dose • Typically, no more than 3 doses of PPV23 in a lifetime</td>
<td>PPV23 0.5 mL IM one time (BII)</td>
<td>N/A</td>
</tr>
<tr>
<td>Syphilis</td>
<td>• For individuals exposed to a sex partner with a diagnosis of primary, secondary, or early latent syphilis within past 90 days (AII), or • For individuals exposed to a sex partner &gt;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)</td>
<td>Benzathine penicillin G 2.4 million units IM for 1 dose (AII)</td>
<td>For penicillin-allergic patients: • Doxycycline 100 mg PO BID for 14 days (BII), or • Ceftriaxone 1 g IM or IV daily for 8–10 days (BII), or • Azithromycin 2 g PO for 1 dose (BII) – not recommended for MSM or pregnant women (AII)</td>
</tr>
<tr>
<td>Talaromycosis (Penicilliosis)</td>
<td>Persons with HIV and CD4 cell counts &lt;100 cells/mm³, who are unable to have ART, or have treatment failure without access to effective ART options, and 1) Who reside in the highly endemic regions in northern Thailand, northern or southern Vietnam, or southern China (BII), or 2) Who are from countries outside of the endemic region, and must travel to the region (BIII) a Particularly in highland regions during the rainy and humid months</td>
<td>For persons who reside in endemic areas, itraconazole 200 mg PO once daily (BIII). For those traveling to the highly endemic regions, begin itraconazole 200 mg PO once daily 3 days before travel, and continue for 1 week after leaving the endemic area (BIII). For persons who reside in endemic areas, fluconazole 400 mg PO once weekly (BIII). For those traveling to the highly endemic regions, take the first dose of fluconazole 400 mg 3 days before travel, continue 400 mg once weekly, and take the final dose after leaving the endemic area (BIII).</td>
<td></td>
</tr>
<tr>
<td>Opportunistic Infections</td>
<td>Indication</td>
<td>Preferred</td>
<td>Alternative</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>-----------------------------------------------------------------------------</td>
<td>-----------------------------------------------</td>
<td>----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Toxoplasma gondii Encephalitis</td>
<td>• Toxoplasma IgG-positive patients with CD4 count &lt;100 cells/µL (AII)</td>
<td>TMP-SMX&lt;sup&gt;c&lt;/sup&gt; 1 DS PO daily (AII)</td>
<td>• TMP-SMX&lt;sup&gt;c&lt;/sup&gt; 1 DS PO three times weekly (BIII), or</td>
</tr>
<tr>
<td></td>
<td><strong>Note:</strong> All regimens recommended for primary prophylaxis against toxoplasmosis are also effective as PCP prophylaxis.</td>
<td></td>
<td>• TMP-SMX&lt;sup&gt;c&lt;/sup&gt; 1 SS PO daily (BIII), or</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Dapsone&lt;sup&gt;d&lt;/sup&gt; 50 mg PO daily + (pyrimethamine&lt;sup&gt;e&lt;/sup&gt; 50 mg + leucovorin 25 mg) PO weekly (BI), or</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• (Dapsone&lt;sup&gt;d&lt;/sup&gt; 200 mg + pyrimethamine&lt;sup&gt;e&lt;/sup&gt; 75 mg + leucovorin 25 mg) PO weekly (BI); or</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Atovaquone 1500 mg PO daily (CIII); or</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• (Atovaquone 1500 mg + pyrimethamine&lt;sup&gt;e&lt;/sup&gt; 25 mg + leucovorin 10 mg) PO daily (CIII)</td>
</tr>
</tbody>
</table>
| Varicella Zoster Virus (VZV)      | **Pre-Exposure Prevention:** • Patients with CD4 counts ≥200 cells/mm<sup>3</sup> who have not been vaccinated, have no history of varicella or herpes zoster, or who are seronegative for VZV (BIII) | **Pre-Exposure Prevention:** • Primary varicella vaccination (Varivax™), two doses (0.5 mL SQ each) administered 3 months apart (BIII). If vaccination results in disease because of vaccine virus, treatment with acyclovir is recommended (AIII). **Post-Exposure Prevention of Primary Varicella Infection:** • Varicella-zoster immune globulin (VariZIG™) 125 IU per 10 kg (maximum 625 IU) IM, administered as soon as possible, preferably within 96 hours, but up to 10 days after exposure (AIII). **Note:** VariZIG can be obtained through (FFF Enterprises 800-843-7477 or ASD Healthcare 800-746-6273). 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. | **Pre-Exposure Prevention:** • VZV-susceptible household contacts of susceptible HIV-infected persons should be vaccinated to prevent potential transmission of VZV to their HIV-infected contacts (BIII). **Alternative Post-Exposure Prevention:** • Acyclovir 800 mg PO five times a day for 5–7 days beginning 7-10 days after exposure (BIII); or • Valacyclovir 1 g PO three times a day for 5–7 days (BIII) These alternatives have not been studied in the HIV population.
Table 1. Prophylaxis to Prevent First Episode of Opportunistic Disease (page 7 of 7)

- Refer to the Drug Interactions section in the Adult and Adolescent Antiretroviral Guidelines for dosing recommendations.
- Screening tests for LTBI include TST or IGRA.
- TMP-SMX DS once daily also confers protection against toxoplasmosis and many respiratory bacterial infections; lower dose also likely confers protection.
- Patients should be tested for G6PD before administration of dapsone or primaquine. Alternative agent should be used in patients found to have G6PD deficiency.
- Refer to Daraprim Direct for information regarding how to access pyrimethamine.

**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; EFV = efavirenz; G6PD = glucose-6-phosphate dehydrogenase; HAV = hepatitis A virus; HBV = hepatitis B virus; HPV = human papillomavirus; IgG = immunoglobulin G; IgM = immunoglobulin M; IGRA = interferon-gamma release assays; IM = intramuscular; INH = isoniazid; IU = international units; IV= intravenously; IVIG = intravenous immunoglobulin; LTBI = latent tuberculosis infection; MAC = Mycobacterium avium complex; N/A = not applicable PCP = Pneumocystis pneumonia; PCV13 = 13-valent pneumococcal conjugate vaccine; PO = orally; PPV23 = 23-valent pneumococcal polysaccharides vaccine; RAL= raltegravir; SQ = subcutaneous; SS = single strength; TB = tuberculosis; TMP-SMX = trimethoprim-sulfamethoxazole; TST = tuberculin skin test; VZV = varicella zoster virus

**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)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacterial Enteric Infections</strong></td>
<td><em>Empiric therapy pending definitive diagnosis</em></td>
<td><strong>Empiric Therapy:</strong></td>
<td>Oral or IV rehydration (if indicated) should be given to patients with diarrhea (AIII). Antimotility agents should be avoided if there is concern about inflammatory diarrhea, including <em>Clostridium difficile</em>-associated diarrhea (BIII). 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. IV antibiotics and hospitalization should be considered in patients with marked nausea, vomiting, diarrhea, electrolyte abnormalities, acidosis, and blood pressure instability.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (AIII)</td>
<td>For Mild-to-Moderate Disease (If Susceptible):</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Therapy should be adjusted based on the results of diagnostic work-up. For patients with chronic diarrhea (&gt;14 days) without severe clinical signs, empiric antibiotics therapy is not necessary, can withhold treatment until a diagnosis is made.</td>
<td>• Levofloxacin 750 mg (PO or IV) q24h (BIII), or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For patients with chronic diarrhea (&gt;14 days) without severe clinical signs, empiric antibiotics therapy is not necessary, can withhold treatment until a diagnosis is made.</td>
<td>• Moxifloxacin 400 mg (PO or IV) q24h (BIII)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Azithromycin 500 mg PO daily (BIII) (Note: Not for patients with bacteremia (AIII))</td>
<td>Add an aminoglycoside to fluoroquinolone in bacteremic patients (BIII).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For Campylobacter Bacteremia:</td>
<td>Effective ART may reduce the frequency, severity, and recurrence of campylobacter infections.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (BIII) + an aminoglycoside (BIII)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Duration of Therapy:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Gastroenteritis: 7–10 days (AIII) (5 days with azithromycin)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Bacteremia: ≥14 days (BIII)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Recurrent bacteremia: 2–6 weeks (BIII)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Empiric Therapy:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ceftriaxone 1 g IV q24h (BIII), or</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cefotaxime 1 g IV q8h (BIII)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>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. Empiric antibiotic therapy is indicated for advanced HIV patients (CD4 count &lt;200 cells/µL or concomitant AIDS-defining illnesses), with clinically severe diarrhea (≥6 stools/day or bloody stool) and/or accompanying fever or chills.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>For Mild Disease and If CD4 Count &gt;200 cells/µL:</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• No therapy unless symptoms persist for more than several days (CIII)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>For Mild-to-Moderate Disease Disease (If Susceptible):</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (BIII), or</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Azithromycin 500 mg PO daily (BIII) (Note: Not for patients with bacteremia (AIII))</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>For Campylobacter Bacteremia:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (BIII) + an aminoglycoside (BIII)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Duration of Therapy:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Gastroenteritis: 7–10 days (AIII) (5 days with azithromycin)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Bacteremia: ≥14 days (BIII)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Recurrent bacteremia: 2–6 weeks (BIII)</td>
<td></td>
</tr>
</tbody>
</table>

Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV  
Downloaded from https://aidsinfo.nih.gov/guidelines on 11/25/2019
### Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 2 of 23)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacterial Enteric Infections, continued</strong></td>
<td>Clostridium difficile Infection (CDI)</td>
<td>Vancomycin 125 mg (PO) QID for 10–14 days (AI)</td>
<td>For mild, outpatient disease: metronidazole 500 mg (PO) TID for 10–14 days (CII). Recurrent CDI: 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.</td>
</tr>
<tr>
<td>Salmonellosis</td>
<td>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).</td>
<td>Oral or IV rehydration if indicated (AIII). Antimotility agents should be avoided (BIII). The role of long-term secondary prophylaxis in patients with recurrent Salmonella bacteremia is not well established. Must weigh benefit against risks of long-term antibiotic exposure (BIII). Effective ART may reduce the frequency, severity, and recurrence of salmonella infections.</td>
<td></td>
</tr>
</tbody>
</table>

#### Salmonellosis

- **Ciprofloxacin**: 500–750 mg PO (or 400 mg IV) q12h, if susceptible (AIII)
- **Duration of Therapy:**
  - For gastroenteritis without bacteremia:
    - If CD4 count ≥200 cells/µL: 7–14 days (BIII)
    - If CD4 count <200 cells/µL: 2–6 weeks (BIII)
  - For gastroenteritis with bacteremia:
    - If CD4 count ≥200/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)

*Secondary Prophylaxis Should Be Considered For:*

- Patients with recurrent Salmonella gastroenteritis +/- bacteremia (CIII), or
- Patients with CD4 <200 cells/µL with severe diarrhea (CIII)

- **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), or
- **Ceftriaxone**: 1 g IV q24h (BIII), or
- **Cefotaxime**: 1 g IV q8h (BIII)
Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 3 of 23)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Shigelloides</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bacterial Enteric Infections, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Shigellosis</strong></td>
<td>• Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (AII)</td>
<td>• Levofloxacin 750 mg (PO or IV) q24h (BIII), or</td>
<td>Therapy is indicated both to shorten duration of illness and prevent spread of infection (AII). Given increasing antimicrobial resistance and limited data showing that antibiotic therapy limits transmission, antibiotic treatment may be withheld in patients with CD4 &gt;500 cells/mm³ whose diarrhea resolves prior to culture confirmation of Shigella infection (CIII). Oral or IV rehydration if indicated (AIII). Antimotility agents should be avoided (BIII). If no clinical response after 5–7 days, consider follow-up stool culture, alternative diagnosis, or antibiotic resistance. Effective ART may decrease the risk of recurrence of Shigella infections.</td>
</tr>
<tr>
<td></td>
<td>Duration of Therapy:</td>
<td>• Moxifloxacin 400 mg (PO or IV) q24h (BIII), or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Gastroenteritis: 7–10 days (AII)</td>
<td>• TMP 160 mg-SMX 800 mg (PO or IV) q12h (BIII) (Note: Shigella infections acquired outside of the United States have high rates of TMP-SMX resistance), or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Bacteremia: ≥14 days (BIII)</td>
<td>• Azithromycin 500 mg PO daily for 5 days (BIII) (Note: azithromycin is not recommended for patients with bacteremia (AIII))</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Recurrent Infections: up to 6 weeks (BIII)</td>
<td>Note: Azithromycin-resistant Shigella spp has been reported in HIV-infected MSM.</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Note:</strong> Increased resistance of Shigella to fluoroquinolones is occurring in the United States. Avoid fluoroquinolones if ciprofloxacin MIC is ≥0.12 ug/ml even if the laboratory identifies the isolate as sensitive. Many Shigella strains resistant to fluoroquinolones exhibit resistance to other commonly used antibiotics. Thus, antibiotic sensitivity testing of Shigella isolates from HIV-infected individuals should be performed routinely.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Note:</strong></td>
<td><strong>Note:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Therapy is indicated both to shorten duration of illness and prevent spread of infection (AIII).</strong></td>
<td><strong>When RIF is used, take into consideration the potential for significant interaction with ARV drugs and other medications (see Table 5 for dosing recommendations).</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Given increasing antimicrobial resistance and limited data showing that antibiotic therapy limits transmission, antibiotic treatment may be withheld in patients with CD4 &gt;500 cells/mm³ whose diarrhea resolves prior to culture confirmation of Shigella infection (CIII).</strong></td>
<td><strong>If relapse occurs after initial (&gt;3 month) course of therapy, long-term suppression with doxycycline or a macrolide is recommended as long as CD4 count &lt;200 cells/µL (AIII).</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Bartonellosis</strong></td>
<td>For Bacillary Angiomatosis, Peliosis Hepatitis, Bacteremia, and Osteomyelitis:</td>
<td>For Bacillary Angiomatosis, Peliosis Hepatitis, Bacteremia, And Osteomyelitis:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Doxycycline 100 mg PO or IV q12h (AII), or</td>
<td>• Azithromycin 500 mg PO daily (BIII)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Erythromycin 500 mg PO or IV q6h (AII)</td>
<td>• Clarithromycin 500 mg PO BID (BIII)</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>CNS Infections:</strong></td>
<td><strong>Confirmed Bartonella Endocarditis but with Renal Insufficiency:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Doxycycline 100 mg +/- RIF 300 mg PO or IV q12h (AII))</td>
<td>(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)</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Confirmed Bartonella Endocarditis:</strong></td>
<td>Other Severe Infections:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(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)</td>
<td>• (Doxycycline 100 mg PO +/- RIF 300 mg PO or IV) q12h (BIII), or</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Other Severe Infections:</strong></td>
<td>• (Erythromycin 500 mg PO or IV q6h) +/- RIF 300 mg PO or IV q12h (BIII)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• (Doxycycline 100 mg PO or IV +/- RIF 300 mg PO or IV) q12h (BIII), or</td>
<td><strong>Duration of Therapy:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• (Erythromycin 500 mg PO or IV q6h) +/- RIF 300 mg PO or IV q12h (BIII)</td>
<td>• At least 3 months (AII)</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Duration of Therapy:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• At least 3 months (AII)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opportunistic Infection</td>
<td>Preferred Therapy</td>
<td>Alternative Therapy</td>
<td>Other Comments</td>
</tr>
<tr>
<td>-------------------------</td>
<td>------------------</td>
<td>---------------------</td>
<td>---------------</td>
</tr>
</tbody>
</table>
| **Candidiasis** (Mucocutaneous)** | **For Oropharyngeal Candidiasis: Initial Episodes (For 7–14 Days):**<br>**Oral Therapy**<br>• Fluconazole 100 mg PO daily (AI)**<br>**For Esophageal Candidiasis (For 14–21 Days):**<br>• Fluconazole 100 mg (up to 400 mg) PO or IV daily (AI), or<br>• Itraconazole oral solution 200 mg PO daily (AI)<br>**For Uncomplicated Vulvo-Vaginal Candidiasis:**<br>• Oral fluconazole 150 mg for 1 dose (AI), or<br>• Topical azoles ( clotrimazole, butoconazole, miconazole, tioconazole, or terconazole) for 3–7 days (AI)**<br>**For Severe or Recurrent Vulvo-Vaginal Candidiasis:**<br>• Fluconazole 100–200 mg PO daily for ≥7 days (AI), or<br>• Topical antifungal ≥7 days (AI)**<br> | **For Oropharyngeal Candidiasis: Initial Episodes (For 7–14 Days):**<br>**Oral Therapy**<br>• Itraconazole oral solution 200 mg PO daily (BI), or<br>• Posaconazole oral suspension 400 mg PO BID for 1 day, then 400 mg daily (BI)<br>**Topical Therapy**<br>• Clotrimazole troches, 10 mg PO 5 times daily (BI), or<br>• Miconazole mucoadhesive buccal 50-mg tablet—apply to mucosal surface over the canine fossa once daily (do not swallow, chew, or crush) (BI), or<br>• Nystatin suspension 4–6 mL QID or 1–2 flavored pastilles 4–5 times daily (BII)<br>**For Esophageal Candidiasis (For 14–21 Days):**<br>• Voriconazole 200 mg PO or IV BID (BI), or<br>• Isavuconazole 200 mg PO as a loading dose, followed by 50 mg PO daily (BI), or<br>• Isavuconazole 400 mg PO as a loading dose, followed by 100 mg PO daily (BI), or<br>• Isavuconazole 400 mg PO once-weekly (BI), or<br>• Anidulafungin 100 mg IV 1 time, then 50 mg IV daily (BI), or<br>• Caspofungin 50 mg IV daily (BI), or<br>• Micafungin 150 mg IV daily (BI), or<br>• Amphotericin B deoxycholate 0.6 mg/kg IV daily (BI), or<br>• Lipid formulation of amphotericin B 3–4 mg/kg IV daily (BIII)<br>**For Uncomplicated Vulvo-Vaginal Candidiasis:**<br>• Itraconazole oral solution 200 mg PO daily for 3–7 days (BII)** | Chronic or prolonged use of azoles may promote development of resistance.<br>Higher relapse rate for esophageal candidiasis seen with echinocandins than with fluconazole use.<br>Suppressive therapy usually not recommended (BIII) unless patients have frequent or severe recurrences.<br>If Decision Is to Use Suppressive Therapy: Oropharyngeal candidiasis:<br>• Fluconazole 100 mg PO daily or three times weekly (BI), or<br>• Itraconazole oral solution 200 mg PO daily (CI)<br>Esophageal candidiasis:<br>• Fluconazole 100–200 mg PO daily (BI), or<br>• Posaconazole 400 mg PO BID (BII)<br>Vulvo-vaginal candidiasis:<br>• 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 5 of 23)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chagas Disease</strong></td>
<td>For Acute, Early Chronic, and Reactivated Disease:</td>
<td>For Acute, Early Chronic, and Reactivated Disease:</td>
<td>Treatment is effective in reducing parasitemia and preventing clinical symptoms or slowing disease progression. It is ineffective in achieving parasitological cure. Duration of therapy has not been studied in HIV-infected patients. Initiate or optimize ART in patients undergoing treatment for Chagas disease, once they are clinically stable (AIII).</td>
</tr>
<tr>
<td></td>
<td>• 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 <a href="mailto:drugservice@cdc.gov">drugservice@cdc.gov</a> or (404) 639-3670, or the CDC emergency operations center at (770) 488-7100)</td>
<td>• 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 <a href="mailto:drugservice@cdc.gov">drugservice@cdc.gov</a> or (404) 639-3670, or the CDC emergency operations center at (770) 488-7100)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Treatment is effective in reducing parasitemia and preventing clinical symptoms or slowing disease progression. It is ineffective in achieving parasitological cure. Duration of therapy has not been studied in HIV-infected patients. Initiate or optimize ART in patients undergoing treatment for Chagas disease, once they are clinically stable (AIII).</td>
<td></td>
</tr>
<tr>
<td><strong>Coccidioidomycosis</strong></td>
<td>Cliniacally Mild Infections (e.g., Focal Pneumonia):</td>
<td>For Patients Who Failed to Respond to Fluconazole or Itraconazole:</td>
<td>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 (BII).</td>
</tr>
<tr>
<td></td>
<td>• Fluconazole 400 mg* PO daily (AII), or</td>
<td>• Posaconazole 300 mg delayed-release tablet* PO BID x 1 day, then once daily (BIII), or</td>
<td>Therapy should be lifelong in patients with meningal infections because relapse occurs in 80% of HIV-infected patients after discontinuation of triazole therapy (AII).</td>
</tr>
<tr>
<td></td>
<td>• Itraconazole 200 mg* PO BID (BII)</td>
<td>• Posaconazole 400 mg oral suspension* PO BID (BII), or</td>
<td>*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.</td>
</tr>
<tr>
<td>Bone or Joint Infections:</td>
<td>• Itraconazole 200 mg* PO BID (AII)</td>
<td>• Voriconazole 200 mg* PO BID (BII)</td>
<td>Intrathecal amphotericin B should only be given in consultation with a specialist and administered by an individual with experience with the technique.</td>
</tr>
<tr>
<td>Severe, Non-Meningeal Infection</td>
<td>• Lipid formulation amphotericin B 3-5 mg/kg IV daily (AIII), or</td>
<td>• Posaconazole 300 mg delayed-release tablet* PO BID x 1 day, then once daily (BIII), or</td>
<td></td>
</tr>
<tr>
<td>(Diffuse Pulmonary Infection or</td>
<td>• Amphotericin B deoxycholate 0.7–1.0 mg/kg IV daily (AII)</td>
<td>• Posaconazole 400 mg oral suspension* PO BID (CIII), or</td>
<td></td>
</tr>
<tr>
<td>Severely Ill Patients with</td>
<td>Duration of therapy: continue until clinical improvement, then switch to a triazole (BII)</td>
<td>• Intrathecal amphotericin B deoxycholate, when triazole antifungals are ineffective (AII)</td>
<td></td>
</tr>
<tr>
<td>Extrathoracic, Disseminated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningeal Infections:</td>
<td>• Fluconazole 400–800 mg* IV or PO daily (AII)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 6 of 23)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community-Acquired Pneumonia (CAP)</td>
<td>Empiric antibiotic therapy should be initiated promptly for patients presenting with clinical and radiographic evidence consistent with bacterial pneumonia. The recommendations listed are suggested empiric therapy. The regimen should be modified as needed once microbiologic results are available (BIII). Providers must also consider the risk of opportunistic lung infections (e.g., PCP, TB), which may alter the empiric therapy. Empiric Outpatient Therapy: • A PO beta-lactam plus a PO macrolide (azithromycin or clarithromycin) (AII) Preferred Beta-Lactams: • High-dose amoxicillin or amoxicillin/clavulanate Alternative Beta-Lactams: • Cefpodoxime or cefuroxime, or • Levofloxacin 750 mg PO once daily (AII), or moxifloxacin 400 mg PO once daily (AII), especially for patients with penicillin allergies. Empiric Therapy for Hospitalized Patients with Non-Severe CAP: • An IV beta-lactam plus a macrolide (azithromycin or clarithromycin) (AI) Preferred Beta-Lactams: • Ceftriaxone, cefotaxime, or ampicillin-sulbactam Levofloxacin 750 mg IV once daily (AI), or moxifloxacin, 400 mg IV once daily (AI), especially for patients with penicillin allergies. Empiric Therapy for Hospitalized Patients with Severe CAP: • An IV beta-lactam plus IV azithromycin (AI), or • An IV beta-lactam plus (levofloxacin 750 mg IV once daily or moxifloxacin 400 mg IV once daily) (AI) Preferred Beta-Lactams: • Ceftriaxone, cefotaxime, or ampicillin-sulbactam</td>
<td>Empiric antibiotic therapy should be initiated promptly for patients presenting with clinical and radiographic evidence consistent with bacterial pneumonia. The recommendations listed are suggested empiric therapy. The regimen should be modified as needed once microbiologic results are available (BIII). Providers must also consider the risk of opportunistic lung infections (e.g., PCP, TB), which may alter the empiric therapy. Empiric Outpatient Therapy: • A PO beta-lactam plus PO doxycycline (CIII) Preferred Beta-Lactams: • High-dose amoxicillin or amoxicillin/clavulanate Alternative Beta-Lactams: • Cefpodoxime or cefuroxime Empiric Therapy for Hospitalized Patients with Non-Severe CAP: • An IV beta-lactam plus doxycycline (CIII) Empiric Therapy for Hospitalized Patients with Severe CAP: For Penicillin-Allergic Patients: • Aztreonam IV plus (levofloxacin 750 mg IV once daily or moxifloxacin 400 mg IV once daily) (BIII) Empiric Therapy for Patients at Risk of Pseudomonas Pneumonia: • An IV antipseudomonal beta-lactam plus an IV aminoglycoside plus azithromycin (BII), or An IV antipseudomoccal, antipseudomonal beta-lactam plus an aminoglycoside plus levofoxacin 750 mg IV once daily or moxifloxacin 400 mg IV once daily (BIII) For Penicillin-Allergic Patients: Replace the beta-lactam with aztreonam (BIII).</td>
<td>Duration: • For most patients, 5–7 days. • Patients should be afebrile for 48–72 hours and clinically stable before stopping antibiotics. • Longer duration is often required if severe CAP or bacteremia is present, and particularly if due to S. pneumoniae or complicated S. aureus pneumonia. Fluoroquinolones should be used with caution in patients in whom TB is suspected but is not being treated. Empiric therapy with a macrolide alone is not routinely recommended, because of increasing pneumococcal resistance (up to 30%) (BIII). Patients receiving a macrolide for MAC prophylaxis may have bacterial resistance to macrolide due to chronic exposure For patients begun on IV antibiotic therapy, switching to PO should be considered when they are clinically improved and able to tolerate oral medications. Antibiotic chemoprophylaxis is generally not recommended because of the potential for developing drug resistance and drug toxicities (AI).</td>
</tr>
</tbody>
</table>

Duration: • For most patients, 5–7 days. • Patients should be afebrile for 48–72 hours and clinically stable before stopping antibiotics. • Longer duration is often required if severe CAP or bacteremia is present, and particularly if due to S. pneumoniae or complicated S. aureus pneumonia. Fluoroquinolones should be used with caution in patients in whom TB is suspected but is not being treated. Empiric therapy with a macrolide alone is not routinely recommended, because of increasing pneumococcal resistance (up to 30%) (BIII). Patients receiving a macrolide for MAC prophylaxis may have bacterial resistance to macrolide due to chronic exposure For patients begun on IV antibiotic therapy, switching to PO should be considered when they are clinically improved and able to tolerate oral medications. Antibiotic chemoprophylaxis is generally not recommended because of the potential for developing drug resistance and drug toxicities (AI).
<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community-Acquired Pneumonia (CAP), continued</td>
<td>Empiric Therapy for Patients at Risk of Pseudomonas Pneumonia: • An IV antipneumococcal, antipseudomonal beta-lactam plus (ciprofloxacin 400 mg IV every 8–12 hours or levofloxacin 750 mg IV once daily) (AI) Preferred Beta-Lactams: • Piperacillin-tazobactam, cefepime, imipenem, or meropenem Empiric Therapy for Patients at Risk for Methicillin-Resistant Staphylococcus aureus Pneumonia: • Add vancomycin IV or linezolid (IV or PO) to the baseline regimen (AII) • Addition of clindamycin to vancomycin (but not to linezolid) can be considered for severe necrotizing pneumonia to minimize bacterial toxin production (CII).</td>
<td>Cryptococcosis Cryptococcal Meningitis Induction Therapy (for at least 2 weeks, followed by consolidation therapy): • 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.) Consolidation Therapy (for at least 8 weeks (AI), followed by maintenance therapy): • Fluconazole 400 mg PO (or IV) daily (AI) Maintenance Therapy: • Fluconazole 200 mg PO daily for at least 12 months (AI) For Non-CNS, Extrapulmonary Cryptococcosis and Diffuse Pulmonary Disease: • Treatment same as for cryptococcal meningitis (BIII) Non-CNS Cryptococcosis with Mild-to-Moderate Symptoms and Focal Pulmonary Infiltrates: • Fluconazole, 400 mg PO daily for 12 months (BIII)</td>
<td>Cryptococcal meningitis Induction Therapy (for at least 2 weeks, followed by consolidation therapy): • 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 (BII), 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) Consolidation Therapy (for at least 8 weeks (AI), followed by maintenance therapy): • Itraconazole 200 mg PO BID for 8 weeks—less effective than fluconazole (CI) Maintenance Therapy: • No alternative therapy recommendation</td>
</tr>
<tr>
<td>Opportunistic Infection</td>
<td>Preferred Therapy</td>
<td>Alternative Therapy</td>
<td>Other Comments</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-----------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Cryptosporidiosis</td>
<td>• Initiate or optimize ART for immune restoration to CD4 count &gt;100 cells/μL (AI), and&lt;br&gt;• Aggressive oral or IV rehydration and replacement of electrolyte loss (AI), and&lt;br&gt;• Symptomatic treatment of diarrhea with anti-motility agents (AI).</td>
<td>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: &lt;br&gt;• Nitazoxanide 500–1000 mg PO BID for 14 days (CIII), or&lt;br&gt;• Paromomycin 500 mg PO QID for 14–21 days (CIII)&lt;br&gt;• With optimized ART, symptomatic treatment and rehydration and electrolyte replacement</td>
<td>Tincture of opium may be more effective than loperamide in management of diarrhea (CII).</td>
</tr>
<tr>
<td>Cystoisosporiasis (Formerly Isosporiasis)</td>
<td>For Acute Infection: &lt;br&gt;• TMP-SMX (160 mg/800 mg) PO (or IV) QID for 10 days (AI), or&lt;br&gt;• TMP-SMX (160 mg/800 mg) PO (or IV) BID for 7–10 days (BI)&lt;br&gt;• Can start with BID dosing first and increase daily dose and/or duration (up to 3–4 weeks) if symptoms worsen or persist (BIII)&lt;br&gt;• IV therapy may be used for patients with potential or documented malabsorption.&lt;br&gt;Chronic Maintenance Therapy (Secondary Prophylaxis):&lt;br&gt;• In patients with CD4 count &lt;200/μL, TMP-SMX (160 mg/800 mg) PO TIW (AI)</td>
<td>For Acute Infection: &lt;br&gt;• Pyrimethamine 50–75 mg PO daily + leucovorin 10–25 mg PO daily (BIII), or&lt;br&gt;• Ciprofloxacin 500 mg PO BID for 7 days (CI) as a second line alternative&lt;br&gt;Chronic Maintenance Therapy (Secondary Prophylaxis):&lt;br&gt;• TMP-SMX (160 mg/800 mg) PO daily or (320 mg/1600 mg) three times weekly (BIII)&lt;br&gt;• Pyrimethamine 25 mg PO daily + leucovorin 5–10 mg PO daily (BII)&lt;br&gt;• Ciprofloxacin 500 mg three times weekly (CI) as a second-line alternative</td>
<td>Fluid and electrolyte management in patients with dehydration (AI).&lt;br&gt;Nutritional supplementation for malnourished patients (AIII).&lt;br&gt;Immune reconstitution with ART may result in fewer relapses (AIII).</td>
</tr>
<tr>
<td>Cytomegalovirus (CMV) Disease</td>
<td>CMV Retinitis Induction Therapy (followed by Chronic Maintenance Therapy):&lt;br&gt;For Immediate Sight-Threatening Lesions (within 1500 microns of the fovea):&lt;br&gt;• 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&lt;br&gt;• Valganciclovir 900 mg PO BID for 14–21 days, then 900 mg once daily (AI):&lt;br&gt;For Peripheral Lesions:&lt;br&gt;• Valganciclovir 900 mg PO BID for 14–21 days, then 900 mg once daily (AI)&lt;br&gt;Chronic Maintenance:&lt;br&gt;• Valganciclovir 900 mg PO daily (AI) for 3–6 months until ART induced immune recovery (see Table 4)</td>
<td>CMV Retinitis&lt;br&gt;For Immediate Sight-Threatening Lesions (within 1500 microns of the fovea): Intravitreal therapy as listed in the Preferred section, plus one of the following:&lt;br&gt;Alternative Symptomatic Induction Therapy (followed by Chronic Maintenance Therapy):&lt;br&gt;• Ganciclovir 5 mg/kg IV q12h for 14–21 days (AI), or&lt;br&gt;• Foscarnet 90 mg/kg IV q12h or 60 mg/kg q8h for 14–21 days (AI), or&lt;br&gt;• 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) (BII). (Note: This regimen should be avoided in patients with sulfa allergy because of cross hypersensitivity with probenecid.)&lt;br&gt;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).&lt;br&gt;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.&lt;br&gt;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.</td>
<td>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).&lt;br&gt;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.&lt;br&gt;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.</td>
</tr>
</tbody>
</table>
### Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 9 of 23)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cytomegalovirus (CMV) Disease</strong>, continued</td>
<td>CMV Esophagitis or Colitis:</td>
<td>Chronic Maintenance (for 3-6 months until ART induced immune recovery (see Table 4):</td>
<td>Routine (i.e., every 3 months) ophthalmologic follow-up is recommended after stopping chronic maintenance therapy for early detection of relapse or IRU, and then periodically after sustained immune reconstitution (AIII). IRU may develop in the setting of immune reconstitution. <strong>Treatment of IRU</strong></td>
</tr>
<tr>
<td></td>
<td>• Ganciclovir 5 mg/kg IV q12h; may switch to valganciclovir 900 mg PO q12h once the patient can tolerate oral therapy (BII) • Duration: 21–42 days or until symptoms have resolved (CII) • Maintenance therapy is usually not necessary, but should be considered after relapses (BII).</td>
<td>• Ganciclovir 5 mg/kg IV 5–7 times weekly (AII), or • Foscarnet 90–120 mg/kg IV once daily (AII), or • Cidofovir 5 mg/kg IV every other week with saline hydration and probenecid as above (BII).</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Well-Documented, Histologically Confirmed CMV Pneumonia:</td>
<td>CMV Esophagitis or Colitis:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 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.</td>
<td>• Foscarnet 90 mg/kg IV q12h or 60 mg/kg q8h (BII) 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 (CIII) • For mild disease, if ART can be initiated without delay, consider withholding CMV therapy (CIII).</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CMV Neurological Disease Note: Treatment should be initiated promptly.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 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) • The optimal duration of therapy and the role of oral valganclovir have not been established. • Optimize ART to achieve viral suppression and immune reconstitution (BIII).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

Downloaded from https://aidsinfo.nih.gov/guidelines on 11/25/2019
### Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis B Virus (HBV) Disease</strong></td>
<td>ART is recommended for all HIV/ HBV-co-infected patients regardless of CD4 cell count (AII). ART regimen should include 2 drugs that are active against both HBV and HIV, with [(tenofovir DF 300 mg or tenofovir alafenamide* 10 or 25mg) + (emtricitabine 200 mg or lamivudine 300 mg)] PO once daily (+ additional drug(s) for HIV) (AIII). Please refer to Table 7 for dosing recommendations in patients with renal impairment. <strong>Duration:</strong> Continue treatment indefinitely (CIII) * Tenofovir alafenamide (TAF) 10 mg dose is in the fixed dose combination tablets of elvitegravir/cobicistat/TAF/emtricitabine and darunavir/cobicistat/TAF/emtricitabine; when TAF is used with other ARVs, the dose is 25 mg.</td>
<td>For Patients Who Refuse or Are Unable to Take ART or Who Are HIV Long-Term Non-Progressors: HBV treatment is indicated for all those who meet criteria for treatment according to the AASLD 2018 guidelines. • 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)</td>
<td>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 (AII). Cross-resistance to emtricitabine or telbivudine should be assumed in patients with suspected or proven lamivudine-resistance. When changing ART regimens, continue agents with anti-HBV activity (BIII). If anti-HBV therapy is discontinued and a flare occurs, therapy should be re-instiututed because it can be potentially life-saving (AIII). As HBV reactivation can occur during treatment for HCV with directly active agents (DAAs) in the absence of HBV-active drugs, all patients with HIV/ HBV coinfection who will be treated for HCV should be on HBV-active ART at the time of HCV treatment initiation (AIII).</td>
</tr>
<tr>
<td><strong>Hepatitis C Virus (HCV) Disease</strong></td>
<td>The field of HCV drug development is evolving rapidly. The armamentarium of approved drugs is likely to expand considerably in the next few years. Clinicians should refer to the most recent HCV treatment guidelines (<a href="http://www.hcvguidelines.org">http://www.hcvguidelines.org</a>) for the most updated recommendations.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 11 of 23)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
</table>
| Herpes Simplex Virus (HSV) Disease | Orolabial Lesions (For 5–10 Days):  
• Valacyclovir 1 g PO BID (AIII), or  
• Famciclovir 500 mg PO BID (AIII), or  
• Acyclovir 400 mg PO TID (AIII)  
Initial or Recurrent Genital HSV (For 5–14 Days):  
• Valacyclovir 1 g PO BID (A), or  
• Famciclovir 500 mg PO BID (A), or  
• Acyclovir 400 mg PO TID (A)  
Severe Mucocutaneous HSV:  
• 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.  
Chronic Suppressive Therapy  
For patients with severe recurrences of genital herpes (A) or patients who want to minimize frequency of recurrences (A):  
• Valacyclovir 500 mg PO BID (A)  
• Famciclovir 500 mg PO BID (A)  
• Acyclovir 400 mg PO BID (A)  
• Continue indefinitely regardless of CD4 cell count. | For Acyclovir-Resistant HSV  
Preferred Therapy:  
• Foscarnet 80–120 mg/kg/day IV in 2–3 divided doses until clinical response (A)  
Alternative Therapy (CIII):  
• IV cidofovir (dosage as in CMV retinitis), or  
• Topical trifluridine, or  
• Topical cidofovir, or  
• Topical imiquimod  
Duration of Therapy:  
• 21–28 days or longer | Patients with HSV infections can be treated with episodic therapy when symptomatic lesions occur, or with daily suppressive therapy to prevent recurrences.  
Topical formulations of trifluridine and cidofovir are not commercially available.  
Extemporaneous compounding of topical products can be prepared using trifluridine ophthalmic solution and the IV formulation of cidofovir. |
## Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histoplasmosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Moderately Severe to Severe Disseminated Disease</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Induction Therapy:</strong></td>
<td>• For at least 2 weeks or until clinically improved</td>
<td>• Amphotericin B lipid complex 5 mg/kg IV daily (AIII), or</td>
<td>Itraconazole, posaconazole, and voriconazole may have significant interactions with certain ARV agents. These interactions are complex and can be bi-directional. Refer to Drug-Drug Interactions in the Adult and Adolescent Antiretroviral Guidelines for dosage recommendations. Therapeutic drug monitoring and dosage adjustment may be necessary to ensure triazole antifungal and ARV efficacy and reduce concentration-related toxicities. Random serum concentration of itraconazole between 1-2 mcg/mL is recommended. Frequency and severity of toxicities increase when concentration is &gt;4 mcg/mL. Acute pulmonary histoplasmosis in HIV-infected patients with CD4 counts &gt;300 cells/mm³ should be managed as non-immunocompromised host (AIII).</td>
</tr>
<tr>
<td></td>
<td>• Liposomal amphotericin B 3 mg/kg IV daily (AII)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Maintenance Therapy:</strong></td>
<td>• Itraconazole 200 mg PO three times a day for 3 days, then 200 mg PO twice a day (AII)</td>
<td>• Posaconazole extended release 300 mg PO twice a day for 1 day, then 300 mg PO once daily (BII), or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Itraconazole 200 mg PO three times a day for 3 days, then 200 mg PO twice a day (AII)</td>
<td>• Voriconazole 400 mg PO twice a day for 1 day, then 200 mg twice a day (BII), or</td>
<td></td>
</tr>
<tr>
<td><strong>Duration of Therapy:</strong></td>
<td>• At least 12 months</td>
<td>• Fluconazole 800 mg PO daily (CII)</td>
<td></td>
</tr>
<tr>
<td>Meningitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Induction Therapy (4–6 weeks):</strong></td>
<td>• Liposomal amphotericin B: 5 mg/kg/day (AIII)</td>
<td>• Posaconazole extended release 300 mg PO twice a day for 1 day, then 300 mg PO once daily (BII), or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Itraconazole 200 mg PO twice a day to three times a day for ≥12 months and until resolution of abnormal CSF findings (AII)</td>
<td>• Voriconazole 400 mg PO twice a day for 1 day, then 200 mg twice a day (BII), or</td>
<td></td>
</tr>
<tr>
<td><strong>Maintenance Therapy:</strong></td>
<td>• Itraconazole 200 mg PO daily (AII)</td>
<td>• Fluconazole 800 mg PO daily (CII)</td>
<td></td>
</tr>
<tr>
<td><strong>Long-Term Suppression Therapy:</strong></td>
<td>• Itraconazole 200 mg PO daily (AII)</td>
<td>• Posaconazole 300 mg extended release tablet PO once daily (BII), or</td>
<td></td>
</tr>
<tr>
<td><strong>For patients with severe disseminated or CNS infection (AIII) after completion of at least 12 months of therapy and who relapse despite appropriate therapy (BII):</strong></td>
<td></td>
<td>• Voriconazole 200 mg PO twice daily (BIII), or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Posaconazole 300 mg extended release tablet PO once daily (BII), or</td>
<td>• Fluconazole 400 mg PO once daily (CII)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Voriconazole 200 mg PO twice daily (BIII), or</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Fluconazole 400 mg PO once daily (CII)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opportunistic Infection</td>
<td>Preferred Therapy</td>
<td>Alternative Therapy</td>
<td>Other Comments</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-------------------</td>
<td>---------------------</td>
<td>----------------</td>
</tr>
<tr>
<td><strong>Human Herpesvirus-8 Diseases</strong>&lt;br&gt;(Kaposi Sarcoma [KS], Primary Effusion Lymphoma [PEL], Multicentric Castleman’s Disease [MCD])</td>
<td>Mild To Moderate KS (localized involvement of skin and/or lymph nodes):&lt;br&gt;• Initiate or optimize ART (AII)</td>
<td>MCD&lt;br&gt;• Rituximab (375 mg/m² given weekly for 4–8 weeks) may be an alternative to or used adjunctively with antiviral therapy (CII).</td>
<td>• Corticosteroids should be avoided in patients with KS, including those with KS-IRis (AII)</td>
</tr>
<tr>
<td>Advanced KS (visceral [AI] or disseminated cutaneous KS [BIII]):&lt;br&gt;• Chemotherapy (per oncology consult) + ART&lt;br&gt;• Liposomal doxorubicin first line chemotherapy (AI)</td>
<td></td>
<td></td>
<td>• Corticosteroids are potentially effective as adjunctive therapy for MCD, but should be used with caution, esp. in patients with concurrent KS.</td>
</tr>
<tr>
<td>Primary Effusion Lymphoma:&lt;br&gt;• Chemotherapy (per oncology consult) + ART (AIII)&lt;br&gt;• PO valganciclovir or IV ganciclovir can be used as adjunctive therapy (CIII).</td>
<td></td>
<td></td>
<td>• Patients who received rituximab for MCD may experience subsequent exacerbation or emergence of KS.</td>
</tr>
<tr>
<td><strong>MCD Therapy Options (in consultation with specialist, depending on HIV/HHV-8 status, presence of organ failure, and refractory nature of disease):</strong>&lt;br&gt;ART (AIII) along with one of the following</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Valganciclovir 900 mg PO BID for 3 weeks (CII), or&lt;br&gt;• Ganciclovir 5 mg/kg IV q12h for 3 weeks (CII), or&lt;br&gt;• Valganciclovir PO or Ganciclovir IV + zidovudine 600 mg PO q6h for 7–21 days (CII)&lt;br&gt;• Rituximab +/- Prednisone (CII)&lt;br&gt;• Monoclonal antibody targeting IL-6 or IL-6 receptor (BII)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concurrent KS and MCD&lt;br&gt;• Rituximab + liposomal doxorubicin (BII)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 14 of 23)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Papillomavirus (HPV) Disease</td>
<td>Treatment of Condyloma Acuminata (Genital Warts)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient-Applied Therapy for Uncomplicated External Warts That Can Be Easily Identified by Patients:</td>
<td></td>
<td></td>
<td>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.</td>
</tr>
<tr>
<td>• 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), or</td>
<td></td>
<td></td>
<td>Topical cidofovir has activity against genital warts, but the product is not commercially available (CIII).</td>
</tr>
<tr>
<td>• Imiquimod 5% cream: Apply to lesion at bedtime and remove in the morning on 3 non-consecutive nights weekly for up to 16 weeks, until lesions are no longer visible. Each treatment should be washed with soap and water 6–10 hours after application (BII), or</td>
<td></td>
<td></td>
<td>Intralesional interferon-alpha is usually not recommended because of high cost, difficult administration, and potential for systemic side effects (CIII).</td>
</tr>
<tr>
<td>• Sinecatechins 15% ointment: Apply to affected areas TID for up to 16 weeks, until warts are completely cleared and not visible (BIII).</td>
<td></td>
<td></td>
<td>The rate of recurrence of genital warts is high despite treatment in HIV-infected patients.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Provider-Applied Therapy for Complex or Multicentric Lesions, or Lesions Inaccessible to Patient Applied Therapy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 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 (BII), or</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Trichloroacetic acid or bichloroacetic acid cauterization: 80%–90% aqueous solution, apply to wart only, allow to dry until a white frost develops. Repeat weekly for up to 6 weeks, until lesions are no longer visible (BIII), or</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Surgical excision (BIII) or laser surgery (CIII) to external or anal warts, or</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Podophyllin 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>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 15 of 23)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leishmaniasis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Visceral                | For Initial Infection:  
  • Liposomal amphotericin B 2–4 mg/kg IV daily (AII), or  
  • Liposomal amphotericin B interrupted schedule (e.g., 4 mg/kg on days 1–5, 10, 17, 24, 31, 38) (AII)  
  • To achieve total dose of 20–60 mg/kg (AII)  
  Chronic Maintenance Therapy: Secondary Prophylaxis): Especially in Patients with CD4 Count <200 cells/µL:  
  • Liposomal amphotericin B 4 mg/kg every 2–4 weeks (AII), or  
  • Amphotericin B lipid complex (AII) 3 mg/kg every 21 days (AII) | For Initial Infection:  
  • Other lipid formulation of amphotericin B, dose and schedule as in Preferred Therapy, or  
  • Amphotericin B deoxycholate 0.5–1.0 mg/kg IV daily for total dose of 1.5–2.0 g (BII), or  
  • Sodium stibogluconate (pentavalent antimony) (BII) 20 mg/kg IV or IM daily for 28 days.  
  Another Option:  
  • Miltefosine 100 mg PO daily for 4 weeks (available in the United States under a treatment IND) (CIII)  
  Chronic Maintenance Therapy: Secondary Prophylaxis):  
  • Sodium stibogluconate 20 mg/kg IV or IM every 4 weeks (BII) | ART should be initiated or optimized (AIII).  
For sodium stibogluconate, contact the CDC Drug Service at (404) 639-3670 or drugservice@cdc.gov. |
| Cutaneous               | • Liposomal amphotericin B 2–4 mg/kg IV daily for 10 days (BII), or  
  • Liposomal amphotericin B interrupted schedule (e.g., 4 mg/kg on days 1–5, 10, 17, 24, 31, 38) to achieve total dose of 20–60 mg/kg (BII), or  
  • Sodium stibogluconate 20 mg/kg IV or IM daily for 3–4 weeks (BIII)  
  Chronic Maintenance Therapy:  
  May be indicated in immunocompromised patients with multiple relapses (CIII) | Possible Options Include:  
  • Oral miltefosine (can be obtained via a treatment IND), or  
  • Topical paromomycin, or  
  • Intrallesional sodium stibogluconate, or  
  • Local heat therapy  
  No data exist for any of these agents in HIV-infected patients; choice and efficacy dependent on species of Leishmania. | None. |
| Malaria                 | Because *Plasmodium falciparum* malaria can progress within hours from mild symptoms or low-grade fever to severe disease or death, all HIV-infected patients with confirmed or suspected *P. falciparum* infection should be hospitalized for evaluation, initiation of treatment, and observation (AIII).  
  Treatment recommendations for HIV-infected patients are the same as HIV-uninfected patients (AIII).  
  When suspicion for malaria is low, antimalarial treatment should not be initiated until the diagnosis is confirmed.  
  For treatment recommendations for specific regions, clinicians should refer to the following web link:  
  [http://www.cdc.gov/malaria/](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 |
Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 16 of 23)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Malaria, continued</strong></td>
<td>Choice of therapy is guided by the degree of parasitemia, the species of <em>Plasmodium</em>, the patient's clinical status, region of infection, and the likely drug susceptibility of the infected species, and can be found at <a href="http://www.cdc.gov/malaria">http://www.cdc.gov/malaria</a>.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Microsporidiosis</strong></td>
<td>For GI Infections Caused by <em>Enterocytozoon bieneusi</em>:</td>
<td></td>
<td>Anti-motility agents can be used for diarrhea control if required (BIII).</td>
</tr>
<tr>
<td></td>
<td>• Initiate or optimize ART with immune restoration to CD4 count &gt;100 cells/mm³ (AII); plus</td>
<td></td>
<td>Fumagillin is available in France as FLISINT® 20 mg capsules. Only available as compassionate use; see the Sanofi Compassionate Use/Managed Access Program website.</td>
</tr>
<tr>
<td></td>
<td>• Manage severe dehydration, malnutrition, and wasting by fluid support (AII) and nutritional supplement (AIII)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>For Intestinal and Disseminated (Not Ocular) Infections Caused by <em>Microsporidia Other Than E. bieneusi</em> and <em>Vittaforma corneae</em>:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Albendazole 400 mg PO twice daily (AII), continue until CD4 count &gt;200 cells/mm³ for &gt;6 months after initiation of ART (BIII)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>For Disseminated Disease Caused by <em>Trachipleistophora or Annacalia</em>:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Itraconazole 400 mg PO daily plus albendazole 400 mg PO twice daily (CIII)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>For Ocular Infection:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Topical fumagillin bicyclohexylammonium (Fumidil B) eye drops 3 mg/mL in saline (fumagillin 70 µg/mL): two drops every 2 hours for 4 days, then two drops four times daily (investigational use only in United States) (BII) plus albendazole 400 mg PO twice daily, for management of systemic infection (BII)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If CD4 count &gt;200 cells/mm³:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Continue until symptoms resolved (CIII).</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If CD4 count ≤200 cells/mm³:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Continue until resolution of ocular symptoms and CD4 count increases to &gt;200 cells/mm³ for &gt;6 months in response to ART (BIII).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opportunistic Infection</td>
<td>Preferred Therapy</td>
<td>Alternative Therapy</td>
<td>Other Comments</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-------------------</td>
<td>---------------------</td>
<td>---------------</td>
</tr>
</tbody>
</table>
| Mycobacterium avium Complex (MAC) Disease | At Least 2 Drugs as Initial Therapy to Prevent or Delay Emergence of Resistance:  
- Clarithromycin 500 mg PO BID (AI)  
+ ethambutol 15 mg/kg PO daily (AI), or  
- If drug interaction or intolerance precludes the use of clarithromycin, (azithromycin 500–600 mg + ethambutol 15 mg/kg) PO daily (AII) | Some experts recommend addition of a third or fourth drug for patients with high mycobacterial loads (>2 log CFU/mL of blood), or in the absence of effective ART (CIII).  
Third or Fourth Drug Options May Include:  
- Rifabutin 300 mg PO daily (dose adjustment may be necessary based on drug interactions) (CI), or  
- A fluoroquinolone such as moxifloxacin 400 mg PO daily (CIII) or levofloxacin 500 mg PO daily (CIII), or  
- An injectable aminoglycoside such as amikacin 10–15 mg/kg IV daily (CIII) or streptomycin 1 g IV or IM daily (CIII) | Testing of susceptibility to clarithromycin and azithromycin is recommended (BIII).  
NSAIDs can be used for moderate to severe symptoms attributed to IRIS (CIII).  
If IRIS symptoms persist, short course (i.e., 4 weeks–8 weeks) systemic corticosteroid (equivalent to 20–40 mg prednisone) can be used (CII). |
| Mycobacterium tuberculosis (TB) Disease | After collecting specimen for culture and molecular diagnostic tests, empiric TB treatment should be started in individuals with clinical and radiographic presentation suggestive of TB (AIII).  
Refer to Table 3 for dosing recommendations.  
Initial Phase (2 Months, Given Daily by DOT) (AI):  
- INH (plus pyridoxine) plus (RIF or RFB) plus PZA plus EMB (AI).  
Continuation Phase (Duration Depends on Site and Severity of Infection [as noted below]):  
- INH (plus pyridoxine) plus (RIF or RFB) daily (AI).  
Total Duration of Therapy (For Drug-Susceptible TB):  
* Pulmonary, Drug-Susceptible TB:  
  - 6 months (BII)  
* Pulmonary TB with Positive Culture After 2 Months of TB Treatment, or Severe Cavity or Disseminated Extrapulmonary TB:  
  - 9 months (BII)  
* Extra-Pulmonary TB with CNS Infection:  
  - 9–12 months (BII) | If rapid drug susceptibility testing (DST) indicates resistance to rifampin with or without other drugs:  
- INH (plus pyridoxine) plus EMB plus PZA plus (moxifloxacin or levofloxacin) plus an aminoglycoside, or  
- Capreomycin (BIII); adjust regimen as conventional DST become available | DOT is recommended for all patients (AII).  
All patients with HIV and TB should be started on ART. Refer to text for recommendations on when to start ART while on TB treatment.  
All rifamycins may have significant pharmacokinetic interactions with ARV drugs, please refer to the Drug-Drug Interactions section in the Adult and Adolescent Antiretroviral Guidelines for dosing recommendations.  
Therapeutic drug monitoring should be considered in patients receiving rifamycin and interacting ART.  
Adjunctive corticosteroids improve survival for TB with CNS involvement (AII). See text for drug, dose, and duration recommendations.  
Paradoxical IRIS that is not severe can be treated with NSAIDs without a change in TB or HIV therapy (BIII).  
See text for prednisone dosing recommendations for pre-emptive treatment or management of IRIS. |
<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
</table>
| **Mycobacterium tuberculosis (TB) Disease, continued** | Extra-Pulmonary TB in Other Sites:  
- 6 months (BII) | For Moderate-to-Severe PCP:  
- Pentamidine 4 mg/kg IV daily infused over ≥60 minutes (AI); can reduce dose to 3 mg/kg IV daily in the event of toxicities (BI), or  
- Primaquine 30 mg (base) PO daily plus (clindamycin 600 mg IV every 6 hours or 900 mg IV every 8 hours) or (clindamycin 450 mg PO every 6 hours or 600 mg PO every 8 hours) (AI) | **Indications for Adjunctive Corticosteroids (AI):**  
- PaO2 <70 mmHg at room air, or  
- Alveolar-arterial DO2 gradient >35 mmHg  
**Prednisone Doses (Beginning as Early as Possible and Within 72 Hours of PCP Therapy) (AI):**  
- Days 1–5: 40 mg PO twice daily  
- Days 6–10: 40 mg PO daily  
- Days 11–21: 20 mg PO daily  
**IV methylprednisolone can be administered as 75% of prednisone dose.**  
**Benefit of corticosteroid if started after 72 hours of treatment is unknown, but some clinicians will use it for moderate-to-severe PCP (BIII).**  
**Whenever possible, patients should be tested for G6PD before use of dapsone or primaquine. Alternative therapy should be used in patients found to have G6PD deficiency.**  
**Patients who are receiving pyrimethamine/sulfadiazine for treatment or suppression of toxoplasmosis do not require additional PCP prophylaxis (AII).**  
**If TMP-SMX is discontinued because of a mild adverse reaction, re-institution should be considered after the reaction resolves (AII). The dose can be increased gradually (desensitization) (BI), reduced, or the frequency modified (CIII).**  
**TMP-SMX should be permanently discontinued in patients with possible or definite Stevens-Johnson Syndrome or toxic epidermal necrosis (AII).** |
| **Pneumocystis Pneumonia (PCP)** | Patients who develop PCP despite TMP-SMX prophylaxis can usually be treated with standard doses of TMP-SMX (BIII).  
**Duration of PCP treatment: 21 days (AII)**  
**For Moderate to Severe PCP:**  
- TMP-SMX: (TMP 15–20 mg and SMX 75–100 mg)/kg/day IV given every 6 hours or every 8 hours (AI); may switch to PO formulations after clinical improvement (AI).  
- Primaquine 30 mg (base) PO daily plus (clindamycin 600 mg IV every 6 hours or 900 mg IV every 8 hours) or (clindamycin 450 mg PO every 6 hours or 600 mg PO every 8 hours) (AI) | For Mild to Moderate PCP:  
- Dapsone 100 mg PO daily plus TMP 5 mg/kg PO TID (BI), or  
- Primaquine 30 mg (base) PO daily plus (clindamycin 450 mg PO every 6 hours or 600 mg PO every 8 hours) (BI), or  
- Atovaquone 750 mg PO twice daily with food (BI)  
**Secondary Prophylaxis, After Completion of PCP Treatment:**  
- TMP-SMX DS: 1 tablet PO daily (AI), or  
- TMP-SMX (80 mg/400 mg or SS): 1 tablet PO daily (AI)  
**Secondary Prophylaxis, After Completion of PCP Treatment:**  
- TMP-SMX DS: 1 tablet PO three times weekly (BI), or  
- Dapsone 100 mg PO daily (BI), or  
- Dapsone 50 mg PO daily with (pyrimethamine1 50 mg plus leucovorin 25 mg) PO weekly (BI), or  
- (Dapsone 200 mg plus pyrimethamine1 75 mg plus leucovorin 25 mg) PO weekly (BI), or  
- Aerosolized pentamidine 300 mg monthly via Respigrad™ nebulizer (BI), or  
- Atovaquone 1500 mg PO daily (BI), or  
- (Atovaquone 1500 mg plus pyrimethamine1 25 mg plus leucovorin 10 mg) PO daily (CIII) | |
Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 19 of 23)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progressive Multifocal Leukoencephalopathy (PML)/JC Virus Infections</td>
<td>There is no specific antiviral therapy for JC virus infection. The main treatment approach is to reverse the immunosuppression caused by HIV. Initiate ART immediately in ART-naive patients (AII). Optimize ART in patients who develop PML in phase of HIV viremia on ART (AIII).</td>
<td>None.</td>
<td>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).</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Early Stage (Primary, Secondary, and Early-Latent Syphilis):</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Benzathine penicillin G 2.4 million units IM for 1 dose (AII)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Late-Latent Disease (&gt;1 year or of Unknown Duration, and No Signs of Neurosyphilis):</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Benzathine penicillin G 2.4 million units IM weekly for 3 doses (AII)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Late-Stage (Tertiary—Cardiovascular or Gummatous Disease):</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Benzathine penicillin G 2.4 million units IM weekly for 3 doses (AII)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Late-Stage (Tertiary—Cardiovascular or Gummatous Disease):</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 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)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Early Stage (Primary, Secondary, and Early-Latent Syphilis):</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>For penicillin-allergic patients:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Doxycycline 100 mg PO BID for 14 days (BII), or</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Ceftriaxone 1 g IM or IV daily for 10–14 days (BII), or</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Azithromycin 2 g PO for 1 dose (BII) (Note: azithromycin is not recommended for men who have sex with men or pregnant women (AII)).</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Late-Latent Disease (&gt;1 year or of Unknown Duration, and No Signs of Neurosyphilis):</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>For penicillin-allergic patients:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Doxycycline 100 mg PO BID for 28 days (BIII)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neurosyphilis:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 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), or</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• For penicillin-allergic patients: Desensitization to penicillin is the preferred approach (BIII); if not feasible, ceftriaxone, 2 g IV daily for 10–14 days (BII)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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.
### Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 20 of 23)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
</table>
| Talaromycosis (Penicilliosis) | **Induction Therapy:**  
- Liposomal amphotericin B 3–5 mg/kg/day IV (AI)  
**Duration:**  
- 2 weeks (AI), followed by consolidation therapy  
**Consolidation Therapy:**  
- Itraconazole 200 mg PO twice daily for 10 weeks (AI), followed by chronic maintenance therapy  
**Chronic Maintenance Therapy:**  
- Itraconazole 200 mg PO once daily, until CD4 count >100 cells/mm³ for ≥6 months (AII)  | **Induction Therapy:**  
- Amphotericin B deoxycholate 0.7 mg/kg/day IV for 2 weeks (if liposomal amphotericin B is not available) (AI)  
**If Amphotericin B is Not Available:**  
- Voriconazole 6 mg/kg IV every 12 hours for 1 day (loading dose), then 4 mg/kg IV every 12 hours (BII), or  
- Voriconazole 600 mg PO twice daily for 1 day (loading dose), then 400 mg PO twice daily (BII)  
**Duration:**  
- 2 weeks (BII) followed by consolidation therapy with itraconazole (preferred) or voriconazole  
**Consolidation Therapy:**  
- Voriconazole 200 mg PO twice daily for 10 weeks (BII), followed by chronic maintenance therapy  
**Chronic Maintenance Therapy:**  
- Itraconazole should be used (AII). Chronic maintenance therapy with voriconazole has not been studied.  | Itraconazole is not recommended as induction therapy for talaromycosis (AI).  
ART can be initiated as early as 1 week after initiation of treatment for talaromycosis (BII).  
Itraconazole and voriconazole may have significant interactions with certain ARV agents. These interactions are complex and can be bi-directional. Refer to Drug-Drug Interactions in the Adult and Adolescent Antiretroviral Guidelines for dosage recommendations.  
TDM and dosage adjustment may be necessary to ensure triazole antifungal and ARV efficacy and reduce concentration-related toxicities. The goals of itraconazole and voriconazole trough concentrations are >0.5 mcg/mL and >1.0 mcg/mL respectively. |
Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy)  

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
</table>
| Toxoplasma gondii Encephalitis | Treatment of Acute Infection (AI):  
- Pyrimethamine^a 200 mg PO 1 time, followed by weight-based therapy:  
  - 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.  
Duration for Acute Therapy:  
- At least 6 weeks (BII); longer duration if clinical or radiologic disease is extensive or response is incomplete at 6 weeks  
- After completion of acute therapy, all patients should be initiated on chronic maintenance therapy  
Chronic Maintenance Therapy:  
- Pyrimethamine^a 25–50 mg PO daily + sulfadiazine 2000–4000 mg PO daily (in 2–4 divided doses) + leucovorin 10–25 mg PO daily (AI) | Treatment of Acute Infection:  
- Pyrimethamine^a (leucovorin)* + clindamycin 600 mg IV or PO q6h (AI), or  
- TMP-SMX (TMP 5 mg/kg and SMX 25 mg/kg) IV or PO BID (BI), or  
- Atovaquone 1500 mg PO BID with food + pyrimethamine^a (leucovorin)* (BII), or  
- Atovaquone 1500 mg PO BID with food + sulfadiazine 1000–1500 mg PO q6h (weight-based dosing, as in preferred therapy) (BII), or  
- Atovaquone 1500 mg PO BID with food (BII)  
Chronic Maintenance Therapy:  
- Clindamycin 600 mg PO q8h + (pyrimethamine^a 25–50 mg + leucovorin 10–25 mg) PO daily (BII), or  
- TMP-SMX DS 1 tablet BID (BII), or  
- TMP-SMX DS 1 tablet once daily (BIII); or  
- Atovaquone 750–1500 mg PO BID + (pyrimethamine^a 25 mg + leucovorin 10 mg) PO daily (BII), or  
- Atovaquone 750–1500 mg PO BID + sulfadiazine 2000–4000 mg PO daily (in 2–4 divided doses) (BII), or  
- Atovaquone 750–1500 mg PO BID with food (BII)  
- Pyrimethamine^a and leucovorin doses are the same as for preferred therapy. | If pyrimethamine is unavailable or there is a delay in obtaining it, TMP-SMX should be utilized in place of pyrimethamine-sulfadiazine (BI).  
For patients with a history of sulfa allergy, sulfa desensitization should be attempted using one of several published strategies (BI).  
Atovaquone should be administered until therapeutic doses of TMP-SMX are achieved (CIII).  
Adjunctive corticosteroids (e.g., dexamethasone) should only be administered when clinically indicated to treat mass effect associated with focal lesions or associated edema (BIII); discontinue as soon as clinically feasible.  
Anticonvulsants should be administered to patients with a history of seizures (AIII) and continued through acute treatment, but should not be used as seizure prophylaxis (AIII).  
If clindamycin is used in place of sulfadiazine, additional therapy must be added to prevent PCP (AII). |
Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 22 of 23)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Varicella-Zoster Virus (VZV) Disease</strong></td>
<td>Primary Varicella Infection (Chickenpox)</td>
<td>Primary Varicella Infection (Chickenpox)</td>
<td>In managing VZV of the eyes, consultation with an ophthalmologist experienced in management of VZV retinitis is strongly recommended (AIII).</td>
</tr>
<tr>
<td>Uncomplicated Cases:</td>
<td>• Initiate as soon as possible after symptom onset and continue for 5 to 7 days:</td>
<td>• Acyclovir 800 mg PO 5 times a day (BII)</td>
<td>Duration of therapy for VZV retinitis is not well defined, and should be determined based on clinical, virologic, and immunologic responses and ophthalmologic responses.</td>
</tr>
<tr>
<td></td>
<td>• Valacyclovir 1 g PO three times a day (AII), or</td>
<td>Herpes Zoster (Shingles)</td>
<td>Optimization of ART is recommended for serious and difficult-to-treat VZV infections (e.g., retinitis, encephalitis) (AIII).</td>
</tr>
<tr>
<td></td>
<td>• Famciclovir 500 mg PO three times a day (AII)</td>
<td>Acute Localized Dermatomal:</td>
<td>In patients with herpes zoster ophthalmicus who have stromal keratitis and anterior uveitis, topical corticosteroids to reduce inflammation may be necessary. The role of ART has not been established in these cases.</td>
</tr>
<tr>
<td>Severe or Complicated Cases:</td>
<td>• Acyclovir 10 mg/kg IV every 8 hours for 7–10 days (AIII)</td>
<td>• For 7–10 days; consider longer duration if lesions are slow to resolve</td>
<td>In patients with herpes zoster ophthalmicus who have stromal keratitis and anterior uveitis, topical corticosteroids to reduce inflammation may be necessary. The role of ART has not been established in these cases.</td>
</tr>
<tr>
<td></td>
<td>• May switch to oral valacyclovir, famciclovir, or acyclovir after defervescence if no evidence of visceral involvement (BIII).</td>
<td>• Acyclovir 800 mg PO 5 times a day (BII)</td>
<td></td>
</tr>
<tr>
<td><strong>Herpes Zoster (Shingles)</strong></td>
<td>Acute Localized Dermatomal:</td>
<td><strong>Symptomatic Relief</strong>:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• For 7–10 days; consider longer duration if lesions are slow to resolve</td>
<td>• Acyclovir 10 mg/kg IV every 8 hours until clinical improvement is evident (AII)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Valacyclovir 1 g PO three times a day (AII), or</td>
<td>• 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).</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Famciclovir 500 mg three times a day (AII)</td>
<td><strong>Extensive Cutaneous Lesion or Visceral Involvement:</strong></td>
<td></td>
</tr>
<tr>
<td>Extensive Cutaneous Lesion or Visceral Involvement:</td>
<td>• Acyclovir 10 mg/kg IV every 8 hours until clinical improvement is evident (AII)</td>
<td>• Acyclovir 10 mg/kg IV every 8 hours for 10–14 days, followed by valacyclovir 1 g PO three times a day for &gt;14 weeks (AIII), plus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 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).</td>
<td>• Intravitreal ganciclovir 2 mg/0.05 mL twice weekly for 1-2 doses (BIII)</td>
<td></td>
</tr>
<tr>
<td><strong>ARN:</strong></td>
<td></td>
<td><strong>ARN:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Acyclovir 10 mg/kg IV every 8 hours for 10–14 days, followed by valacyclovir 1 g PO three times a day for &gt;14 weeks (AIII), plus</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Intravitreal ganciclovir 2 mg/0.05 mL twice weekly for 1-2 doses (BIII)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PORN:</strong></td>
<td></td>
<td><strong>PORN:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Acyclovir 10 mg/kg IV every 8 hours or ganciclovir 5 mg/kg IV every 12 hours (AIII), plus</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy) (page 23 of 23)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Preferred Therapy</th>
<th>Alternative Therapy</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varicella-Zoster Virus (VZV) Disease, continued</td>
<td>≥1 intravitreal antiviral injection: ganciclovir 2 mg/0.05 mL or foscarnet 1.2 mg/0.05 mL twice weekly (AIII)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Initiate or optimize ART (AIII)</td>
</tr>
</tbody>
</table>

* Refer to [Daraprim Direct](https://www.daraprimdirect.com) for information on accessing pyrimethamine.

### Key to Acronyms:
- ACTG = AIDS Clinical Trials Group
- ARN = acute retinal necrosis
- 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
- ddI = didanosine
- DOT = directly-observed therapy
- DS = double strength
- EFV = efavirenz
- EMB = ethambutol
- g = gram
- 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
- 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

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

(Last updated September 27, 2019; last reviewed September 27, 2019)

<table>
<thead>
<tr>
<th>TB Drug</th>
<th>ARV Drugs</th>
<th>Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>All ARVs</td>
<td>5 mg/kg (usual dose 300 mg)</td>
</tr>
<tr>
<td>Rifampin</td>
<td>With HIV PIs, DOR, ETR, RPV, BIC, or EVG/c</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Note:</strong> DTG, RAL, and MVC doses need to be adjusted when used with rifampin</td>
<td>With TAF</td>
<td>Use with caution at dose indicated below</td>
</tr>
<tr>
<td></td>
<td>With other ARV drugs</td>
<td>10 mg/kg (usual dose 600 mg)</td>
</tr>
<tr>
<td>Rifabutin</td>
<td>With PI with COBI, TAF, BIC, or EVG/c containing regimens</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Note:</strong> DOR and RPV doses need to be adjusted when used with rifabutin</td>
<td>With DTG, RAL, EFV, DOR, RPV</td>
<td>5 mg/kg (usual dose 300 mg)</td>
</tr>
<tr>
<td></td>
<td>With HIV PIs with RTV</td>
<td>150 mg</td>
</tr>
<tr>
<td></td>
<td>With EFV</td>
<td>450–600 mg</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>All ARVs</td>
<td>Weight-Based Dosing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Weighing 40–55 kg: 1,000 mg (18.2–25.0 mg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Weighing 56–75 kg: 1,500 mg (20.0–26.8 mg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Weighing 76–90 kg: 2,000 mg (22.2–26.3 mg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Weighing &gt;90 kg: 2,000 mg</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>All ARVs</td>
<td>Weight-Based Dosing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Weighing 40–55 kg: 800 mg (14.5–20.0 mg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Weighing 56–75 kg: 1,200 mg (16.0–21.4 mg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Weighing 76–90 kg: 1,600 mg (17.8–21.1 mg/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Weighing &gt;90 kg: 1,600 mg</td>
</tr>
</tbody>
</table>

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

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

* This combination has not been tested in patients to confirm PK and virologic efficacy among patients taking full dose ART and TB regimens.

* Acquired rifamycin resistance has been reported in patients with inadequate rifabutin levels while on 150 mg twice weekly dosing together with RTV-boosted PIs. May consider TDM when rifabutin is used with an RTV-boosted PI and adjust dose accordingly.

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

**Key:** ARV = antiretroviral; ART = antiretroviral therapy; BIC = bictegravir; COBI = cobicistat; DOR = doravirine; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; MVC = maraviroc; PI = protease inhibitor; PK = pharmacokinetic; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TB = tuberculosis; TDM = therapeutic drug monitoring.
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 November 21, 2019; last reviewed November 21, 2019)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Indication for Discontinuing Primary Prophylaxis</th>
<th>Indication for Restarting Primary Prophylaxis</th>
<th>Indication for Discontinuing Secondary Prophylaxis/Chronic Maintenance Therapy</th>
<th>Indication for Restarting Secondary Prophylaxis/Chronic Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial Enteric Infections: Salmonellosis</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>Resolution of <em>Salmonella</em> infection and after response to ART with sustained viral suppression and CD4 counts &gt;200 cells/µL (CII)</td>
<td>No recommendation</td>
</tr>
</tbody>
</table>
| Bartonellosis | Not applicable | Not applicable | • Received at least 3–4 months of treatment, *and*  
• CD4 count >200 cells/µL for ≥6 months (CIII)  
• Some specialists would only discontinue therapy if *Bartonella* titers have also decreased by four-fold (CIII). | No recommendation |
| Candidiasis (Mucocutaneous) | Not applicable | Not applicable | If used, reasonable to discontinue when CD4 count >200 cells/µL (AIII). | No recommendation |
| Coccidioidomycosis | CD4 count ≥250 cells/µL and with viral suppression while on ART (CIII) | Restart at CD4 count <250 cells/µL (BIII) | Only for patients with focal coccidioidal pneumonia (AII):  
• 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.  
For patients with diffuse pulmonary (BIII), disseminated non-meningeal (BIII):  
• 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  
For meningeal diseases (AII):  
Suppressive therapy should be continued indefinitely, even with increase in CD4 count on ART. | No recommendation |
| Cryptococcal Meningitis | Not applicable | Not applicable | If the following criteria are fulfilled (BII):  
• Completed initial (induction and consolidation) therapy, *and*  
• Received at least 1 year of maintenance therapy, *and*  
• Remain asymptomatic of cryptococcal infection, *and*  
• CD4 count ≥100 cells/µL for >3 months, and with suppressed plasma HIV RNA in response to ART | CD4 count <100 cells/µL (AIII) |
### Table 4. Indications for Discontinuing and Restarting Opportunistic Infection Secondary Prophylaxis or Chronic Maintenance in HIV-Infected Adults and Adolescents (page 2 of 3)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Indication for Discontinuing Primary Prophylaxis</th>
<th>Indication for Restarting Primary Prophylaxis</th>
<th>Indication for Discontinuing Secondary Prophylaxis/Chronic Maintenance Therapy</th>
<th>Indication for Restarting Secondary Prophylaxis/Chronic Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystoisosporiasis (Formerly Isosporiasis)</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>Sustained increase in CD4 count to &gt;200 cells/µL for &gt;6 months in response to ART and without evidence of <em>I. belli</em> infection (BIII)</td>
<td>No recommendation</td>
</tr>
<tr>
<td>Cytomegalovirus Retinitis</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>• CMV treatment for at least 3 to 6 months; and with CD4 count &gt;100 cells/µL for &gt;3 to 6 months in response to ART (AII).&lt;br&gt;• 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.&lt;br&gt;• 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).&lt;br&gt;CD4 count &lt;100 cells/µL (AIII)</td>
<td></td>
</tr>
<tr>
<td>Histoplasmosis</td>
<td>On ART, with CD4 count &gt;150 cells/mm³ and undetectable HIV-1 viral load for 6 months (BIII)</td>
<td>For patients at high risk of acquiring histoplasmosis, restart if CD4 count falls to &lt;150 cells/mm³ (CIII)</td>
<td>If the following criteria (AI) are fulfilled:&lt;br&gt;• Received azole therapy for &gt;1 year, and&lt;br&gt;• Negative fungal blood cultures, and&lt;br&gt;• Serum or urine <em>Histoplasma</em> antigen below the level of quantification, and&lt;br&gt;• Undetectable HIV viral load, and&lt;br&gt;• CD4 count ≥150 cells/mm³ for ≥6 months in response to ART&lt;br&gt;CD4 count &lt;150 cells/mm³ (BIII)</td>
<td></td>
</tr>
<tr>
<td>Leishmaniasis: Visceral (and possibly cutaneous leishmaniasis in immunocompromised patients with multiple relapses)</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>There is no consensus regarding when to stop secondary prophylaxis. Some investigators suggest that therapy can be stopped if CD4 count increases to &gt;200 to 350 cells/µL for 3–6 months in response to ART, but others suggest that therapy should be continued indefinitely.</td>
<td>No recommendation</td>
</tr>
<tr>
<td>Microsporidiosis</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>No signs and symptoms of non-ocular (BIII) or ocular (CIII) microsporidiosis and CD4 count &gt;200 cells/µL for &gt;6 months in response to ART.</td>
<td>No recommendation</td>
</tr>
<tr>
<td><em>Mycobacterium avium</em> Complex Disease</td>
<td>Initiation of effective ART (AI)</td>
<td>CD4 count &lt;50 cells/mm³; only if not on fully suppressive ART (AIII)</td>
<td>If the Following Criteria are Fulfilled (AI):&lt;br&gt;• Completed ≥12 months of therapy, and&lt;br&gt;• No signs and symptoms of MAC disease, and&lt;br&gt;• Have sustained (&gt;6 months) CD4 count &gt;100 cells/mm³ in response to ART.&lt;br&gt;CD4 count &lt;100 cells/mm³ (AIII)</td>
<td></td>
</tr>
</tbody>
</table>
### Table 4. Indications for Discontinuing andRestarting Opportunistic Infection Secondary Prophylaxis or Chronic Maintenance in HIV-Infected Adults and Adolescents (page 3 of 3)

<table>
<thead>
<tr>
<th>Opportunistic Infection</th>
<th>Indication for Discontinuing Primary Prophylaxis</th>
<th>Indication for Restarting Primary Prophylaxis</th>
<th>Indication for Discontinuing Secondary Prophylaxis/Chronic Maintenance Therapy</th>
<th>Indication for Restarting Secondary Prophylaxis/Chronic Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pneumocystis Pneumonia</strong></td>
<td>CD4 count increased from &lt;200 to &gt;200 cells/mm³ for &gt;3 months in response to ART (AI) Can consider when CD4 count is 100–200 cells/mm³ if HIV RNA remains below limits of detection for ≥3 months–6 months (BII).</td>
<td>CD4 count &lt;100 cells/mm³ (AII) CD4 count 100–200 cells/mm³ and HIV RNA above detection limit of the assay (AII).</td>
<td>CD4 count increased from &lt;200 cells/mm³ to &gt;200 cells/mm³ for &gt;3 months in response to ART (BII) Can consider when CD4 count is 100–200 cells/mm³ if HIV RNA remains below limits of detection for ≥3 months–6 months (BII). If PCP occurs at a CD4 count &gt;200 cells/mm³ while not on ART, discontinuation of prophylaxis can be considered once HIV RNA levels are suppressed to below limits of detection for ≥3 months–6 months (CII). If PCP occurs at a CD4 count &gt;200 cells/mm³ while on ART, continue PCP prophylaxis for life, regardless of how high the CD4 cell count rises as a consequence of ART (BIII).</td>
<td>CD4 count &lt;100 cells/mm³ (AIII) CD4 count 100–200 cells/mm³ and with HIV RNA above detection limit of the assay (AIII).</td>
</tr>
<tr>
<td><strong>Talaromycosis (Penicilliosis)</strong></td>
<td>CD4 count &gt;100 cells/mm³ for &gt;6 months in response to ART (BII) or If achieved sustained HIV viral suppression for &gt;6 months (BIII)</td>
<td>CD4 count &lt;100 cells/mm³ (BII)—if patient is unable to have ART, or has treatment failure without access to effective ART options, and still resides in or travels to the endemic area</td>
<td>CD4 count &gt;100 cells/mm³ for ≥6 months in response to ART (BII) or If achieved sustained HIV viral suppression for &gt;6 months (BIII)</td>
<td>CD4 count &lt;100 cells/mm³ (BII)</td>
</tr>
<tr>
<td><strong>Toxoplasma gondii Encephalitis</strong></td>
<td>CD4 count increased to &gt;200 cells/µL for &gt;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)</td>
<td>CD4 count &lt;100 cells/µL, (AIII) CD4 count 100-200 cells/µL and with HIV RNA above detection limit of the assay (AIII).</td>
<td>Successfully completed initial therapy, remain free of signs and symptoms of TE, and CD4 count &gt;200 cells/µL for &gt;6 months in response to ART (BII).</td>
<td>CD4 count &lt;200 cells/µL (AIII)</td>
</tr>
</tbody>
</table>

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

**Evidence Rating:**

*Strength of Recommendation:*
- A: Strong recommendation for the statement
- B: Moderate recommendation for the statement
- C: Optional recommendation for the statement

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

In cases where there are no data for the prevention or treatment of an OI based on studies conducted in HIV-infected populations, but data derived from HIV-uninfected patients exist that can plausibly guide management decisions for patients with HIV/AIDS, the data will be rated as III but will be assigned recommendations of A, B, C depending on the strength of recommendation.
**Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections**  
(page 1 of 15)  
(Last updated October 22, 2019; last reviewed October 22, 2019)

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

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

**Do not coadminister.**

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

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

**Coadministration should be avoided, if possible.**

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

**Use with caution.**

Drug combinations are recommended to be used with caution when:

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

**Rifamycin Antibiotics-Related Interactions**

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

**Note:** To avoid redundancy, drug-drug interactions are listed only once by primary drug (listed alphabetically). Subsequently, when an interacting agent becomes the primary drug, guideline users are referred to the entry for the initial primary drug. See the Clarithromycin row for the first example of this format.
### Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 2 of 15)

<table>
<thead>
<tr>
<th>Primary Drug</th>
<th>Interacting Agent</th>
<th>Effect on Primary and/or Concomitant Drug Concentrations</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Artemether/Lumefantrine</strong></td>
<td>Clarithromycin</td>
<td>↑ lumefantrine expected</td>
<td>Coadministration should be avoided, if possible. Consider azithromycin in place of clarithromycin.</td>
</tr>
<tr>
<td></td>
<td>Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td>↑ artemether and lumefantrine possible</td>
<td>Use with caution. Monitor for artemether and lumefantrine toxicities.</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>↑ lumefantrine possible</td>
<td><strong>Do not coadminister.</strong> Consider azithromycin in place of erythromycin.</td>
</tr>
<tr>
<td></td>
<td>Fluconazole</td>
<td>↑ lumefantrine possible</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for lumefantrine toxicities.</td>
</tr>
<tr>
<td></td>
<td>Isavuconazole</td>
<td>↑ lumefantrine possible</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for lumefantrine toxicities.</td>
</tr>
<tr>
<td></td>
<td>Itraconazole</td>
<td>↑ lumefantrine expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for lumefantrine toxicities.</td>
</tr>
<tr>
<td></td>
<td>Mefloquine</td>
<td>↓ lumefantrine possible</td>
<td>If mefloquine is administered immediately before artemether/lumefantrine, monitor for decreased efficacy of artemether/lumefantrine and encourage food intake.</td>
</tr>
<tr>
<td></td>
<td>Posaconazole</td>
<td>↑ lumefantrine expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for lumefantrine toxicities.</td>
</tr>
<tr>
<td></td>
<td>Rifabutina</td>
<td>↓ artemether, DHA, and lumefantrine expected</td>
<td>Use with caution. Monitor for antimalarial efficacy.</td>
</tr>
<tr>
<td></td>
<td>Rifampina</td>
<td>Artemether AUC ↓ 89%</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>DHA AUC ↓ 85%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lumefantrine AUC ↓ 68%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rifapentinea</td>
<td>↓ artemether, DHA, and lumefantrine expected</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td>Voriconazole</td>
<td>↑ lumefantrine expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for lumefantrine toxicities.</td>
</tr>
<tr>
<td><strong>Atovaquone</strong></td>
<td>Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td>↔ atovaquone (based on interaction data for atovaquone oral solution with ATV/r)</td>
<td>No dosage adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>Doxycycline</td>
<td>Atovaquone concentration ↑ approximately equal to 40% with tetracycline</td>
<td>Dose adjustment not established; if coadministered, instruct patient to take atovaquone with fatty meal and monitor for decreased atovaquone efficacy.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No interaction study with doxycycline</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rifabutina</td>
<td>Atovaquone C_{SS} ↓ 34%</td>
<td>Dose adjustment not established; if coadministered, instruct patient to take atovaquone with fatty meal and monitor for decreased atovaquone efficacy.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rifabutin C_{SS} ↓ 19%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rifampina</td>
<td>Atovaquone C_{SS} ↓ 52%</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rifampin C_{SS} ↑ 37%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rifapentinea</td>
<td>↓ atovaquone expected</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
</tbody>
</table>
Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections  (page 3 of 15)

<table>
<thead>
<tr>
<th>Primary Drug</th>
<th>Interacting Agent</th>
<th>Effect on Primary and/or Concomitant Drug Concentrations</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atovaquone/Proguanil</td>
<td>Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td>↓ atovaquone and proguanil AUC (when coadministered with ATV/r or LPV/r)</td>
<td>Consider alternative drug for malaria prophylaxis.</td>
</tr>
<tr>
<td>Bedaquiline</td>
<td>Clarithromycin</td>
<td>↑ bedaquiline expected</td>
<td>Do not coadminister. Consider azithromycin in place of clarithromycin.</td>
</tr>
<tr>
<td></td>
<td>Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td>↑ bedaquiline expected</td>
<td>Coadministration should be avoided, if possible. Consider alternative HCV regimen.</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>↑ bedaquiline possible</td>
<td>Do not coadminister. Consider azithromycin in place of erythromycin.</td>
</tr>
<tr>
<td></td>
<td>Fluconazole</td>
<td>↑ bedaquiline possible</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for bedaquiline toxicities.</td>
</tr>
<tr>
<td></td>
<td>Isavuconazole</td>
<td>↑ bedaquiline possible</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for bedaquiline toxicities.</td>
</tr>
<tr>
<td></td>
<td>Itraconazole</td>
<td>↑ bedaquiline expected</td>
<td>Coadministration should be avoided, if possible. If coadministration is required for &gt;14 days, weigh the benefits of therapy against the risks of bedaquiline toxicities. If coadministered, monitor for bedaquiline toxicities.</td>
</tr>
<tr>
<td></td>
<td>Posaconazole</td>
<td>↑ bedaquiline expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for bedaquiline toxicities.</td>
</tr>
<tr>
<td></td>
<td>Rifabutin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>↔ bedaquiline</td>
<td>If coadministered, monitor for rifabutin toxicities.</td>
</tr>
<tr>
<td></td>
<td>Rifampin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Bedaquiline AUC ↓ 53%</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>Rifapentine&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Bedaquiline AUC ↓ 55% (with daily rifapentine)</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>Voriconazole</td>
<td>↑ bedaquiline expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for bedaquiline toxicities.</td>
</tr>
<tr>
<td>Caspofungin</td>
<td>Rifabutin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>No data ↓ caspofungin possible</td>
<td>Monitor for antifungal efficacy. Dose not established. Consider increasing caspofungin dose to 70 mg/day or switch to another echinocandin (e.g., micafungin or anidulafungin).</td>
</tr>
<tr>
<td></td>
<td>Rifampin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Caspofungin C&lt;sub&gt;min&lt;/sub&gt; ↓ 30%</td>
<td>If coadministered, caspofungin dose should be increased to 70 mg/day. Consider alternative echinocandin (e.g., micafungin or anidulafungin).</td>
</tr>
<tr>
<td></td>
<td>Rifapentine&lt;sup&gt;a&lt;/sup&gt;</td>
<td>No data ↓ caspofungin possible</td>
<td>Monitor for antifungal efficacy. Dose not established. Consider increasing caspofungin dose to 70 mg/day or switch to another echinocandin (e.g., micafungin or anidulafungin).</td>
</tr>
</tbody>
</table>
Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections  

<table>
<thead>
<tr>
<th>Primary Drug</th>
<th>Interacting Agent</th>
<th>Effect on Primary and/or Concomitant Drug Concentrations</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroquine</td>
<td>Clarithromycin</td>
<td>↑ chloroquine expected</td>
<td>Do not coadminister. Consider azithromycin in place of clarithromycin.</td>
</tr>
<tr>
<td>Erythromycin</td>
<td></td>
<td>↑ chloroquine possible</td>
<td>Do not coadminister. Consider azithromycin in place of erythromycin.</td>
</tr>
<tr>
<td>Fluconazole</td>
<td></td>
<td>↑ chloroquine possible</td>
<td>Coadministration should be avoided, if possible. If co-administered, monitor for chloroquine toxicities.</td>
</tr>
<tr>
<td>Isavuconazole</td>
<td></td>
<td>↑ chloroquine possible</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for chloroquine toxicities.</td>
</tr>
<tr>
<td>Itraconazole</td>
<td></td>
<td>↑ chloroquine expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for chloroquine toxicities.</td>
</tr>
<tr>
<td>Posaconazole</td>
<td></td>
<td>↑ chloroquine expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for chloroquine toxicities.</td>
</tr>
<tr>
<td>Rifabutina</td>
<td></td>
<td>↓ chloroquine expected</td>
<td>Monitor for chloroquine efficacy.</td>
</tr>
<tr>
<td>Rifampina</td>
<td></td>
<td>↓ chloroquine expected</td>
<td>Monitor for chloroquine efficacy.</td>
</tr>
<tr>
<td>Rifapentinea</td>
<td></td>
<td>↓ chloroquine expected</td>
<td>Monitor for chloroquine efficacy.</td>
</tr>
<tr>
<td>Voriconazole</td>
<td></td>
<td>↑ chloroquine expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for chloroquine toxicities.</td>
</tr>
</tbody>
</table>

Clarithromycin

<table>
<thead>
<tr>
<th>Interacting Agent</th>
<th>Effect on Clarithromycin</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artemether/ Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
</tr>
<tr>
<td>Bedaquiline</td>
<td>See Bedaquiline</td>
<td>See Bedaquiline</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>See Chloroquine</td>
<td>See Chloroquine</td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>↑ daclatasvir expected</td>
<td>Decrease daclatasvir dose to 30 mg once daily.</td>
</tr>
<tr>
<td>Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir</td>
<td>↑ clarithromycin and paritaprevir expected ↑ ombitasvir and dasabuvir possible</td>
<td>Coadministration should be avoided, if possible. Consider azithromycin in place of clarithromycin.</td>
</tr>
<tr>
<td>Elbasvir/Grazoprevir</td>
<td>↑ elbasvir and grazoprevir expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor closely for hepatotoxicity. Consider azithromycin in place of clarithromycin.</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>Clarithromycin AUC ↑ 18% and Cmin ↑ 33%</td>
<td>No dose adjustment necessary in patients with normal renal function. Monitor for clarithromycin toxicity.</td>
</tr>
<tr>
<td>Isavuconazole</td>
<td>↑ isavuconazole and clarithromycin expected</td>
<td>Coadministration should be avoided, if possible. Consider azithromycin in place of clarithromycin. If coadministered, monitor for toxicities of both isavuconazole and clarithromycin. Role of isavuconazole TDM has not been established.</td>
</tr>
</tbody>
</table>
### Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections

<table>
<thead>
<tr>
<th>Primary Drug, continued</th>
<th>Interacting Agent</th>
<th>Effect on Primary and/or Concomitant Drug Concentrations</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarithromycin, continued</td>
<td>Itraconazole</td>
<td>↑ itraconazole and clarithromycin expected</td>
<td>Coadministration should be avoided, if possible. Consider azithromycin in place of clarithromycin. If coadministered, monitor for toxicities of both itraconazole and clarithromycin; consider monitoring itraconazole concentration and adjust dose accordingly.</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>↑ mefloquine expected</td>
<td>Use with caution. Consider azithromycin in place of clarithromycin. If coadministered, monitor for mefloquine toxicity.</td>
<td></td>
</tr>
<tr>
<td>Posaconazole</td>
<td>↑ clarithromycin expected</td>
<td>Coadministration should be avoided, if possible. Consider azithromycin in place of clarithromycin.</td>
<td></td>
</tr>
<tr>
<td>Quinine</td>
<td>↑ quinine expected, ↑ clarithromycin possible</td>
<td><strong>Do not coadminister.</strong> Consider azithromycin in place of clarithromycin.</td>
<td></td>
</tr>
<tr>
<td>Rifabutin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Clarithromycin AUC ↓ 44%, 14-OH AUC ↑ 57%, Rifabutin AUC ↑ 76% to 99%, des-Rbt AUC ↑ 375%</td>
<td>Use with caution. Consider azithromycin in place of clarithromycin. If coadministered, consider reducing rifabutin dose, monitoring clarithromycin and rifabutin concentrations, and monitoring for rifabutin toxicities.</td>
<td></td>
</tr>
<tr>
<td>Rifampin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Clarithromycin concentration ↓ 87%, Rifampin AUC ↑ 60%</td>
<td><strong>Do not coadminister.</strong> Use azithromycin in place of clarithromycin.</td>
<td></td>
</tr>
<tr>
<td>Rifapentine&lt;sup&gt;a&lt;/sup&gt;</td>
<td>↓ clarithromycin expected, ↑ 14-OH and rifapentine expected</td>
<td>Use with caution. Consider azithromycin in place of clarithromycin. If coadministered, monitor for rifapentine toxicities; consider monitoring clarithromycin and rifapentine concentrations and adjusting doses accordingly.</td>
<td></td>
</tr>
<tr>
<td>Voriconazole</td>
<td>↑ clarithromycin expected</td>
<td>Coadministration should be avoided, if possible. Consider azithromycin in place of clarithromycin.</td>
<td></td>
</tr>
</tbody>
</table>

### Daclatasvir

<table>
<thead>
<tr>
<th>Daclatasvir</th>
<th>Clarithromycin</th>
<th>See Clarithromycin</th>
<th>See Clarithromycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythromycin</td>
<td>↑ daclatasvir possible</td>
<td>No dosage adjustment. Monitor for daclatasvir toxicities.</td>
<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td>↑ daclatasvir possible</td>
<td>No dosage adjustment. Monitor for daclatasvir toxicities.</td>
<td></td>
</tr>
<tr>
<td>Isavuconazole</td>
<td>↑ daclatasvir possible</td>
<td>Dose not established. Monitor for daclatasvir toxicities.</td>
<td></td>
</tr>
<tr>
<td>Itraconazole</td>
<td>↑ daclatasvir expected</td>
<td>Reduce daclatasvir dose to 30 mg once daily.</td>
<td></td>
</tr>
<tr>
<td>Posaconazole</td>
<td>↑ daclatasvir expected</td>
<td>Reduce daclatasvir dose to 30 mg once daily.</td>
<td></td>
</tr>
<tr>
<td>Rifabutin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>↓ daclatasvir expected</td>
<td>Dose not established. Consider increasing daclatasvir dose to 90 mg once daily and monitor for therapeutic efficacy.</td>
<td></td>
</tr>
<tr>
<td>Rifampin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Daclatasvir AUC ↓ 79%</td>
<td><strong>Do not coadminister.</strong></td>
<td></td>
</tr>
<tr>
<td>Rifapentine&lt;sup&gt;a&lt;/sup&gt;</td>
<td>↓ daclatasvir expected</td>
<td>Dose not established. Consider increasing daclatasvir dose to 90 mg once daily and monitor for therapeutic efficacy.</td>
<td></td>
</tr>
</tbody>
</table>
### Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 6 of 15)

<table>
<thead>
<tr>
<th>Primary Drug</th>
<th>Interacting Agent</th>
<th>Effect on Primary and/or Concomitant Drug Concentrations</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daclatasvir, continued</td>
<td>TDF</td>
<td>TFV AUC ↑ 10%</td>
<td>No dosage adjustment.</td>
</tr>
<tr>
<td></td>
<td>Voriconazole</td>
<td>↑ daclatasvir expected</td>
<td>Reduce daclatasvir dose to 30 mg once daily.</td>
</tr>
<tr>
<td>Dapsone</td>
<td>Rifabutina</td>
<td>Dapsone AUC ↓ 27% to 40%</td>
<td>Coadministration should be avoided, if possible. Consider alternatives for dapsone.</td>
</tr>
<tr>
<td></td>
<td>Rifampinb</td>
<td>Dapsone concentration 7-fold to 10-fold and t1/2 ↓ from 24 hours to 11 hours</td>
<td>Coadministration should be avoided, if possible. Consider alternatives for dapsone.</td>
</tr>
<tr>
<td></td>
<td>Rifapentinea</td>
<td>↓ dapsone expected</td>
<td>Coadministration should be avoided, if possible. Consider alternatives for dapsone.</td>
</tr>
<tr>
<td>Dasabuvir/ Ombitasvir/ Paritaprevir/ Ritonavir</td>
<td>Artemether/ Lumefantrine</td>
<td>See Artemether/lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
</tr>
<tr>
<td></td>
<td>Atovaquone (oral solution)</td>
<td>See Atovaquone (oral solution)</td>
<td>See Atovaquone (oral solution)</td>
</tr>
<tr>
<td></td>
<td>Bedaquiline</td>
<td>See Bedaquiline</td>
<td>See Bedaquiline</td>
</tr>
<tr>
<td></td>
<td>Clarithromycin</td>
<td>See Clarithromycin</td>
<td>See Clarithromycin</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>↑ erythromycin and paritaprevir expected</td>
<td>Coadministration should be avoided, if possible. Consider azithromycin in place of erythromycin.</td>
</tr>
<tr>
<td></td>
<td>or ↑ ombitasvir and dasabuvir possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Isavuconazole</td>
<td>Isavuconazole ↑ 96% and RTV AUC ↓ 31% (when studied with LPV/r)</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for isavuconazole toxicity and HCV regimen-associated toxicities and efficacy.</td>
</tr>
<tr>
<td></td>
<td>or ↓ paritaprevir, ombitasvir, and dasabuvir possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Itraconazole</td>
<td>↑ itraconazole and paritaprevir expected</td>
<td>Itraconazole doses &gt;200 mg/day are not recommended unless dosing is guided by itraconazole concentration. Monitor for itraconazole- and HCV regimen-associated toxicities.</td>
</tr>
<tr>
<td></td>
<td>↑ ombitasvir and dasabuvir possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mefloquine</td>
<td>RTV AUC ↓ 31% (based on study with RTV 200 mg twice daily)</td>
<td>Monitor for HCV antiviral activity.</td>
</tr>
<tr>
<td></td>
<td>Posaconazole</td>
<td>↑ posaconazole and paritaprevir expected</td>
<td>Monitor for posaconazole- and HCV regimen-associated toxicities. Monitor posaconazole concentration and adjust dose if necessary.</td>
</tr>
<tr>
<td></td>
<td>↑ ombitasvir and dasabuvir possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rifabutinb</td>
<td>↑ rifabutin expected</td>
<td>Coadministration should be avoided, if possible. With coadministration, decrease rifabutin dose to 150 mg/day and monitor rifabutin concentration. Monitor HCV regimen for efficacy.</td>
</tr>
<tr>
<td></td>
<td>↓ paritaprevir possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rifampinb</td>
<td>↓ paritaprevir, rifatnavir, ombitasvir, and dasabuvir expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>Rifapentinea</td>
<td>↓ paritaprevir, rifatnavir, ombitasvir, and dasabuvir expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>Voriconazole</td>
<td>Voriconazole AUC ↓ 39% (when given with RTV 100 mg twice daily)</td>
<td>Coadminister only if the benefits outweigh the risk. Monitor voriconazole concentration to guide dosage adjustments.</td>
</tr>
<tr>
<td></td>
<td>↑ paritaprevir expected</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections

<table>
<thead>
<tr>
<th>Primary Drug</th>
<th>Interacting Agent</th>
<th>Effect on Primary and/or Concomitant Drug Concentrations</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxycycline</td>
<td>Atovaquone</td>
<td>See Atovaquone</td>
<td>See Atovaquone</td>
</tr>
<tr>
<td></td>
<td>Rifabutina</td>
<td>No data</td>
<td>Monitor closely for doxycycline efficacy or consider alternative therapy.</td>
</tr>
<tr>
<td></td>
<td>Rifampina</td>
<td>Doxycycline AUC ↓ 59%</td>
<td>Use with caution. Monitor closely for doxycycline efficacy or consider alternative therapy.</td>
</tr>
<tr>
<td></td>
<td>Rifapentina</td>
<td>No data</td>
<td>Monitor closely for doxycycline efficacy or consider alternative therapy.</td>
</tr>
<tr>
<td></td>
<td>Elbasvir/Grazoprevir</td>
<td>Clarithromycin</td>
<td>See Clarithromycin</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>↑ elbasvir and grazoprevir expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor closely for hepatotoxicity. Consider azithromycin in place of erythromycin.</td>
</tr>
<tr>
<td></td>
<td>Isavuconazole</td>
<td>↑ elbasvir and grazoprevir expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor closely for hepatotoxicity.</td>
</tr>
<tr>
<td></td>
<td>Itraconazole</td>
<td>↑ elbasvir and grazoprevir expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor closely for hepatotoxicity.</td>
</tr>
<tr>
<td></td>
<td>Posaconazole</td>
<td>↑ elbasvir and grazoprevir expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor closely for hepatotoxicity.</td>
</tr>
<tr>
<td></td>
<td>Rifabutina</td>
<td>↓ elbasvir and grazoprevir possible</td>
<td>Coadministration should be avoided if possible. Consider alternative HCV regimen.</td>
</tr>
<tr>
<td></td>
<td>Rifampina</td>
<td>Grazoprevir AUC ↓ 7% and C24h ↓ 90%</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td>Rifapentina</td>
<td>↓ elbasvir and grazoprevir expected</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td>Voriconazole</td>
<td>↑ elbasvir and grazoprevir expected</td>
<td>Coadministration should be avoided if possible. If coadministered, monitor closely for hepatotoxicity.</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Artemether/ Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
</tr>
<tr>
<td></td>
<td>Bedaquiline</td>
<td>See Bedaquiline</td>
<td>See Bedaquiline</td>
</tr>
<tr>
<td></td>
<td>Chloroquine</td>
<td>See Chloroquine</td>
<td>See Chloroquine</td>
</tr>
<tr>
<td></td>
<td>Daclatasvir</td>
<td>See Daclatasvir</td>
<td>See Daclatasvir</td>
</tr>
<tr>
<td></td>
<td>Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
</tr>
<tr>
<td></td>
<td>Elbasvir/Grazoprevir</td>
<td>See Elbasvir/Grazoprevir</td>
<td>See Elbasvir/Grazoprevir</td>
</tr>
<tr>
<td></td>
<td>Fluconazole</td>
<td>↑ erythromycin possible</td>
<td><strong>Do not coadminister.</strong> Consider azithromycin in place of erythromycin.</td>
</tr>
<tr>
<td></td>
<td>Isavuconazole</td>
<td>↑ erythromycin and isavuconazole possible</td>
<td><strong>Do not coadminister.</strong> Consider azithromycin in place of erythromycin.</td>
</tr>
<tr>
<td></td>
<td>Itraconazole</td>
<td>Itraconazole AUC ↑ 36% and ↑ erythromycin possible</td>
<td><strong>Do not coadminister.</strong> Consider azithromycin in place of erythromycin.</td>
</tr>
</tbody>
</table>
Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections

<table>
<thead>
<tr>
<th>Primary Drug</th>
<th>Interacting Agent</th>
<th>Effect on Primary and/or Concomitant Drug Concentrations</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythromycin, continued</td>
<td>Mefloquine</td>
<td>↑ mefloquine possible</td>
<td>Do not coadminister. Consider azithromycin in place of erythromycin.</td>
</tr>
<tr>
<td></td>
<td>Posaconazole</td>
<td>↑ erythromycin expected</td>
<td>Do not coadminister. Consider azithromycin in place of erythromycin.</td>
</tr>
<tr>
<td></td>
<td>Quinine</td>
<td>↑ quinine expected, ↑ erythromycin possible</td>
<td>Do not coadminister. Consider azithromycin in place of erythromycin.</td>
</tr>
<tr>
<td></td>
<td>Rifabutina</td>
<td>↓ erythromycin possible, ↑ rifabutin possible</td>
<td>Use with caution. Consider azithromycin in place of erythromycin. Monitor for erythromycin efficacy or rifabutin toxicities.</td>
</tr>
<tr>
<td></td>
<td>Rifampinb</td>
<td>↓ erythromycin expected</td>
<td>Consider azithromycin in place of erythromycin. If coadministered, monitor for erythromycin efficacy.</td>
</tr>
<tr>
<td></td>
<td>Rifapentinea</td>
<td>↓ erythromycin expected</td>
<td>Consider azithromycin in place of erythromycin. If coadministered, monitor for erythromycin efficacy.</td>
</tr>
<tr>
<td></td>
<td>Voriconazole</td>
<td>↑ erythromycin expected</td>
<td>Do not coadminister. Consider azithromycin in place of erythromycin.</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>Artemether/Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
</tr>
<tr>
<td></td>
<td>Bedaquiline</td>
<td>See Bedaquiline</td>
<td>See Bedaquiline</td>
</tr>
<tr>
<td></td>
<td>Chloroquine</td>
<td>See Chloroquine</td>
<td>See Chloroquine</td>
</tr>
<tr>
<td></td>
<td>Clarithromycin</td>
<td>See Clarithromycin</td>
<td>See Clarithromycin</td>
</tr>
<tr>
<td></td>
<td>Daclatasvir</td>
<td>See Daclatasvir</td>
<td>See Daclatasvir</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>See Erythromycin</td>
<td>See Erythromycin</td>
</tr>
<tr>
<td></td>
<td>Mefloquine</td>
<td>↑ mefloquine possible</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for mefloquine toxicities.</td>
</tr>
<tr>
<td></td>
<td>Quinine</td>
<td>↑ quinine expected, ↑ fluconazole possible</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for quinine and fluconazole toxicity.</td>
</tr>
<tr>
<td></td>
<td>Rifabutina</td>
<td>Rifabutin AUC ↑ 80% ↔ fluconazole</td>
<td>Use with caution. Monitor for rifabutin toxicities. Consider monitoring rifabutin concentration; may need to decrease rifabutin dose to 150 mg/day.</td>
</tr>
<tr>
<td></td>
<td>Rifampinb</td>
<td>Fluconazole AUC ↓ 23% to 56%</td>
<td>Monitor for antifungal efficacy; may need to increase fluconazole dose.</td>
</tr>
<tr>
<td></td>
<td>Rifapentinea</td>
<td>↓ fluconazole expected</td>
<td>Monitor for antifungal efficacy; may need to increase fluconazole dose.</td>
</tr>
<tr>
<td></td>
<td>Gilecaprevir/Pibrentasvir</td>
<td>Rifabutina</td>
<td>↓ gilecaprevir and pibrentasvir possible</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rifampinb</td>
<td>Gilecaprevir AUC ↓ 88% Pibrentasvir AUC ↓ 87%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rifapentinea</td>
<td>↓ gilecaprevir and pibrentasvir possible</td>
</tr>
<tr>
<td></td>
<td>TDF</td>
<td>TFV AUC ↑ 29% when coadministered as EFV/TDF/FTC</td>
<td>Use usual dose. Monitor renal function or consider TAF.</td>
</tr>
</tbody>
</table>
### Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections

<table>
<thead>
<tr>
<th>Primary Drug</th>
<th>Interacting Agent</th>
<th>Effect on Primary and/or Concomitant Drug Concentrations</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glecaprevir/ Pibrentasvir, continued</strong></td>
<td>TAF</td>
<td>↔ TFV concentration when coadministered as EVG/c/TAF/FTC</td>
<td>No dose adjustment.</td>
</tr>
<tr>
<td><strong>Isavuconazole</strong></td>
<td>Artemether/ Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
</tr>
<tr>
<td>Bedaquiline</td>
<td>See Bedaquiline</td>
<td>See Bedaquiline</td>
<td></td>
</tr>
<tr>
<td>Chloroquine</td>
<td>See Chloroquine</td>
<td>See Chloroquine</td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>See Clarithromycin</td>
<td>See Clarithromycin</td>
<td></td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>See Daclatasvir</td>
<td>See Daclatasvir</td>
<td></td>
</tr>
<tr>
<td>Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td></td>
</tr>
<tr>
<td>Elbasvir/Grazoprevir</td>
<td>See Elbasvir/Grazoprevir</td>
<td>See Elbasvir/Grazoprevir</td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>See Erythromycin</td>
<td>See Erythromycin</td>
<td></td>
</tr>
<tr>
<td>Mefloquine</td>
<td>† mefloquine expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for mefloquine toxicities.</td>
<td></td>
</tr>
<tr>
<td>Quinine</td>
<td>† quinine expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for quinine and isavuconazole toxicities.</td>
<td></td>
</tr>
<tr>
<td>Rifabutin</td>
<td>‡ isavuconazole expected</td>
<td>Consider alternative agent(s). If alternative agents are not available, use with close monitoring for isavuconazole anti-fungal activity and rifabutin toxicity.</td>
<td></td>
</tr>
<tr>
<td>Rifampin</td>
<td>Isavuconazole AUC ↓ 97%</td>
<td><em>Do not coadminister.</em> Consider alternative antifungal and/or antimycobacterial agent(s).</td>
<td></td>
</tr>
<tr>
<td>Rifapentine</td>
<td>Significant ‡ isavuconazole expected</td>
<td><em>Do not coadminister.</em> Consider alternative antifungal and/or antimycobacterial agent(s).</td>
<td></td>
</tr>
<tr>
<td><strong>Itraconazole</strong></td>
<td>Artemether/ Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
</tr>
<tr>
<td>Bedaquiline</td>
<td>See Bedaquiline</td>
<td>See Bedaquiline</td>
<td></td>
</tr>
<tr>
<td>Chloroquine</td>
<td>See Chloroquine</td>
<td>See Chloroquine</td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>See Clarithromycin</td>
<td>See Clarithromycin</td>
<td></td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>See Daclatasvir</td>
<td>See Daclatasvir</td>
<td></td>
</tr>
<tr>
<td>Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td></td>
</tr>
<tr>
<td>Elbasvir/Grazoprevir</td>
<td>See Elbasvir/Grazoprevir</td>
<td>See Elbasvir/Grazoprevir</td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>See Erythromycin</td>
<td>See Erythromycin</td>
<td></td>
</tr>
<tr>
<td>Mefloquine</td>
<td>† Mefloquine expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for mefloquine toxicities.</td>
<td></td>
</tr>
<tr>
<td>Quinine</td>
<td>† quinine expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for quinine and itraconazole toxicities; monitor itraconazole concentration and adjust dose accordingly.</td>
<td></td>
</tr>
</tbody>
</table>
### Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 10 of 15)

<table>
<thead>
<tr>
<th>Primary Drug</th>
<th>Interacting Agent</th>
<th>Effect on Primary and/or Concomitant Drug Concentrations</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Itraconazole, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Itraconazole</td>
<td>Rifabutina</td>
<td>Itraconazole AUC ↓ 70% † rifabutin expected</td>
<td><strong>Do not coadminister.</strong> Consider alternative antifungal and/or antimycobacterial agent(s).</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>Rifampina</td>
<td>Itraconazole AUC ↓ 64% to 88%</td>
<td><strong>Do not coadminister.</strong> Consider alternative antifungal and/or antimycobacterial agent(s).</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>Rifapentinea</td>
<td>↓ itraconazole expected</td>
<td><strong>Do not coadminister.</strong> Consider alternative antifungal and/or antimycobacterial agent(s).</td>
</tr>
<tr>
<td><strong>Ledipasvir/ Sofosbuvir</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ledipasvir/ Sofosbuvir</td>
<td>Rifabutina</td>
<td>↓ ledipasvir and sofosbuvir expected</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td>Ledipasvir/ Sofosbuvir</td>
<td>Rifampina</td>
<td>Ledipasvir AUC ↓ 59% Sofosbuvir AUC ↓ 72%</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td>Ledipasvir/ Sofosbuvir</td>
<td>Rifapentinea</td>
<td>↓ ledipasvir and sofosbuvir expected</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td>TAF</td>
<td></td>
<td>Ledipasvir AUC † 79% (when given with EVG/c/TAF/FTC)</td>
<td>No dosage adjustment.</td>
</tr>
<tr>
<td>TDF</td>
<td></td>
<td>TFV AUC † 98% (when given with EFV/FTC) TFV AUC † 40% (when given with RPV/FTC) TFV AUC † 50% (when given with DRV/r/FTC)</td>
<td>Monitor for TDF toxicities. Consider TAF in place of TDF.</td>
</tr>
<tr>
<td><strong>Linezolid</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linezolid</td>
<td>Rifabutina</td>
<td>↓ linezolid possible</td>
<td>Monitor for linezolid efficacy.</td>
</tr>
<tr>
<td>Linezolid</td>
<td>Rifampina</td>
<td>Linezolid AUC ↓ 32%</td>
<td>Monitor for linezolid efficacy.</td>
</tr>
<tr>
<td>Linezolid</td>
<td>Rifapentinea</td>
<td>↓ linezolid possible</td>
<td>Monitor for linezolid efficacy.</td>
</tr>
<tr>
<td><strong>Mefloquine</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Artemether/ Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Clarithromycin</td>
<td>See Clarithromycin</td>
<td>See Clarithromycin</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/Paritaprevir/ Ritonavir</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Erythromycin</td>
<td>See Erythromycin</td>
<td>See Erythromycin</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Fluconazole</td>
<td>See Fluconazole</td>
<td>See Fluconazole</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Isavuconazole</td>
<td>See Isavuconazole</td>
<td>See Isavuconazole</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Itraconazole</td>
<td>See Itraconazole</td>
<td>See Itraconazole</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Posaconazole</td>
<td>↑ mefloquine expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for mefloquine toxicities.</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Rifabutina</td>
<td>↓ mefloquine possible</td>
<td>Monitor for mefloquine efficacy.</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Rifampina</td>
<td>Mefloquine AUC ↓ 68%</td>
<td><strong>Do not coadminister.</strong> Use alternative antimalarial drug or rifabutin.</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Rifapentinea</td>
<td>↓ mefloquine expected</td>
<td><strong>Do not coadminister.</strong> Use alternative antimalarial drug or rifabutin.</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Voriconazole</td>
<td>↑ mefloquine expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for mefloquine toxicities.</td>
</tr>
<tr>
<td><strong>Posaconazole</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posaconazole</td>
<td>Artemether/ Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
</tr>
<tr>
<td>Posaconazole</td>
<td>Bedaquiline</td>
<td>See Bedaquiline</td>
<td>See Bedaquiline</td>
</tr>
</tbody>
</table>
### Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 11 of 15)

<table>
<thead>
<tr>
<th>Primary Drug</th>
<th>Interacting Agent</th>
<th>Effect on Primary and/or Concomitant Drug Concentrations</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Posaconazole</strong>&lt;br&gt;continued</td>
<td>Chloroquine</td>
<td>See Chloroquine</td>
<td>See Chloroquine</td>
</tr>
<tr>
<td></td>
<td>Clarithromycin</td>
<td>See Clarithromycin</td>
<td>See Clarithromycin</td>
</tr>
<tr>
<td></td>
<td>Daclatasvir</td>
<td>See Daclatasvir</td>
<td>See Daclatasvir</td>
</tr>
<tr>
<td></td>
<td>Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
</tr>
<tr>
<td></td>
<td>Elbasvir/Grazoprevir</td>
<td>See Elbasvir/Grazoprevir</td>
<td>See Elbasvir/Grazoprevir</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>See Erythromycin</td>
<td>See Erythromycin</td>
</tr>
<tr>
<td></td>
<td>Mefloquine</td>
<td>See Mefloquine</td>
<td>See Mefloquine</td>
</tr>
<tr>
<td></td>
<td>Quinine</td>
<td>↑ quinine expected&lt;br&gt;↑ posaconazole possible</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for quinine toxicities.</td>
</tr>
<tr>
<td></td>
<td>Rifabutina</td>
<td>Posaconazole AUC ↓ 49%&lt;br&gt;Rifabutin AUC ↑ 72%</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor posaconazole and rifabutin concentrations and adjust doses accordingly; monitor for clinical response to posaconazole and rifabutin toxicities.</td>
</tr>
<tr>
<td></td>
<td>Rifampina</td>
<td>Significant ↓ posaconazole expected</td>
<td><strong>Do not coadminister when treating invasive fungal infections.</strong> If coadministered for treatment of non-invasive fungal infections, monitor posaconazole concentration and adjust dose accordingly; monitor for clinical response.</td>
</tr>
<tr>
<td></td>
<td>Rifapentinea</td>
<td>↓ posaconazole expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor posaconazole concentration and adjust dose accordingly; monitor clinical response.</td>
</tr>
<tr>
<td><strong>Quinine</strong></td>
<td>Clarithromycin</td>
<td>See Clarithromycin</td>
<td>See Clarithromycin</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>See Erythromycin</td>
<td>See Erythromycin</td>
</tr>
<tr>
<td></td>
<td>Fluconazole</td>
<td>See Fluconazole</td>
<td>See Fluconazole</td>
</tr>
<tr>
<td></td>
<td>Itraconazole</td>
<td>See Itraconazole</td>
<td>See Itraconazole</td>
</tr>
<tr>
<td></td>
<td>Posaconazole</td>
<td>See Posaconazole</td>
<td>See Posaconazole</td>
</tr>
<tr>
<td></td>
<td>Rifabutina</td>
<td>↓ quinine possible&lt;br&gt;↑ rifabutin possible</td>
<td>Monitor for quinine efficacy.&lt;br&gt;Monitor rifabutin concentration and toxicity.</td>
</tr>
<tr>
<td></td>
<td>Rifampina</td>
<td>Quinine AUC ↓ 75% to 85%</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td>Rifapentinea</td>
<td>↓ quinine expected</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td>Voriconazole</td>
<td>↑ quinine expected</td>
<td>Coadministration should be avoided, if possible. If coadministered, monitor for quinine toxicities.</td>
</tr>
<tr>
<td><strong>Rifabutina</strong></td>
<td>Artemether/Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
</tr>
<tr>
<td></td>
<td>Atovaquone</td>
<td>See Atovaquone</td>
<td>See Atovaquone</td>
</tr>
<tr>
<td></td>
<td>Bedaquiline</td>
<td>See Bedaquiline</td>
<td>See Bedaquiline</td>
</tr>
<tr>
<td></td>
<td>Caspofungin</td>
<td>See Caspofungin</td>
<td>See Caspofungin</td>
</tr>
<tr>
<td></td>
<td>Chloroquine</td>
<td>See Chloroquine</td>
<td>See Chloroquine</td>
</tr>
</tbody>
</table>
Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 12 of 15)

<table>
<thead>
<tr>
<th>Primary Drug</th>
<th>Interacting Agent</th>
<th>Effect on Primary and/or Concomitant Drug Concentrations</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rifabutin</strong>*, continued</td>
<td>Clarithromycin</td>
<td>See Clarithromycin</td>
<td>See Clarithromycin</td>
</tr>
<tr>
<td></td>
<td>Daclatasvir</td>
<td>See Daclatasvir</td>
<td>See Daclatasvir</td>
</tr>
<tr>
<td></td>
<td>Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
</tr>
<tr>
<td></td>
<td>Dapsone</td>
<td>See Dapsone</td>
<td>See Dapsone</td>
</tr>
<tr>
<td></td>
<td>Doxycycline</td>
<td>See Doxycycline</td>
<td>See Doxycycline</td>
</tr>
<tr>
<td></td>
<td>Elbasvir/Grazoprevir</td>
<td>See Elbasvir/Grazoprevir</td>
<td>See Elbasvir/Grazoprevir</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>See Erythromycin</td>
<td>See Erythromycin</td>
</tr>
<tr>
<td></td>
<td>Fluconazole</td>
<td>See Fluconazole</td>
<td>See Fluconazole</td>
</tr>
<tr>
<td></td>
<td>Gilecaprevir/Pibrentasvir</td>
<td>See Gilecaprevir/Pibrentasvir</td>
<td>See Gilecaprevir/Pibrentasvir</td>
</tr>
<tr>
<td></td>
<td>Isavuconazole</td>
<td>See Isavuconazole</td>
<td>See Isavuconazole</td>
</tr>
<tr>
<td></td>
<td>Itraconazole</td>
<td>See Itraconazole</td>
<td>See Itraconazole</td>
</tr>
<tr>
<td></td>
<td>Ledipasvir/Sofosbuvir</td>
<td>See Ledipasvir/Sofosbuvir</td>
<td>See Ledipasvir/Sofosbuvir</td>
</tr>
<tr>
<td></td>
<td>Linezolid</td>
<td>See Linezolid</td>
<td>See Linezolid</td>
</tr>
<tr>
<td></td>
<td>Mefloquine</td>
<td>See Mefloquine</td>
<td>See Mefloquine</td>
</tr>
<tr>
<td></td>
<td>Posaconazole</td>
<td>See Posaconazole</td>
<td>See Posaconazole</td>
</tr>
<tr>
<td></td>
<td>Quinine</td>
<td>See Quinine</td>
<td>See Quinine</td>
</tr>
<tr>
<td></td>
<td>Sofosbuvir</td>
<td>↓ sofosbuvir expected</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td>Sofosbuvir/Velpatasvir +/- Voxilaprevir</td>
<td>↓ velpatasvir, voxilaprevir, and sofosbuvir expected</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td>TAF</td>
<td>↓ TAF expected</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td>Voriconazole</td>
<td>Voriconazole AUC ↓ 79% Rifabutin AUC ↑ 4-fold</td>
<td><strong>Do not coadminister.</strong> Consider alternative antifungal and/or antimycobacterial agent(s). If coadministration is absolutely necessary, monitor voriconazole and rifabutin concentrations to guide therapy.</td>
</tr>
<tr>
<td><strong>Rifampin</strong>*</td>
<td>Artemether/ Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
</tr>
<tr>
<td></td>
<td>Atovaquone</td>
<td>See Atovaquone</td>
<td>See Atovaquone</td>
</tr>
<tr>
<td></td>
<td>Bedaquiline</td>
<td>See Bedaquiline</td>
<td>See Bedaquiline</td>
</tr>
<tr>
<td></td>
<td>Caspofungin</td>
<td>See Caspofungin</td>
<td>See Caspofungin</td>
</tr>
<tr>
<td></td>
<td>Chloroquine</td>
<td>See Chloroquine</td>
<td>See Chloroquine</td>
</tr>
<tr>
<td></td>
<td>Clarithromycin</td>
<td>See Clarithromycin</td>
<td>See Clarithromycin</td>
</tr>
<tr>
<td></td>
<td>Daclatasvir</td>
<td>See Daclatasvir</td>
<td>See Daclatasvir</td>
</tr>
<tr>
<td></td>
<td>Dapsone</td>
<td>See Dapsone</td>
<td>See Dapsone</td>
</tr>
<tr>
<td></td>
<td>Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
</tr>
<tr>
<td></td>
<td>Doxycycline</td>
<td>See Doxycycline</td>
<td>See Doxycycline</td>
</tr>
<tr>
<td></td>
<td>Elbasvir/Grazoprevir</td>
<td>See Elbasvir/Grazoprevir</td>
<td>See Elbasvir/Grazoprevir</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>See Erythromycin</td>
<td>See Erythromycin</td>
</tr>
<tr>
<td></td>
<td>Fluconazole</td>
<td>See Fluconazole</td>
<td>See Fluconazole</td>
</tr>
<tr>
<td></td>
<td>Gilecaprevir/Pibrentasvir</td>
<td>See Gilecaprevir/Pibrentasvir</td>
<td>See Gilecaprevir/Pibrentasvir</td>
</tr>
</tbody>
</table>
Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections (page 13 of 15)

<table>
<thead>
<tr>
<th>Primary Drug</th>
<th>Interacting Agent</th>
<th>Effect on Primary and/or Concomitant Drug Concentrations</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampin, continued</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isavuconazole</td>
<td>See Isavuconazole</td>
<td>See Isavuconazole</td>
<td></td>
</tr>
<tr>
<td>Itraconazole</td>
<td>See Itraconazole</td>
<td>See Itraconazole</td>
<td></td>
</tr>
<tr>
<td>Ledipasvir/Sofosbuvir</td>
<td>See Ledipasvir/Sofosbuvir</td>
<td>See Ledipasvir/Sofosbuvir</td>
<td></td>
</tr>
<tr>
<td>Linezolid</td>
<td>See Linezolid</td>
<td>See Linezolid</td>
<td></td>
</tr>
<tr>
<td>Mefloquine</td>
<td>See Mefloquine</td>
<td>See Mefloquine</td>
<td></td>
</tr>
<tr>
<td>Posaconazole</td>
<td>See Posaconazole</td>
<td>See Posaconazole</td>
<td></td>
</tr>
<tr>
<td>Quinine</td>
<td>See Quinine</td>
<td>See Quinine</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir</td>
<td>Sofosbuvir AUC ↓ 72%</td>
<td>Do not coadminister.</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir +/- Voxilaprevir</td>
<td>Sofosbuvir AUC ↓ 72%</td>
<td>Do not coadminister.</td>
<td></td>
</tr>
<tr>
<td>TAF</td>
<td>TAF plus Rifampin: • TAF AUC ↓ 56%, • TFV AUC ↓ 53% • TFV-DP AUC ↓ 36% Intracellular TFV-DP concentration is 4.2-fold greater than with TDF alone.</td>
<td>If coadministered, monitor for HIV and HBV efficacy. <strong>Note:</strong> FDA labeling recommends not to coadminister.</td>
<td></td>
</tr>
<tr>
<td>Voriconazole</td>
<td>Voriconazole AUC ↓ 96%</td>
<td>Do not coadminister. Consider alternative antifungal and/or antimycobacterial agent(s).</td>
<td></td>
</tr>
<tr>
<td>Rifapentine*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artemether/Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
<td></td>
</tr>
<tr>
<td>Atovaquone</td>
<td>See Atovaquone</td>
<td>See Atovaquone</td>
<td></td>
</tr>
<tr>
<td>Bedaquiline</td>
<td>See Bedaquiline</td>
<td>See Bedaquiline</td>
<td></td>
</tr>
<tr>
<td>Caspofungin</td>
<td>See Caspofungin</td>
<td>See Caspofungin</td>
<td></td>
</tr>
<tr>
<td>Chloroquine</td>
<td>See Chloroquine</td>
<td>See Chloroquine</td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>See Clarithromycin</td>
<td>See Clarithromycin</td>
<td></td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>See Daclatasvir</td>
<td>See Daclatasvir</td>
<td></td>
</tr>
<tr>
<td>Dapsone</td>
<td>See Dapsone</td>
<td>See Dapsone</td>
<td></td>
</tr>
<tr>
<td>Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir</td>
<td></td>
</tr>
<tr>
<td>Doxycycline</td>
<td>See Doxycycline</td>
<td>See Doxycycline</td>
<td></td>
</tr>
<tr>
<td>Elbasvir/Grazoprevir</td>
<td>See Elbasvir/Grazoprevir</td>
<td>See Elbasvir/Grazoprevir</td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>See Erythromycin</td>
<td>See Erythromycin</td>
<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td>See Fluconazole</td>
<td>See Fluconazole</td>
<td></td>
</tr>
<tr>
<td>Glecaprevir/Pibrentasvir</td>
<td>See Glecaprevir/Pibrentasvir</td>
<td>See Glecaprevir/Pibrentasvir</td>
<td></td>
</tr>
<tr>
<td>Isavuconazole</td>
<td>See Isavuconazole</td>
<td>See Isavuconazole</td>
<td></td>
</tr>
<tr>
<td>Itraconazole</td>
<td>See Itraconazole</td>
<td>See Itraconazole</td>
<td></td>
</tr>
<tr>
<td>Ledipasvir/Sofosbuvir</td>
<td>See Ledipasvir/Sofosbuvir</td>
<td>See Ledipasvir/Sofosbuvir</td>
<td></td>
</tr>
<tr>
<td>Linezolid</td>
<td>See Linezolid</td>
<td>See Linezolid</td>
<td></td>
</tr>
<tr>
<td>Mefloquine</td>
<td>See Mefloquine</td>
<td>See Mefloquine</td>
<td></td>
</tr>
<tr>
<td>Posaconazole</td>
<td>See Posaconazole</td>
<td>See Posaconazole</td>
<td></td>
</tr>
</tbody>
</table>
### Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections

<table>
<thead>
<tr>
<th>Primary Drug</th>
<th>Interacting Agent</th>
<th>Effect on Primary and/or Concomitant Drug Concentrations</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifapentine*, continued</td>
<td>Quinine</td>
<td>See Quinine</td>
<td>See Quinine</td>
</tr>
<tr>
<td>Sofosbuvir</td>
<td>↓ sofosbuvir expected</td>
<td>Do not coadminister.</td>
<td></td>
</tr>
<tr>
<td>TAF</td>
<td>↓ TAF expected</td>
<td>Do not coadminister.</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir +/- Voxilaprevir</td>
<td>↓ sofosbuvir, velpatasvir, and voxilaprevir expected</td>
<td>Do not coadminister.</td>
<td></td>
</tr>
<tr>
<td>Voriconazole</td>
<td>↓ voriconazole expected</td>
<td>Do not coadminister. Consider alternative antifungal and/or antimycobacterial agent(s).</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir</td>
<td>Rifabutina</td>
<td>See Rifabutin</td>
<td>See Rifabutin</td>
</tr>
<tr>
<td>Rifampina</td>
<td>See Rifampin</td>
<td>See Rifampin</td>
<td></td>
</tr>
<tr>
<td>Rifapentinea</td>
<td>See Rifapentine</td>
<td>See Rifapentine</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir/ Velpatasvir +/- Voxilaprevir</td>
<td>Rifabutina</td>
<td>See Rifabutin</td>
<td>See Rifabutin</td>
</tr>
<tr>
<td>Rifampina</td>
<td>See Rifampin</td>
<td>See Rifampin</td>
<td></td>
</tr>
<tr>
<td>Rifapentinea</td>
<td>See Rifapentine</td>
<td>See Rifapentine</td>
<td></td>
</tr>
<tr>
<td>TAF</td>
<td>TVF AUC † 52% (when RPV/TAF/FTC given with SOF/VEL/VOX)</td>
<td>No dosage adjustment.</td>
<td></td>
</tr>
<tr>
<td>TDF</td>
<td>TVF AUC † 35% to 40% (when given with EVG/c/FTC or RPV/FTC)</td>
<td>Monitor for TDF toxicities. Consider TAF in place of TDF.</td>
<td></td>
</tr>
<tr>
<td>Tenofovir Alafenamide</td>
<td>Ledipasvir/Sofosbuvir</td>
<td>See Ledipasvir/Sofosbuvir</td>
<td>See Ledipasvir/Sofosbuvir</td>
</tr>
<tr>
<td>Gлечaprevir/Pibrentasvir</td>
<td>See Gлечaprevir/Pibrentasvir</td>
<td>See Gлечaprevir/Pibrentasvir</td>
<td></td>
</tr>
<tr>
<td>Rifabutina</td>
<td>See Rifabutin</td>
<td>See Rifabutin</td>
<td></td>
</tr>
<tr>
<td>Rifampina</td>
<td>See Rifampin</td>
<td>See Rifampin</td>
<td></td>
</tr>
<tr>
<td>Rifapentinea</td>
<td>See Rifapentine</td>
<td>See Rifapentine</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir +/- Voxilaprevir</td>
<td>See Sofosbuvir/Velpatasvir +/- Voxilaprevir</td>
<td>See Sofosbuvir/Velpatasvir +/- Voxilaprevir</td>
<td></td>
</tr>
<tr>
<td>Tenofovir Disoproxil Fumarate</td>
<td>Daclatasvir</td>
<td>See Daclatasvir</td>
<td>See Daclatasvir</td>
</tr>
<tr>
<td>Gлечaprevir/Pibrentasvir</td>
<td>See Gлечaprevir/Pibrentasvir</td>
<td>See Gлечaprevir/Pibrentasvir</td>
<td></td>
</tr>
<tr>
<td>Ledipasvir/Sofosbuvir</td>
<td>See Ledipasvir/Sofosbuvir</td>
<td>See Ledipasvir/Sofosbuvir</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir</td>
<td>See Sofosbuvir/Velpatasvir +/- Voxilaprevir</td>
<td>See Sofosbuvir/Velpatasvir +/- Voxilaprevir</td>
<td></td>
</tr>
<tr>
<td>Voriconazole</td>
<td>Artemether/ Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
<td>See Artemether/Lumefantrine</td>
</tr>
<tr>
<td>Bedaquiline</td>
<td>See Bedaquiline</td>
<td>See Bedaquiline</td>
<td></td>
</tr>
<tr>
<td>Chloroquine</td>
<td>See Chloroquine</td>
<td>See Chloroquine</td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>See Clarithromycin</td>
<td>See Clarithromycin</td>
<td></td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>See Daclatasvir</td>
<td>See Daclatasvir</td>
<td></td>
</tr>
<tr>
<td>Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/ Paritaprevir/Ritonavir</td>
<td>See Dasabuvir/Ombitasvir/Paritaprevir/ Ritonavir</td>
<td></td>
</tr>
<tr>
<td>Elbasvir/Grazoprevir</td>
<td>See Elbasvir/Grazoprevir</td>
<td>See Elbasvir/Grazoprevir</td>
<td></td>
</tr>
</tbody>
</table>
Table 5. Significant Pharmacokinetic Interactions between Drugs Used to Treat or Prevent Opportunistic Infections

<table>
<thead>
<tr>
<th>Primary Drug</th>
<th>Interacting Agent</th>
<th>Effect on Primary and/or Concomitant Drug Concentrations</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voriconazole, continued</td>
<td>Erythromycin</td>
<td>See Erythromycin</td>
<td>See Erythromycin</td>
</tr>
<tr>
<td></td>
<td>Mefloquine</td>
<td>See Mefloquine</td>
<td>See Mefloquine</td>
</tr>
<tr>
<td></td>
<td>Quinine</td>
<td>See Quinine</td>
<td>See Quinine</td>
</tr>
<tr>
<td></td>
<td>Rifabutin</td>
<td>See Rifabutin</td>
<td>See Rifabutin</td>
</tr>
<tr>
<td></td>
<td>Rifampin</td>
<td>See Rifampin</td>
<td>See Rifampin</td>
</tr>
<tr>
<td></td>
<td>Rifapentine</td>
<td>See Rifapentine</td>
<td>See Rifapentine</td>
</tr>
</tbody>
</table>

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

Key to Symbols:
- † = increase
- ‡ = decrease
- ↔ = no change

Key: 14-OH = active metabolite of clarithromycin; ARV = antiretroviral; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{24h} = concentration at 24 hours post dose; C_{min} = minimum concentration; C_{ss} = concentration at steady state; CYP3A4 = Cytochrome P450 3A4; des-Rbt = desacetyl rifabutin; DHA = dihydroartemisinin; DRV/r = darunavir/ritonavir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; HCV = hepatitis C virus; LPV/r = lopinavir/ritonavir; PI = protease inhibitor; PK = pharmacokinetic; RPV = rilpivirine; RTV = ritonavir; SOF = sofosbuvir; T_{1/2} = half-life; TAF = tenofovir alafenamide; TB = tuberculosis; TDF = tenofovir disoproxil fumarate; TDM = therapeutic drug monitoring; TFV = tenofovir; TFV-DP = tenofovir diphosphate; VEL = velpastavir; VOX = voxilaprevir
Table 6. Common or Serious Adverse Reactions Associated with Systemically Administered Drugs Used to Treat Opportunistic Infections (page 1 of 6)  (Last updated October 22, 2019; last reviewed October 22, 2019)

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Common or Serious Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir</td>
<td>Crystalluria associated with high doses, dehydration, or pre-existing renal impairment; nephrotoxicity secondary to obstructive urolithiasis, particularly after high dose rapid IV infusion; neurotoxicity (e.g., agitation, confusion, hallucination, seizure, coma) with high doses, especially in patients with renal impairment and/or older patients; thrombophlebitis at peripheral IV infusion site; nausea; vomiting; headache</td>
</tr>
<tr>
<td>Adefovir</td>
<td>Nausea, asthenia, nephrotoxicity (especially in patients with underlying renal insufficiency or predisposing comorbidities, or in patients who are currently taking nephrotoxic drugs)</td>
</tr>
</tbody>
</table>
| 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/Sublactam | Diarrhea, nausea, vomiting, abdominal pain, Clostridium difficile-associated diarrhea and colitis, hypersensitivity reactions (immediate or delayed reactions, including anaphylaxis), bone marrow suppression, drug fever, neurotoxicity (seizure) at high doses (especially in patients with renal dysfunction) |
| Amphotericin B Deoxycholate and Lipid Formulations | Nephrotoxicity, infusion-related reactions (e.g., fever, chills, rigors, back pain, hypotension), hypokalemia, hypomagnesemia, anemia, thrombophlebitis, nausea, vomiting  
 Lower incidence of nephrotoxicity and infusion-related reactions with liposomal formulations. |
| Anidulafungin | Generally well-tolerated. Hepatotoxicity, histamine-related infusion reactions (flushing, rash, pruritus, hypotension, and dyspnea are rare when infusion rate <1.1 mg/min), hypokalemia, diarrhea |
| Artemether/Lumefantrine | Generally well-tolerated. Rash, pruritus, nausea, vomiting, abdominal pain, anorexia, diarrhea, arthralgia, myalgia, dizziness, asthenia, headache, QTc prolongation  
 Rarely: Hemolytic anemia |
| Artesunate | Generally well-tolerated. Bradycardia, dizziness, nausea and vomiting, skin rash, pruritus, postartemisinin delayed hemolysis, QTc prolongation |
| Atovaquone | Rash, nausea, vomiting, diarrhea, hepatotoxicity, headache, hyperglycemia, fever |
| Atovaquone/Proguanil | Pruritus, rash, nausea, vomiting, abdominal pain, diarrhea, anorexia, erythema multiforme, asthenia, dizziness, headache, oral ulcers, hepatotoxicity |
| Azithromycin | Nausea, vomiting, diarrhea, hepatotoxicity, ototoxicity (with prolonged use), rash, urticaria, pruritus, abdominal pain, C. difficile-associated diarrhea  
 Rarely: Torsades de Pointes (greatest risk in patients with underlying QTc prolongation) |
| Aztreonam | Diarrhea, thrombophlebitis, neutropenia, increased liver enzymes, C. difficile-associated diarrhea  
 Rarely: Hypersensitivity reaction |
<p>| Benznidazole | Photosensitivity, allergic dermatitis, paresthesia, peripheral neuropathy, nausea, vomiting, abdominal pain, anorexia, weight loss, bone marrow suppression |
| Bedaquiline | Nausea, arthralgia, headache, QTc prolongation, elevated transaminases |
| Capreomycin | Nephrotoxicity, ototoxicity (both hearing loss and vestibular toxicity are possible), pain upon IM injection |
| Caspofungin | Generally well-tolerated. Fever, thrombophlebitis, histamine-related infusion reactions (flushing, rash, pruritus, facial swelling, hypotension, dyspnea), hypokalemia, anemia, headache, hepatotoxicity, diarrhea |</p>
<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Common or Serious Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone</td>
<td>Generally well-tolerated. Cholelithiasis, urolithiasis, pancreatitis, rash, diarrhea, drug fever, hemolytic anemia, <em>C. difficile</em>-associated diarrhea and colitis, injection-site reactions after IM injections</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Hypersensitivity reaction, rash, nausea, vomiting, diarrhea, <em>C. difficile</em>-associated diarrhea and colitis, bone marrow suppression, hemolytic anemia</td>
</tr>
<tr>
<td>See above for Ceftriaxone</td>
<td>Rarely: CNS toxicities (e.g., seizure, confusion) mostly seen with high doses used in patients with renal insufficiency or elderly patients without dose adjustment</td>
</tr>
<tr>
<td>Chloroquine and Hydroxychloroquine</td>
<td>Headache, pruritus, skin pigmentation, nausea, vomiting, abdominal pain, diarrhea, anorexia, photosensitivity, visual disturbances including blurry vision and retinal toxicity, auditory disturbances, QTc prolongation, cardiomyopathy, bone marrow suppression, hemolysis (associated with G6PD deficiency), hypersensitivity reaction (including TEN, SJS, and EM), hepatitis, neuropsychiatric changes (including extrapyramidal reactions and suicidal behavior), convulsive seizures, severe hypoglycemia (which may require adjustment of antidiabetic medications)</td>
</tr>
<tr>
<td></td>
<td>Rarely: Neuromyopathy (which may occur with long-term use)</td>
</tr>
<tr>
<td>Cidofovir</td>
<td>Nephrotoxicity, proteinuria, ocular hypotony, anterior uveitis/iritis, neutropenia, metabolic acidosis (including Fanconi’s syndrome), diarrhea, asthenia, fever, headache, alopecia, anemia</td>
</tr>
<tr>
<td></td>
<td>Side effects most likely related to co-administration with probenecid are rash, nausea, vomiting, anorexia.</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Nausea, vomiting, abdominal pain, diarrhea, <em>C. difficile</em>-associated diarrhea and colitis, headache, dizziness, sleep disturbances, tendonitis and tendon rupture (associated with age &gt;60 and concomitant steroid use), photosensitivity, hypoglycemia, peripheral neuropathy, hepatotoxicity, QTc prolongation, neurotoxicity (especially with high doses, use in elderly patients, or use in patients with renal dysfunction), seizures, and mental health side effects (e.g., disorientation, agitation, memory impairment, delirium)</td>
</tr>
<tr>
<td></td>
<td>Rarely: Aortic dissection</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>Hepatotoxicity, ototoxicity (with high doses or prolonged use), headache, nausea, vomiting, abdominal cramps, diarrhea, <em>C. difficile</em>-associated diarrhea and colitis, rash, QTc prolongation, dysgeusia</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>Nausea, vomiting, abdominal pain, diarrhea, <em>C. difficile</em>-associated diarrhea and colitis, rash, arrhythmia associated with rapid IV infusion, metallic taste (with IV infusion), thrombophlebitis, abnormal liver function tests</td>
</tr>
<tr>
<td>Clotrimazole (Troche)</td>
<td>Generally well-tolerated. Nausea, vomiting, anorexia, metallic taste</td>
</tr>
<tr>
<td></td>
<td>Rarely: Increase in serum transaminases</td>
</tr>
<tr>
<td>Cycloserine</td>
<td>Neuropsychiatric toxicities (e.g., headache, somnolence, lethargy, vertigo, tremor, dysarthria, irritability, confusion, paranoia, psychosis), seizures (particularly in patients with history of chronic alcoholism), allergic dermatitis, rash</td>
</tr>
<tr>
<td>Dapsone</td>
<td>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</td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>Fatigue, headache, nausea, anemia, bradycardia (when co-administered with sofosbuvir and amiodarone)</td>
</tr>
<tr>
<td>Dasabuvir, Ombitasvir, Paritaprevir, and Ritonavir</td>
<td>Hepatotoxicity, nausea, pruritus, rash, insomnia, fatigue, asthenia, dyspnea (associated with ribavirin co-administration)</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>Photosensitivity reaction, nausea, vomiting, diarrhea, esophageal ulceration, thrombophlebitis (with IV infusion), intracranial hypertension, <em>C. difficile</em>-associated diarrhea and colitis, tissue hyperpigmentation</td>
</tr>
<tr>
<td></td>
<td>Rarely: Hepatotoxicity</td>
</tr>
</tbody>
</table>
Table 6. Common or Serious Adverse Reactions Associated with Systemically Administered Drugs Used to Treat Opportunistic Infections (page 3 of 6)

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Common or Serious Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Elbasvir/Grazoprevir</strong></td>
<td>Fatigue, headache, nausea, ALT elevations, anemia (when given with ribavirin)</td>
</tr>
<tr>
<td><strong>Emtricitabine</strong></td>
<td>Generally well-tolerated. Headache, nausea, skin hyperpigmentation, diarrhea, rash</td>
</tr>
<tr>
<td><strong>Entecavir</strong></td>
<td>Generally well-tolerated. Headache, fatigue, dizziness, nausea</td>
</tr>
<tr>
<td><strong>Erythromycin</strong></td>
<td>Nausea, vomiting, diarrhea, abdominal pain, anorexia, rash, hepatotoxicity, cholestatic jaundice, ototoxicity (hearing loss, tinnitus), rash, QTC prolongation and cardiac arrhythmia, <em>C. difficile</em>-associated diarrhea and colitis, thrombophlebitis (with IV infusion)</td>
</tr>
<tr>
<td><strong>Ethambutol</strong></td>
<td>Optic neuritis (dose dependent), peripheral neuropathy, headache, nausea, vomiting, anorexia</td>
</tr>
<tr>
<td><strong>Ethionamide</strong></td>
<td>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</td>
</tr>
<tr>
<td><strong>Famciclovir</strong></td>
<td>Generally well-tolerated. Headache, nausea, vomiting, diarrhea, nephrotoxicity (in patients with underlying renal disease)</td>
</tr>
<tr>
<td><strong>Flucytosine</strong></td>
<td>Concentration-dependent bone marrow suppression (anemia, neutropenia, thrombocytopenia), diarrhea, nausea, vomiting, rash, hepatotoxicity</td>
</tr>
<tr>
<td><strong>Fluconazole</strong></td>
<td>Hepatotoxicity, rash, nausea, vomiting, diarrhea, abdominal discomfort, reversible alopecia (with doses ≥400 mg/day for &gt;2 months), QTC prolongation</td>
</tr>
<tr>
<td><strong>Foscarnet</strong></td>
<td>Nephrotoxicity, electrolyte imbalances (e.g., hypocalcemia, hypomagnesemia, hypophosphatemia, hyperphosphatemia, hypokalemia), penile ulceration, nausea, vomiting, anorexia, headache, seizure (associated with electrolyte imbalances), anemia, injection-site associated thrombophlebitis</td>
</tr>
<tr>
<td><strong>Fumagillin (Investigational)</strong></td>
<td>Oral Therapy: Neutropenia, thrombocytopenia, vertigo, nausea, vomiting, diarrhea, anorexia, abdominal cramps</td>
</tr>
<tr>
<td></td>
<td>Ocular Therapy: Minimal systemic effect or local effect</td>
</tr>
<tr>
<td><strong>Ganciclovir</strong></td>
<td>Neutropenia, thrombocytopenia, anemia, injection-site-associated thrombophlebitis, increased serum creatinine, carcinogenic and teratogenic potential, impaired fertility, neuropathy</td>
</tr>
<tr>
<td><strong>Glecaprevir/Pibrentasvir</strong></td>
<td>Generally well tolerated with only 0.1% discontinuation due to adverse reaction in clinical trials. Mild headache, fatigue, nausea, diarrhea</td>
</tr>
<tr>
<td><strong>Imipenem/Cilastatin</strong></td>
<td>Hypersensitivity reaction (immediate or delayed); nausea; vomiting; diarrhea; <em>C. difficile</em>-associated diarrhea and colitis; thrombophlebitis; headache; bone marrow suppression; drug fever; CNS effects (seizure, myoclonus, and confusion) especially with higher doses, in patients with underlying CNS disorders, or with renal insufficiency</td>
</tr>
<tr>
<td><strong>Interferon-Alfa and Peginterferon-Alfa</strong></td>
<td>Flu-like syndrome (e.g., fever, headache, fatigue, myalgia), neuropsychiatric disorders (e.g., depression, suicidal ideation), neutropenia, anemia, thrombocytopenia, thyroid dysfunction, injection-site reactions, alopecia, nausea, anorexia, diarrhea, weight loss, development or exacerbation of autoimmune disorders, ocula effects (e.g., retinal hemorrhage, retinal artery or vein obstructions, and cotton wool spots)</td>
</tr>
<tr>
<td><strong>Isavuconazonium Sulfate</strong></td>
<td>Hepatotoxicity, cholelithiasis, infusion-related reaction (hypotension, dyspnea, chills, dizziness, paresthesia, and hypoesthesia), hypersensitivity reaction (e.g., anaphylaxis, rash, SJS), nausea, vomiting, diarrhea, headache, hypokalemia, dyspnea, cough. Adverse events primarily reported in immunocompromised patients.</td>
</tr>
<tr>
<td><strong>Isoniazid</strong></td>
<td>Hepatotoxicity, peripheral neuropathy, optic neuritis, psychosis, diarrhea, nausea</td>
</tr>
<tr>
<td></td>
<td>Rarely: Psychosis</td>
</tr>
<tr>
<td><strong>Itraconazole</strong></td>
<td>Hepatotoxicity, congestive heart failure, edema, hypokalemia, nausea, vomiting, diarrhea, abdominal pain, rash, QTC prolongation, neuropathy</td>
</tr>
<tr>
<td><strong>Lamivudine</strong></td>
<td>Generally well-tolerated. Nausea, vomiting.</td>
</tr>
<tr>
<td><strong>Ledipasvir/Sofosbuvir</strong></td>
<td>Fatigue, headache, asthenia (most common), nausea, diarrhea, insomnia, mild transient asymptomatic lipase elevation, mild bilirubin elevation</td>
</tr>
</tbody>
</table>

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

Downloaded from https://aidsinfo.nih.gov/guidelines on 11/25/2019
<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Common or Serious Adverse Reactions</th>
</tr>
</thead>
</table>
| Levofloxacin            | Nausea, vomiting, abdominal pain, diarrhea, *C. difficile*-associated diarrhea and colitis, headache, dizziness, sleep disturbances, tendinitis and tendon rupture (associated with age >60 years and concomitant steroid use), photosensitivity, hypoglycemia, peripheral neuropathy, hepatotoxicity, QTc prolongation, neurotoxicity (especially with high doses, use in older patients, or in patients with renal dysfunction), seizures, and mental health side effects (e.g., disorientation, agitation, memory impairment, delirium)  
Rarely: Aortic dissection |
| Linezolid               | Anemia, neutropenia, thrombocytopenia (especially with treatment lasting longer than 2–4 weeks), peripheral neuropathy, optic neuritis with long-term therapy, serotonin syndrome (especially in patients receiving concomitant serotonergic agents), seizure (in patients with a history of seizure or with risk factors for seizure), diarrhea, headache, nausea, vomiting  
Rarely: Lactic acidosis |
| Mefloquine              | Depression, psychosis, anxiety, rash (reports of TEN and SJS), nausea, vomiting, diarrhea, epigastric pain, agitation, dizziness, headache, insomnia, abnormal dreams, QTc prolongation, arrhythmias (extrasystole, sinus bradycardia), agranulocytosis/aplastic anemia |
| Meropenem               | Generally well-tolerated. Hypersensitivity reaction (immediate or delayed), nausea, vomiting, diarrhea, *C. difficile*-associated diarrhea and colitis, thrombophlebitis, headache, bone marrow suppression, drug fever |
| Micafungin              | Generally well-tolerated. Histamine-related infusion reactions (e.g., flushing, rash, pruritus, hypotension, dyspnea) may occur, but these are rare if infusion lasts over 1 hour; anaphylaxis and anaphylactoid reaction, hepatotoxicity, thrombophlebitis, nausea, vomiting, diarrhea, hypokalemia  
Rarely: Hemolysis |
| Miconazole Buccal Tablets | Dysgeusia, diarrhea, nausea, vomiting, upper abdominal pain, headache, local reactions (oral discomfort, burning, pain, tongue/mouth ulceration, gingival pruritus, swelling, dry mouth)  
Rarely: Hypersensitivity reaction (may occur in patients with known hypersensitivity reaction to milk product concentrate) |
| Miltefosine             | Nausea, vomiting, diarrhea, headache, motion sickness, leukocytosis, thrombocytosis, nephrotoxicity, retinal degeneration, elevated transaminases and bilirubin, teratogenic potential, impaired fertility |
| Moxifloxacin            | Nausea, vomiting, abdominal pain, diarrhea, *C. difficile*-associated diarrhea and colitis, headache, dizziness, sleep disturbances, tendinitis and tendon rupture (associated with age >60 years and concomitant steroid use), photosensitivity, hypoglycemia, peripheral neuropathy, hepatotoxicity, QTc prolongation, neurotoxicity (especially with high doses, use in elderly patients or in patients with renal dysfunction), seizures, and mental health side effects such as disorientation, agitation, memory impairment, delirium  
Rarely: Aortic dissection |
| Nifurtimox             | Anorexia, weight loss, nausea, vomiting, abdominal pain, headache, dizziness, mood changes, insomnia, myalgia, peripheral neuropathy, rash, pruritus, memory loss |
| Nitazoxanide           | Generally well-tolerated. Nausea, vomiting, diarrhea, abdominal pain, headache |
| Nystatin (Oral Preparations) | Unpleasant taste, nausea, vomiting, anorexia, diarrhea  
Rarely: Hypersensitivity reaction |
| Paromomycin            | Nausea, vomiting, cramps, anorexia, rash, headache  
Rarely: Nephrotoxicity and ototoxicity (inflammatory bowel disease and renal insufficiency may increase risk) |
Table 6. Common or Serious Adverse Reactions Associated with Systemically Administered Drugs Used to Treat Opportunistic Infections (page 5 of 6)

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Common or Serious Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin G</td>
<td><strong>All Penicillin G Preparations:</strong> Hypersensitivity reactions (immediate or delayed reactions, including anaphylaxis), bone marrow suppression, nausea, vomiting, diarrhea, <em>C. difficile</em>-associated diarrhea and colitis, drug fever</td>
</tr>
<tr>
<td></td>
<td><strong>Benzathine Penicillin G and Procaine Penicillin G:</strong> IM injection-site reactions (pain and erythema), procaine neuropsychiatric reactions (with high dose), neurovascular damage (due to inadvertent intravascular instead of IM injection)</td>
</tr>
<tr>
<td></td>
<td><strong>Aqueous Crystalline Penicillin G (IV):</strong> Thrombophlebitis, neurotoxicity at high doses, especially in patients with renal dysfunction</td>
</tr>
<tr>
<td>Pentamidine</td>
<td><strong>IV Infusion:</strong> Nephrotoxicity, infusion-related hypotension, thrombophlebitis, QTc prolongation, arrhythmias (including Torsades de Pointes), pancreatitis, hypoglycemia, hyperglycemia, diabetes mellitus, hepatotoxicity, electrolyte abnormalities, leucopenia, thrombocytopenia</td>
</tr>
<tr>
<td></td>
<td><strong>Aerosolized Therapy:</strong> Bronchospasm, cough, dyspnea, tachypnea, metallic taste</td>
</tr>
<tr>
<td></td>
<td><strong>Rarely:</strong> Pancreatitmid</td>
</tr>
<tr>
<td>Pentavalent Antimony (Sodium Stibogluconate)</td>
<td>Nausea, vomiting, abdominal pain, anorexia, headache, hepatotoxicity, arthralgia, myalgia, cardiac toxicity with &gt;20 mg/kg dose (prolonged QTc and T wave inversion), rash, thrombophlebitis, leukopenia, anemia, thrombocytopenia</td>
</tr>
<tr>
<td></td>
<td><strong>Rarely:</strong> Pancreatitmid</td>
</tr>
<tr>
<td>Posaconazole</td>
<td>Nausea, vomiting, diarrhea, abdominal pain, headache, hepatotoxicity, hypokalemia, QTc prolongation, rash</td>
</tr>
<tr>
<td></td>
<td><strong>IV Infusion:</strong> Thrombophlebitis, cyclodextrin accumulation (especially in patients with eGFR &lt;50 mL/min, but an observational study did not show an increased risk of nephrotoxicity)</td>
</tr>
<tr>
<td>Piperacillin-Tazobactam</td>
<td>Generally well-tolerated. Hypersensitivity reaction, rash, diarrhea, nausea, vomiting, <em>C. difficile</em>-associated diarrhea and colitis, thrombophlebitis, impaired platelet aggregation, seizure (with high doses used in patients with renal insufficiency)</td>
</tr>
<tr>
<td></td>
<td><strong>Rarely:</strong> Thrombocytopenia</td>
</tr>
<tr>
<td>Primaquine</td>
<td>Methemoglobinemia, hemolytic anemia (especially in patients with G6PD deficiency), leukopenia, neutropenia, abdominal cramps, nausea, vomiting, QTc prolongation, pruritus, rash, dizziness</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>Hepatotoxicity, hyperuricemia, arthralgia, myalgia, nausea, vomiting, rash</td>
</tr>
<tr>
<td>Pyrimethamine</td>
<td>Neutropenia, thrombocytopenia, megaloblastic anemia, rash</td>
</tr>
<tr>
<td>Quinidine Glucuronate</td>
<td>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)</td>
</tr>
<tr>
<td>Quinine</td>
<td>Headache, nausea, vomiting, diarrhea, cinchonism (tinnitus, vertigo, blurred vision), hypersensitivity reaction, hypoglycemia, thrombocytopenia, QTc prolongation</td>
</tr>
<tr>
<td>Ribavirin</td>
<td>Hemolytic anemia, dyspnea, hyperbilirubinemia, fatigue, myalgia, headache, nausea, vomiting, anorexia, dyspepsia, rash, dry cough, teratogenicity, hypersensitivity reaction, hepatotoxicity</td>
</tr>
<tr>
<td>Rifabutin</td>
<td>Hepatotoxicity, anterior uveitis (dose dependent), red-orange discoloration of body fluids, rash, arthralgia, neutropenia, nausea, vomiting, abdominal pain, diarrhea, anorexia</td>
</tr>
<tr>
<td>Rifampin</td>
<td>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</td>
</tr>
<tr>
<td>Rifapentine</td>
<td>Hypersensitivity reaction, hepatotoxicity, anemia, lymphopenia, neutropenia, arthralgia, conjunctivitis, headache, vomiting, nausea, diarrhea, rash, pruritus, anorexia and lymphadenopathy, red-orange discoloration of body fluids, <em>C. difficile</em>-associated diarrhea and colitis</td>
</tr>
</tbody>
</table>
Table 6. Common or Serious Adverse Reactions Associated with Systemically Administered Drugs Used to Treat Opportunistic Infections (page 6 of 6)

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

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

Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV  CC-55

Downloaded from https://aidsinfo.nih.gov/guidelines on 11/25/2019
### Table 7. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections That Require Dosage Adjustment in Patients with Renal Insufficiency

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Usual Dose</th>
<th>Dosage Adjustment in Renal Insufficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CrCl (mL/min)*</td>
</tr>
<tr>
<td>Acyclovir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV Dose</td>
<td>Serious HSV:</td>
<td>26–50</td>
</tr>
<tr>
<td></td>
<td>• 5 mg/kg IV every 8 hours</td>
<td>10–25</td>
</tr>
<tr>
<td></td>
<td>VZV Infections:</td>
<td>&lt;10</td>
</tr>
<tr>
<td></td>
<td>• 10 mg/kg IV every 8 hours</td>
<td>HD</td>
</tr>
<tr>
<td>PO Dose for Herpes Zoster: 800 mg PO five times/day</td>
<td>10–25</td>
<td>800 mg PO every 8 hours</td>
</tr>
<tr>
<td></td>
<td>&lt;10</td>
<td>800 mg PO every 12 hours</td>
</tr>
<tr>
<td></td>
<td>HD</td>
<td>800 mg PO every 12 hours; administer dose after HD on day of dialysis</td>
</tr>
<tr>
<td>Adefovir</td>
<td>10 mg PO every 24 hours</td>
<td>30–49</td>
</tr>
<tr>
<td></td>
<td>10–29</td>
<td>10 mg PO every 72 hours</td>
</tr>
<tr>
<td></td>
<td>HD</td>
<td>10 mg PO weekly; administer dose after HD</td>
</tr>
<tr>
<td>Amikacin</td>
<td>IV 15 mg/kg per day</td>
<td>N/A</td>
</tr>
<tr>
<td>For mycobacterial infections</td>
<td>or 25 mg/kg three times per week</td>
<td>Use with caution in patients with renal insufficiency and family history of ototoxicity.</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>0.7–1.0 mg/kg IV per day (amphotericin B deoxycholate)</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>or 3–6 mg/kg IV per day (lipid formulation)</td>
<td>Use with caution in patients with renal insufficiency.</td>
</tr>
<tr>
<td>Capreomycin</td>
<td>intravenous (IV) or intramuscular (IM) per day</td>
<td>N/A</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>For Treatment of Acute Malaria:</td>
<td>&lt;10</td>
</tr>
<tr>
<td>(Base)</td>
<td>• 1 g (600 mg base) PO for 1 dose, followed by 500 mg (300 mg base) PO at 6, 24, and 48 hours (for a total dose of 1,500 mg)</td>
<td>Pretreatment SCr &gt;1.5 mg/dL</td>
</tr>
<tr>
<td></td>
<td>or CrCl &lt;55 mL/min</td>
<td>or Proteinuria ≥100 mg/dL (≥2 +)</td>
</tr>
<tr>
<td></td>
<td>or Proteinuria ≥3 +</td>
<td>If SCr increases by 0.3–0.4 mg/dL above baseline</td>
</tr>
<tr>
<td>Cidofovir</td>
<td>5 mg/kg IV on Day 0, repeat 5 mg/kg IV dose on Day 7, then 5 mg/kg IV every 2 weeks</td>
<td>Give each dose with probenecid and saline hydration (see Table 2 for dosing instructions).</td>
</tr>
</tbody>
</table>
### Table 7. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections That Require Dosage Adjustment in Patients with Renal Insufficiency (page 2 of 8)

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

*Note: Please refer to product information for dosing recommendations for other ARV FDC products containing FTC/TAF.
Table 7. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections That Require Dosage Adjustment in Patients with Renal Insufficiency

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Usual Dose</th>
<th>Dosage Adjustment in Renal Insufficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[Drug Name] (Usual Dose)</td>
<td>[CrCl (mL/min)]</td>
</tr>
<tr>
<td>Emtricitabine/Tenofovir Disoproxil Fumarate (FTC/TDF) (FDC Trade Name: Truvada)</td>
<td>One (FTC 200 mg/TDF 300 mg) tablet PO daily</td>
<td>30–49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;30 or HD</td>
</tr>
<tr>
<td>Entecavir</td>
<td>Usual Dose: 0.5 mg PO once daily</td>
<td>30 to &lt;50</td>
</tr>
<tr>
<td></td>
<td>For Treatment of 3TC-Refractory HBV or for Patients with Decompensated Liver Disease: 1 mg PO once daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 to &lt;30</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethambutol</td>
<td>For MAI: 15 mg/kg PO daily</td>
<td>&lt;30 or HD</td>
</tr>
<tr>
<td></td>
<td>For MTB: 15–25 mg/kg PO daily (See Table 3 for additional MTB dosing recommendations.)</td>
<td></td>
</tr>
<tr>
<td>Ethionamide</td>
<td>15–20 mg/kg PO daily (usually 250–500 mg PO once or twice daily)</td>
<td>&lt;30 or HD</td>
</tr>
<tr>
<td>Famciclovir</td>
<td>For Herpes Zoster: 500 mg PO every 8 hours</td>
<td>40–59</td>
</tr>
<tr>
<td></td>
<td>For HSV: 500 mg PO every 12 hours</td>
<td>20–39</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HD</td>
</tr>
</tbody>
</table>

**Note:** Please refer to product information for dosing recommendations for other ARV FDC products containing FTC/TDF.
Table 7. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections That Require Dosage Adjustment in Patients with Renal Insufficiency (page 4 of 8)

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Usual Dose</th>
<th>Dosage Adjustment in Renal Insufficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CrCl (mL/min)*</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>200–1,200 mg PO or IV every 24 hours (dose and route of administration depends on type of OI)</td>
<td>≤50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>21–40</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10–20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td>25 mg/kg PO every 6 hours TDM is recommended for all patients to guide optimal dosing (target peak serum concentration 2 hours after dose: 30–80 mcg/mL).</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foscarnet</td>
<td>Induction Therapy for CMV Infection: 180 mg/kg/day IV in two divided doses</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Maintenance Therapy for CMV Infection or for Treatment of HSV Infections: 90–120 mg/kg IV once daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Induction Therapy: 5 mg/kg IV every 12 hours</td>
<td>50–69</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25–49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10–24</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;10 or HD</td>
</tr>
<tr>
<td></td>
<td>Maintenance Therapy: 5 mg/kg IV every 24 hours</td>
<td>50–69</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25–49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10–24</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;10 or HD</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td>300 mg PO every 24 hours</td>
<td>30–49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>15–29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5–14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;5 or HD</td>
</tr>
<tr>
<td>Lamivudine/Tenofovir Disoproxil Fumarate (3TC/TDF)</td>
<td>One (3TC 300 mg/TDF 300 mg) tablet PO every 24 hours</td>
<td>&lt;50</td>
</tr>
<tr>
<td>(FDC Trade Names: Cimduo or Temixys)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Note: Please refer to product information for dosing recommendations for other ARV FDC products containing 3TC/TDF.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ledipasvir/Sofosbuvir</td>
<td>One (ledipasvir 90 mg/sofosbuvir 400 mg) tablet PO once daily</td>
<td>&lt;30</td>
</tr>
</tbody>
</table>
### Table 7. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections That Require Dosage Adjustment in Patients with Renal Insufficiency

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Usual Dose</th>
<th>CrCl (mL/min)*</th>
<th>Dose</th>
</tr>
</thead>
</table>
| **Levofloxacin**         | 500 mg (low dose) or 750-1,000 mg (high dose) IV or PO daily              | 20–49          | **Low Dose:** 500 mg once, then 250 mg every 24 hours, IV or PO  
<20 or CAPD or HD (administer dose after HD or CAPD on days of dialysis) |
|                          |                                                                           |                | **High Dose:** 750 mg every 48 hours IV or PO                                                               |
| **Para-aminosalicylic acid** | 8–12 g/day PO in two to three divided doses                              | <30 or HD      | 4 g PO twice daily; administer after HD on days of dialysis                                                 |
| **Paromomycin**          | 500 mg PO every 6 hours                                                  | <10            | Minimal systemic absorption. No dosage adjustment necessary, but monitor for worsening renal function and ototoxicity in patients with ESRD. |
| **Peginterferon Alfa-2a** | 180 mcg SQ once weekly                                                   | <30 or HD      | 135 mcg SQ once weekly                                                                                       |
|                          | HD                                                                       |                | 135 mcg SQ once weekly                                                                                       |
| **Peginterferon Alfa-2b** | 1.5 mcg/kg SQ once weekly                                                | 30–50          | Reduce dose by 25%                                                                                           |
|                          | 10–29 and HD                                                             |                | Reduce dose by 50%                                                                                           |
| **Penicillin G**         | **Neurosyphilis, Ocular Syphilis, or OtoSyphilis:**                     | 10–50          | 2–3 million units every 4 hours  
<10                                                                 | 12–18 million units as continuous infusion  
2 million units every 4–6 hours  
HD or CAPD 2 million units every 6 hours  
8 million units as continuous infusion |
| (Potassium or Sodium)    | • 3–4 million units IV every 4 hours, or  
|                          | • 18–24 million units IV daily as continuous infusion                   |                | or                                                                                                             |
|                          |                                                                           | <10            | or                                                                                                             |
| **Pentamidine**          | 4 mg/kg IV every 24 hours                                                 | 10–50          | 3 mg/kg IV every 24 hours                                                                                     |
|                          | <10                                                                      |                | 4 mg/kg IV every 48 hours                                                                                     |
| **Posaconazole**         | **IV:** 300 mg twice daily on Day 1; then 300 mg once daily              | <50            | No dosage adjustment of oral dose in patients with renal insufficiency. Higher variability in serum concentrations observed in patients with CrCl <20 ml/min.  
Monitor posaconazole concentrations (target trough concentration >1.25 mcg/mL).  
IV posaconazole is not recommended by the manufacturer because of potential toxicity due to accumulation of sulfobutylether cyclodextrin (vehicle of IV product). However, an observational study did not find worsening in renal function in patients with CrCl <50 ml/min given sulfobutylether cyclodextrin.  
Switch patients with CrCl <50 ml/min to oral posaconazole when feasible. |
|                          | **Delayed-Release Tablet:** 300 mg PO once daily                          |                |                                                                                                                                |
|                          | **Oral Suspension:** 400 mg PO twice daily                               |                |                                                                                                                                |
| **Pyrazinamide**         | See Table 3 for weight-based dosing guidelines.                          | <30 or HD      | 25–35 mg/kg/dose three times per week; administer dose after HD on dialysis days                             |
### Table 7. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections That Require Dosage Adjustment in Patients with Renal Insufficiency

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Usual Dose</th>
<th>Dosage Adjustment in Renal Insufficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Quinidine Gluconate</strong></td>
<td>10 mg/kg (salt) IV over one to two hours, then 0.02 mg/kg/min (salt) IV for up to 72 hours or until able to take oral meds</td>
<td>CrCl (mL/min)*&lt;br&gt; HD: 75% of usual dose; some clinicians recommend supplementation with 100–200 mg IV after HD on days of dialysis. Consider TDM for all patients to optimize dosing.</td>
</tr>
<tr>
<td>(Salt) Note: 10 mg quinidine gluconate salt = 6.25 mg quinidine base</td>
<td>10 mg/kg (salt) IV over one to two hours, then 0.02 mg/kg/min (salt) IV for up to 72 hours or until able to take oral meds</td>
<td>&lt;10: 75% of usual dose; some clinicians recommend supplementation with 100–200 mg IV after HD on days of dialysis. Consider TDM for all patients to optimize dosing.</td>
</tr>
<tr>
<td><strong>Quinine Sulfate</strong></td>
<td>650 mg salt (524 mg base) PO every 8 hours</td>
<td>CrCl (mL/min)*&lt;br&gt; &lt;10 or HD: 650 mg once, then 325 mg PO every 12 hours</td>
</tr>
<tr>
<td><strong>Ribavirin</strong></td>
<td>For Genotypes 1 and 4: 1,000–1,200 mg PO per day in two divided doses (based on weight; see Table 2 for full dosing recommendation)&lt;br&gt; For Genotypes 2 and 3: 400 mg PO twice daily</td>
<td>CrCl (mL/min)*&lt;br&gt; 30–50: Alternate dosing 200 mg PO and 400 mg PO every other day&lt;br&gt; &lt;30 or HD: 200 mg PO daily (based on limited data)</td>
</tr>
<tr>
<td><strong>Rifabutin</strong></td>
<td>5 mg/kg PO daily (usually 300 mg PO daily)&lt;br&gt; See Table 3 and Drug-Drug Interactions in the Adult and Adolescent Antiretroviral Guidelines for dosage adjustment based on interactions with ARVs.</td>
<td>CrCl (mL/min)*&lt;br&gt; &lt;30: Consider 50% of dose once daily if toxicity is suspected. Monitor serum concentration and adjust dose as needed.</td>
</tr>
<tr>
<td><strong>Rifampin</strong></td>
<td>10 mg/kg PO daily (usually 600 mg PO daily)</td>
<td>CrCl (mL/min)*&lt;br&gt; &lt;30 or HD: 600 mg once daily, or 600 mg three times per week</td>
</tr>
<tr>
<td><strong>Sofosbuvir</strong></td>
<td>400 mg PO daily</td>
<td>CrCl (mL/min)*&lt;br&gt; &lt;30: <strong>Not recommended.</strong> Up to 20-fold higher sofosbuvir metabolite observed in patients with this level of renal impairment.</td>
</tr>
<tr>
<td><strong>Streptomycin</strong></td>
<td>15 mg/kg IM or IV every 24 hours&lt;br&gt; or&lt;br&gt; 25 mg/kg IM or IV three times per week</td>
<td>CrCl (mL/min)*&lt;br&gt; Use with caution in patients with renal insufficiency. Adjust dose based on serum concentrations. Administer dose after dialysis on day of dialysis.</td>
</tr>
<tr>
<td><strong>Sulfadiazine</strong></td>
<td>1,000–1,500 mg PO every 6 hours (1,500 mg every 6 hours for patients &gt;60 kg)</td>
<td>CrCl (mL/min)*&lt;br&gt; 10–50: 1,000–1,500 mg PO every 12 hours (ensure adequate hydration)&lt;br&gt; &lt;10 or HD: 1,000–1,500 mg PO every 24 hours; administer dose after HD on days of dialysis</td>
</tr>
<tr>
<td><strong>Telavancin</strong></td>
<td>10 mg/kg IV every 24 hours</td>
<td>CrCl (mL/min)*&lt;br&gt; 31–50: 7.5 mg/kg IV every 24 hours (decreased clinical cure rate with CrCl &lt;50 mL/minute; use with caution)&lt;br&gt; 10-30: 10 mg/kg IV every 48 hours (decreased clinical cure rate with CrCl &lt;50 mL/minute; use with caution)&lt;br&gt; &lt;10: Insufficient clinical data to recommend routine use. Use with caution due to decreased clinical cure rate with CrCl &lt;50 mL/minute. If no other option, consider 10 mg/kg every 48 hours IV or 10 mg/kg IV post-HD three times a week (based on observational study [n = 10]).</td>
</tr>
<tr>
<td>Drug(s)</td>
<td>Usual Dose</td>
<td>Dosage Adjustment in Renal Insufficiency</td>
</tr>
<tr>
<td>-------------------------</td>
<td>----------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>CrCl (mL/min)</strong></td>
</tr>
<tr>
<td>Telbivudine</td>
<td>600 mg PO daily</td>
<td>30–49</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;30</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>HD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir Alafenamide</td>
<td>25 mg PO daily</td>
<td>&lt;15</td>
</tr>
<tr>
<td>(TAF)</td>
<td></td>
<td>&lt;15 on HD</td>
</tr>
<tr>
<td>Tenofovir Disoproxil</td>
<td>300 mg PO daily</td>
<td>30–49</td>
</tr>
<tr>
<td>Fumarate (TDF)</td>
<td></td>
<td>10–29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;10 and not on dialysis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HD</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>250 mg PO every 6 hours</td>
<td>10–49</td>
</tr>
<tr>
<td></td>
<td>Consider using doxycycline in patients with renal dysfunction.</td>
<td>&lt;10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HD</td>
</tr>
<tr>
<td>Trimethoprim/</td>
<td>For PCP Treatment:</td>
<td>15–30</td>
</tr>
<tr>
<td>Sulfamethoxazole (TMP-SMX)</td>
<td>• 5 mg/kg (of TMP component) IV every 6-8 hours, or</td>
<td>&lt;15</td>
</tr>
<tr>
<td></td>
<td>• Two TMP-SMX DS tablets PO every 8 hours</td>
<td>HD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>For PCP Prophylaxis:</td>
<td>15–30</td>
</tr>
<tr>
<td></td>
<td>• One TMP-SMX DS tablet PO daily;</td>
<td>&lt;15</td>
</tr>
<tr>
<td></td>
<td>• One TMP-SMX DS tablet PO three times per week; or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• One TMP-SMX SS tablet PO daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>For Toxoplasmosis Encephalitis (TE) Treatment:</td>
<td>15–30</td>
</tr>
<tr>
<td></td>
<td>5 mg/kg (TMP component) IV or PO every 12 hours</td>
<td>&lt;15</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 7. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections That Require Dosage Adjustment in Patients with Renal Insufficiency (page 8 of 8)

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Usual Dose</th>
<th>Dosage Adjustment in Renal Insufficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CrCl (mL/min)*</td>
</tr>
<tr>
<td>Trimethoprim/ Sulfamethoxazole (TMP-SMX), continued</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For TE Chronic Maintenance Therapy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• One TMP-SMX DS tablet twice daily, or</td>
<td>15–30</td>
<td>Reduce dose by 50%</td>
</tr>
<tr>
<td>• One TMP-SMX DS tablet daily</td>
<td>&lt;15</td>
<td>Reduce dose by 50% or use alternative agent</td>
</tr>
<tr>
<td>For Toxoplasmosis Primary Prophylaxis: One TMP-SMX DS tablet PO daily</td>
<td>15–30</td>
<td>Reduce dose by 50%</td>
</tr>
<tr>
<td></td>
<td>&lt;15</td>
<td>Reduce dose by 50% or use alternative agent</td>
</tr>
<tr>
<td>Valacyclovir</td>
<td>For Herpes Zoster: 1 g PO three times daily</td>
<td>30–49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10–29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HD</td>
</tr>
<tr>
<td>Valganciclovir</td>
<td>Induction Therapy: 900 mg PO twice daily, Maintenance Therapy: 900 mg PO once daily</td>
<td>40–59</td>
</tr>
<tr>
<td></td>
<td></td>
<td>26–39</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10–25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;10 and not on dialysis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voriconazole</td>
<td>6 mg/kg IV every 12 hours for two doses, then 4 mg/kg IV every 12 hours or 200–300 mg PO every 12 hours</td>
<td>&lt;50</td>
</tr>
</tbody>
</table>

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

* Creatinine Clearance Calculation

<table>
<thead>
<tr>
<th>Male:</th>
<th>Female:</th>
</tr>
</thead>
<tbody>
<tr>
<td>(140 - age in years) x (weight in kg)</td>
<td>(140 - age in years) x (weight in kg) x (0.85)</td>
</tr>
<tr>
<td>72 x (serum creatinine)</td>
<td>72 x (serum creatinine)</td>
</tr>
</tbody>
</table>

Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV  CC-63

Downloaded from https://aidsinfo.nih.gov/guidelines on 11/25/2019
Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy  

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA Category</th>
<th>Pertinent Animal Reproductive and Human Pregnancy Data</th>
<th>Recommended Use During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir</td>
<td>B</td>
<td>No teratogenicity in mice, rats, rabbits at human levels. Large experience in pregnancy (&gt;700 first-trimester exposures reported to registry); well-tolerated.</td>
<td>Treatment of frequent or severe symptomatic herpes outbreaks or varicella</td>
</tr>
<tr>
<td>Adefovir</td>
<td>C</td>
<td>No increase in malformations at 23 times (rats) and 40 times (rabbits) human dose. Limited experience with human use in pregnancy.</td>
<td>Not recommended because of limited data in pregnancy. Report exposures during pregnancy to Antiretroviral Pregnancy Registry: <a href="http://www.APRegistry.com">http://www.APRegistry.com</a></td>
</tr>
<tr>
<td>Albendazole</td>
<td>C</td>
<td>Embryotoxic and teratogenic (skeletal malformations) in rats and rabbits, but not in mice or cows. Limited experience in human pregnancy.</td>
<td>Not recommended, especially in first trimester. Primary therapy for microsporidiosis in pregnancy should be ART.</td>
</tr>
<tr>
<td>Amikacin</td>
<td>C</td>
<td>Not teratogenic in mice, rats, rabbits. Theoretical risk of ototoxicity in fetus; reported with streptomycin but not amikacin.</td>
<td>Drug-resistant TB, severe MAC infections</td>
</tr>
<tr>
<td>Amoxicillin, amox./clavulanate, ampicillin/ sulbactam</td>
<td>B</td>
<td>Not teratogenic in animals. Large experience in human pregnancy does not suggest an increase in adverse events.</td>
<td>Susceptible bacterial infections</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>B</td>
<td>Not teratogenic in animals or in human experience. Preferred over azole antifungals in first trimester if similar efficacy expected.</td>
<td>Documented invasive fungal disease</td>
</tr>
<tr>
<td>Antimonials, pentavalent (stibogluconate, meglumine)</td>
<td>Not FDA approved</td>
<td>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.</td>
<td>Therapy of visceral leishmaniasis not responsive to amphotericin B or pentamidine</td>
</tr>
<tr>
<td>Artesunate, arteether, arteether/ lumefantrine</td>
<td>C</td>
<td>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.</td>
<td>Recommended by WHO as first-line therapy in second/third trimester for <em>P. falciparum</em> 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.</td>
</tr>
<tr>
<td>Atovaquone</td>
<td>C</td>
<td>Not teratogenic in rats or rabbits, limited human experience</td>
<td>Alternate agent for PCP, <em>Toxoplasma gondii</em>, malaria infections</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>B</td>
<td>Not teratogenic in animals. Moderate experience with use in human pregnancy does not suggest adverse events.</td>
<td>Preferred agent for MAC prophylaxis or treatment (with ethambutol), <em>Chlamydia trachomatis</em> infection in pregnancy.</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>B</td>
<td>Not teratogenic in rats, rabbits. Limited human experience, but other beta-lactam antibiotics have not been associated with adverse pregnancy outcomes.</td>
<td>Susceptible bacterial infections</td>
</tr>
<tr>
<td>Bedaquiline</td>
<td>B</td>
<td>Not teratogenic in rats, rabbits. No experience in human pregnancy.</td>
<td>Multidrug resistant TB when effective treatment regimen can not otherwise be provided.</td>
</tr>
<tr>
<td>Drug</td>
<td>FDA Category</td>
<td>Pertinent Animal Reproductive and Human Pregnancy Data</td>
<td>Recommended Use During Pregnancy</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>--------------</td>
<td>------------------------------------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Boceprevir</td>
<td>B</td>
<td>Not teratogenic in rats, rabbits. No human pregnancy data.</td>
<td>Treatment of HCV currently generally not indicated in pregnancy.</td>
</tr>
<tr>
<td>Capreomycin</td>
<td>C</td>
<td>Increase in skeletal variants in rats. Limited experience in human pregnancy; theoretical risk of fetal ototoxicity.</td>
<td>Drug-resistant TB</td>
</tr>
<tr>
<td>Caspofungin</td>
<td>C</td>
<td>Embryotoxic, skeletal defects in rats, rabbits. No experience with human use.</td>
<td>Invasive <em>Candida</em> or <em>Aspergillus</em> infections refractory to amphotericin and azoles</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>B</td>
<td>Not teratogenic in animals. Large experience in human pregnancy has not suggested increase in adverse outcomes.</td>
<td>Bacterial infections; alternate treatment for MAC</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>C</td>
<td>Associated with anophthalmia, microophthalmia at tetotoxic doses in animals. Not associated with increased risk in human pregnancy at doses used for malaria.</td>
<td>Drug of choice for malaria prophylaxis and treatment of sensitive species in pregnancy.</td>
</tr>
<tr>
<td>Cidofovir</td>
<td>C</td>
<td>Embryotoxic and teratogenic (meningocele, skeletal abnormalities) in rats and rabbits. No experience in human pregnancy.</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Ciprofloxacin, other quinolones</td>
<td>C</td>
<td>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.</td>
<td>Severe MAC infections; multidrug resistant TB, anthrax, bacterial infections</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>C</td>
<td>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 &gt;100 first-trimester exposures, did not show increase in defects but one study found an increase in spontaneous abortion.</td>
<td>Treatment or secondary MAC prophylaxis, if other choices exhausted</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>B</td>
<td>No concerns specific to pregnancy in animal or human studies.</td>
<td>Treatment of anaerobic bacterial infections and used with quinine for chloroquine-resistant malaria; alternate agent for secondary prophylaxis of <em>Toxoplasma</em> encephalitis</td>
</tr>
<tr>
<td>Clofazimine</td>
<td>C</td>
<td>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.</td>
<td>No indications.</td>
</tr>
<tr>
<td>Clotrimazole troches</td>
<td>C</td>
<td>Not teratogenic in animals at exposures expected from treatment of oral or vaginal <em>Candida</em>. No increase in adverse pregnancy outcomes with vaginal use.</td>
<td>Oral or vaginal <em>Candida</em> infections and prophylaxis</td>
</tr>
<tr>
<td>Cycloserine</td>
<td>C</td>
<td>Not teratogenic in rats. No data available from human studies.</td>
<td>Drug-resistant TB</td>
</tr>
</tbody>
</table>
Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 3 of 9)

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA Category</th>
<th>Pertinent Animal Reproductive and Human Pregnancy Data</th>
<th>Recommended Use During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dapsone</td>
<td>C</td>
<td>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.</td>
<td>Alternate choice for primary or secondary PCP prophylaxis</td>
</tr>
<tr>
<td>Diphenoxylate</td>
<td>C</td>
<td>Limited animal and human data do not indicate teratogenicity.</td>
<td>Symptomatic treatment of diarrhea</td>
</tr>
<tr>
<td>Doxycycline, other tetracyclines</td>
<td>D</td>
<td>Risk of hepatic toxicity increased with tetracyclines in pregnancy; staining of fetal bones and teeth contraindicates use in pregnancy.</td>
<td>No indications</td>
</tr>
<tr>
<td>Emtricitabine</td>
<td>B</td>
<td>No concerns in pregnancy from limited animal and human data.</td>
<td>As part of fully suppressive combination antiretroviral regimen for treatment of HIV, HBV. Report exposures during pregnancy to Antiretroviral Pregnancy Registry: <a href="http://www.APRegistry.com">http://www.APRegistry.com</a></td>
</tr>
<tr>
<td>Entecavir</td>
<td>C</td>
<td>Animal data do not suggest teratogenicity at human doses; limited experience in human pregnancy.</td>
<td>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: <a href="http://www.APRegistry.com">http://www.APRegistry.com</a></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>B</td>
<td>Hepatotoxicity with erythromycin estolate in pregnancy; other forms acceptable; no evidence of teratogenicity.</td>
<td>Bacterial and chlamydial infections</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>B</td>
<td>Teratogenic, at high doses, in mice, rats, rabbits. No evidence of teratogenicity in 320 cases of human use for treatment of TB.</td>
<td>Active TB and MAC treatment; avoid in first trimester if possible</td>
</tr>
<tr>
<td>Ethionamide</td>
<td>C</td>
<td>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.</td>
<td>Active TB; avoid in first trimester if possible</td>
</tr>
<tr>
<td>Famciclovir</td>
<td>B</td>
<td>No evidence of teratogenicity in rats or rabbits, limited human experience.</td>
<td>Recurrent genital herpes and primary varicella infection. Report exposures during pregnancy to the Famvir Pregnancy Registry (1-888-669-6682).</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>C</td>
<td>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.</td>
<td>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.</td>
</tr>
</tbody>
</table>
### Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy  

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA Category</th>
<th>Pertinent Animal Reproductive and Human Pregnancy Data</th>
<th>Recommended Use During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flucytosine</td>
<td>C</td>
<td>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.</td>
<td>Use after first trimester if indicated for life-threatening fungal infections.</td>
</tr>
<tr>
<td>Fumagillin</td>
<td>Not FDA approved</td>
<td>Caused complete litter destruction or growth retardation in rats, depending on when administered. No data in human pregnancy.</td>
<td>Topical solution can be used for ocular microsporidial infections.</td>
</tr>
<tr>
<td>Ganciclovir, valganciclovir</td>
<td>C</td>
<td>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.</td>
<td>Treatment or secondary prophylaxis of life-threatening or sight-threatening CMV infection. Preferred agent for therapy in children.</td>
</tr>
<tr>
<td>Imipenem, meropenem</td>
<td>C/B</td>
<td>Not teratogenic in animals; limited human experience.</td>
<td>Serious bacterial infections</td>
</tr>
<tr>
<td>Imiquimod</td>
<td>B</td>
<td>Not teratogenic in rats and rabbits; 8 case reports of human use, only 2 in first trimester.</td>
<td>Because of limited experience, other treatment modalities such as cryotherapy or trichloracetic acid recommended for wart treatment during pregnancy.</td>
</tr>
<tr>
<td>Influenza vaccine</td>
<td>C</td>
<td>Not teratogenic. Live vaccines, including intranasal influenza vaccine, are contraindicated in pregnancy.</td>
<td>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.</td>
</tr>
<tr>
<td>Interferons (alfa, beta, gamma)</td>
<td>C</td>
<td>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.</td>
<td>Not indicated. Treatment of HCV currently generally not recommended in pregnancy.</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>C</td>
<td>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.</td>
<td>Active TB; prophylaxis for exposure or skin test conversion</td>
</tr>
<tr>
<td>Drug</td>
<td>FDA Category</td>
<td>Pertinent Animal Reproductive and Human Pregnancy Data</td>
<td>Recommended Use During Pregnancy</td>
</tr>
<tr>
<td>---------------------</td>
<td>--------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>C</td>
<td>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.</td>
<td>Only for documented systemic fungal disease, not prophylaxis. Consider using amphotericin B in first trimester if similar efficacy expected.</td>
</tr>
<tr>
<td>Kanamycin</td>
<td>D</td>
<td>Associated with club feet in mice, inner ear changes in multiple species. Hearing loss in 2.3% of 391 children after long-term <em>in utero</em> therapy.</td>
<td>Drug-resistant TB</td>
</tr>
<tr>
<td>Ketoconazole</td>
<td>C</td>
<td>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.</td>
<td>None</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>C</td>
<td>Not teratogenic in animals. No evidence of teratogenicity with &gt;3700 first-trimester exposures reported to Antiretroviral Pregnancy Registry.</td>
<td>HIV and HBV therapy, only as part of a fully suppressive combination ARV regimen. Report exposures to Antiretroviral Pregnancy Registry: <a href="http://www.APRegistry.com">http://www.APRegistry.com</a>.</td>
</tr>
<tr>
<td>Ledipasvir/sofusbuvir</td>
<td>B</td>
<td>No evidence of teratogenicity in rats or rabbits. No experience in human pregnancy</td>
<td>Treatment of hepatitis C generally not indicated in pregnancy.</td>
</tr>
<tr>
<td>Leucovorin (folic acid)</td>
<td>C</td>
<td>Prevents birth defects of valproic acid, methotrexate, phenytoin, aminopterin in animal models. No evidence of harm in human pregnancies.</td>
<td>Use with pyrimethamine if use of pyrimethamine cannot be avoided.</td>
</tr>
<tr>
<td>Linezolid</td>
<td>C</td>
<td>Not teratogenic in animals. Decreased fetal weight and neonatal survival at ~ human exposures, possibly related to maternal toxicity. Limited human experience.</td>
<td>Serious bacterial infections</td>
</tr>
<tr>
<td>Loperamide</td>
<td>B</td>
<td>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.</td>
<td>Symptomatic treatment of diarrhea after the first trimester</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>C</td>
<td>Animal data and human data do not suggest an increased risk of birth defects, but miscarriage and stillbirth may be increased.</td>
<td>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.</td>
</tr>
<tr>
<td>Meglumine</td>
<td>Not FDA approved</td>
<td>See Antimonials, pentavalent</td>
<td>Anaerobic bacterial infections, bacterial vaginosis, trichomoniasis, giardiasis, amebiasis</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>B</td>
<td>Multiple studies do not indicate teratogenicity. Studies on several hundred women with first-trimester exposure found no increase in birth defects.</td>
<td></td>
</tr>
<tr>
<td>Micafungin</td>
<td>C</td>
<td>Teratogenic in rabbits; no human experience.</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>
Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 6 of 9)

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA Category</th>
<th>Pertinent Animal Reproductive and Human Pregnancy Data</th>
<th>Recommended Use During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miltefosine</td>
<td>Not FDA approved</td>
<td>Embryotoxic in rats, rabbits; teratogenic in rats. No experience with human use.</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Nifurtimox</td>
<td>Not FDA approved</td>
<td>Not teratogenic in mice and rats. Increased chromosomal aberrations in children receiving treatment; uncertain significance. No experience in human pregnancy.</td>
<td>Not indicated in chronic infection; seek expert consultation if acute infection or symptomatic reactivation of T. cruzi in pregnancy.</td>
</tr>
<tr>
<td>Nitazoxanide</td>
<td>B</td>
<td>Not teratogenic in animals; no human data</td>
<td>Severely symptomatic cryptosporidiosis after the first trimester</td>
</tr>
<tr>
<td>Para-amino salicylic acid (PAS)</td>
<td>C</td>
<td>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.</td>
<td>Drug-resistant TB</td>
</tr>
<tr>
<td>Paromomycin</td>
<td>C</td>
<td>Not teratogenic in mice and rabbits. Limited human experience, but poor oral absorption makes toxicity, teratogenicity unlikely.</td>
<td>Amebic intestinal infections, possibly cryptosporidiosis</td>
</tr>
<tr>
<td>Penicillin</td>
<td>B</td>
<td>Not teratogenic in multiple animal species. Vast experience with use in human pregnancy does not suggest teratogenicity, other adverse outcomes.</td>
<td>Syphilis, other susceptible bacterial infections</td>
</tr>
<tr>
<td>Pentamidine</td>
<td>C</td>
<td>Embryocidal but not teratogenic in rats, rabbits with systemic use. Limited experience with systemic use in pregnancy.</td>
<td>Alternate therapy for PCP and leishmaniasis.</td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>B</td>
<td>Not teratogenic in limited animal studies. Limited experience in pregnancy but penicillins generally considered safe.</td>
<td>Bacterial infections</td>
</tr>
<tr>
<td>Pneumococcal vaccine</td>
<td>C</td>
<td>No studies in animal pregnancy. Polysaccharide vaccines generally considered safe in pregnancy. Well-tolerated in third-trimester studies.</td>
<td>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.</td>
</tr>
<tr>
<td>Podophyllin, podofilox</td>
<td>C</td>
<td>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.</td>
<td>Because alternative treatments for genital warts in pregnancy are available, use not recommended; inadvertent use in early pregnancy is not indication for abortion.</td>
</tr>
<tr>
<td>Posaconazole</td>
<td>C</td>
<td>Embryotoxic in rabbits; teratogenic in rats at similar to human exposures. No experience in human pregnancy.</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Prednisone</td>
<td>B</td>
<td>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.</td>
<td>Adjunctive therapy for severe PCP; multiple other non-HIV-related indications</td>
</tr>
</tbody>
</table>
Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 7 of 9)

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA Category</th>
<th>Pertinent Animal Reproductive and Human Pregnancy Data</th>
<th>Recommended Use During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primaquine</td>
<td>C</td>
<td>No animal data. Limited experience with use in human pregnancy; theoretical risk for hemolytic anemia if fetus has G6PD deficiency.</td>
<td>Alternate therapy for PCP, chloroquine-resistant malaria</td>
</tr>
<tr>
<td>Proguanil</td>
<td>C</td>
<td>Not teratogenic in animals. Widely used in malaria-endemic areas with no clear increase in adverse outcomes.</td>
<td>Alternate therapy and prophylaxis of <em>P. falciparum</em> malaria</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>C</td>
<td>Not teratogenic in rats, mice. Limited experience with use in human pregnancy.</td>
<td>Active TB</td>
</tr>
<tr>
<td>Pyrimethamine</td>
<td>C</td>
<td>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.</td>
<td>Treatment and secondary prophylaxis of toxoplastic encephalitis; alternate treatment of PCP</td>
</tr>
<tr>
<td>Quinidine gluconate</td>
<td>C</td>
<td>Generally considered safe in pregnancy; high doses associated with preterm labor. One case of fetal 8th nerve damage reported.</td>
<td>Alternate treatment of malaria, control of fetal arrhythmias</td>
</tr>
<tr>
<td>Quinine sulfate</td>
<td>C</td>
<td>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.</td>
<td>Treatment of chloroquine-resistant malaria</td>
</tr>
<tr>
<td>Ribavirin</td>
<td>X</td>
<td>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.</td>
<td>Contraindicated in early pregnancy; no clear indications in pregnancy. Report exposures during pregnancy to Ribavirin Pregnancy Registry at (800) 593-2214 or <a href="http://www.ribavirinpregnancyregistry.com">www.ribavirinpregnancyregistry.com</a></td>
</tr>
<tr>
<td>Rifabutin</td>
<td>B</td>
<td>Not teratogenic in rats and rabbits; no specific concerns for human pregnancy.</td>
<td>Treatment or prophylaxis of MAC, active TB</td>
</tr>
<tr>
<td>Rifampin</td>
<td>C</td>
<td>Teratogenic at high doses in mice (cleft palate) and rats (spina bifida) but not in rabbits. No clear teratogenicity in humans.</td>
<td>Active TB</td>
</tr>
<tr>
<td>Simeprevir</td>
<td>C</td>
<td>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.</td>
<td>Treatment of HCV currently generally not recommended in pregnancy.</td>
</tr>
<tr>
<td>Sinecatechin ointment</td>
<td>C</td>
<td>No evidence of teratogenicity in rats and rabbits after oral or intravaginal dosing. No experience in human pregnancy.</td>
<td>Not recommended based on lack of data.</td>
</tr>
<tr>
<td>Sofobusvir</td>
<td>B</td>
<td>No evidence of teratogenicity in rats or rabbits. No experience in human pregnancy.</td>
<td>Treatment of HCV generally not indicated in pregnancy. Regimens including ribavirin and interferon are contraindicated in pregnancy.</td>
</tr>
</tbody>
</table>
Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 8 of 9)

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA Category</th>
<th>Pertinent Animal Reproductive and Human Pregnancy Data</th>
<th>Recommended Use During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptomycin</td>
<td>D</td>
<td>No teratogenicity in mice, rats, guinea pigs. Possible increased risk of deafness and VIII nerve damage; no evidence of other defects.</td>
<td>Alternate therapy for active TB</td>
</tr>
<tr>
<td>Sulfadiazine</td>
<td>B</td>
<td>Sulfonamides teratogenic in some animal studies. No clear teratogenicity in humans; potential for increased jaundice, kernicterus if used near delivery.</td>
<td>Secondary prophylaxis of toxoplasmic encephalitis</td>
</tr>
<tr>
<td>Telaprevir</td>
<td>B</td>
<td>Not teratogenic in mice, rats. No human pregnancy data.</td>
<td>Treatment of HCV currently generally not indicated in pregnancy.</td>
</tr>
<tr>
<td>Telbivudine</td>
<td>B</td>
<td>Not teratogenic in rats, rabbits. Limited experience in human pregnancy.</td>
<td>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: <a href="http://www.APRegistry.com">http://www.APRegistry.com</a></td>
</tr>
<tr>
<td>Tenofovir</td>
<td>B</td>
<td>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.</td>
<td>Component of fully suppressive antiretroviral regimen in pregnant women. Report exposures during pregnancy to Antiretroviral Pregnancy Registry: <a href="http://www.APRegistry.com">http://www.APRegistry.com</a></td>
</tr>
<tr>
<td>Trichloracetic acid, bichloracetic acid</td>
<td>Not rated</td>
<td>No studies. Used topically so no systemic absorption expected.</td>
<td>Topical therapy of non-cervical genital warts</td>
</tr>
<tr>
<td>Trifluridine</td>
<td>C</td>
<td>Not teratogenic in rats, rabbits. Minimal systemic absorption expected with topical ocular use.</td>
<td>Topical agent for treatment of ocular herpes infections</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>C</td>
<td>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.</td>
<td>Therapy of PCP during pregnancy. Primary and secondary PCP prophylaxis in the second/third trimester; consider aerosolized pentamidine in first trimester. Recommend fetal ultrasound at 18–20 weeks after first trimester exposure.</td>
</tr>
<tr>
<td>Valacyclovir</td>
<td>B</td>
<td>Not teratogenic in mice, rats, and rabbits. Experience with valacyclovir in pregnancy limited; prodrug of acyclovir, which is considered safe for use in pregnancy.</td>
<td>Treatment of HSV and varicella infections in pregnancy</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>C</td>
<td>Not teratogenic in rats, rabbits. Limited human experience.</td>
<td>Serious bacterial infections</td>
</tr>
</tbody>
</table>
### Table 8. Summary of Pre-Clinical and Human Data on, and Indications for, Opportunistic Infection Drugs During Pregnancy (page 9 of 9)

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

**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