



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

Downloaded from <https://aidsinfo.nih.gov/guidelines> on 7/22/2018

Visit the *AIDSinfo* website to access the most up-to-date guideline.

Register for e-mail notification of guideline updates at <https://aidsinfo.nih.gov/e-news>.

**Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy)** (page 1 of 22) (Last updated May 29, 2018; last reviewed May 29, 2018)

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
<p><b><i>Pneumocystis</i> Pneumonia (PCP)</b></p>	<p>Patients who develop PCP despite TMP-SMX prophylaxis can usually be treated with standard doses of TMP-SMX <b>(BIII)</b>.</p> <p>Duration of PCP treatment: 21 days <b>(AII)</b></p> <p><u>For Moderate-to-Severe PCP:</u></p> <ul style="list-style-type: none"> <li>• TMP-SMX: [TMP 15–20 mg and SMX 75–100 mg]/kg/day IV given q6h or q8h <b>(AI)</b>, may switch to PO after clinical improvement <b>(AI)</b></li> </ul> <p><u>For Mild-to-Moderate PCP:</u></p> <ul style="list-style-type: none"> <li>• TMP-SMX: [TMP 15–20 mg and SMX 75–100 mg]/kg/day, given PO in 3 divided doses <b>(AI)</b>, or</li> <li>• TMP-SMX: (160 mg/800 mg or DS) 2 tablets PO TID <b>(AI)</b></li> </ul> <p><u>Secondary Prophylaxis, after completion of PCP treatment:</u></p> <ul style="list-style-type: none"> <li>• TMP-SMX DS: 1 tablet PO daily <b>(AI)</b>, or</li> <li>• TMP-SMX (80 mg/400 mg or SS): 1 tablet PO daily <b>(AI)</b></li> </ul>	<p><u>For Moderate-to-Severe PCP:</u></p> <ul style="list-style-type: none"> <li>• Pentamidine 4 mg/kg IV daily infused over ≥60 minutes <b>(AI)</b>; can reduce dose to 3 mg/kg IV daily because of toxicities <b>(BI)</b>, or</li> <li>• Primaquine 30 mg (base) PO daily + (clindamycin 600 mg q6h IV or 900 mg IV q8h) or (clindamycin 450 mg PO q6h or 600 mg PO q8h) <b>(AI)</b></li> </ul> <p><u>For Mild-to-Moderate PCP:</u></p> <ul style="list-style-type: none"> <li>• Dapsone 100 mg PO daily + TMP 5 mg/kg PO TID <b>(BI)</b>, or</li> <li>• Primaquine 30 mg (base) PO daily + (clindamycin 450 mg PO q6h or 600 mg PO q8h) <b>(BI)</b>, or</li> <li>• Atovaquone 750 mg PO BID with food <b>(BI)</b></li> </ul> <p><u>Secondary Prophylaxis, after completion of PCP treatment:</u></p> <ul style="list-style-type: none"> <li>• TMP-SMX DS: 1 tablet PO three times weekly <b>(BI)</b>, or</li> <li>• Dapsone 100 mg PO daily <b>(BI)</b>, or</li> <li>• Dapsone 50 mg PO daily + (pyrimethamine<sup>a</sup> 50 mg + leucovorin 25 mg) PO weekly <b>(BI)</b>, or</li> <li>• (Dapsone 200 mg + pyrimethamine<sup>a</sup> 75 mg + leucovorin 25 mg) PO weekly <b>(BI)</b>, or</li> <li>• Aerosolized pentamidine 300 mg monthly via Respigard II™ nebulizer <b>(BI)</b>, or</li> <li>• Atovaquone 1500 mg PO daily <b>(BI)</b>, or</li> <li>• (Atovaquone 1500 mg + pyrimethamine<sup>a</sup> 25 mg + leucovorin 10 mg) PO daily <b>(CIII)</b></li> </ul>	<p><u>Indications for Adjunctive Corticosteroids <b>(AI)</b>:</u></p> <ul style="list-style-type: none"> <li>• PaO<sub>2</sub> &lt;70 mmHg at room air, or</li> <li>• Alveolar-arterial O<sub>2</sub> gradient &gt;35 mm Hg</li> </ul> <p><u>Prednisone Doses (Beginning as Early as Possible and Within 72 Hours of PCP Therapy) <b>(AI)</b>:</u></p> <ul style="list-style-type: none"> <li>• Days 1–5: 40 mg PO BID</li> <li>• Days 6–10: 40 mg PO daily</li> <li>• Days 11–21: 20 mg PO daily</li> </ul> <p>IV methylprednisolone can be administered as 75% of prednisone dose.</p> <p>Benefit of corticosteroid if started after 72 hours of treatment is unknown, but some clinicians will use it for moderate-to-severe PCP <b>(BIII)</b>.</p> <p>Whenever possible, patients should be tested for G6PD before use of dapsone or primaquine. Alternative therapy should be used in patients found to have G6PD deficiency.</p> <p>Patients who are receiving pyrimethamine<sup>a</sup>/sulfadiazine for treatment or suppression of toxoplasmosis do not require additional PCP prophylaxis <b>(AII)</b>.</p> <p>If TMP-SMX is discontinued because of a mild adverse reaction, re-institution should be considered after the reaction resolves <b>(AII)</b>. The dose can be increased gradually (desensitization) <b>(BI)</b>, reduced, or the frequency modified <b>(CIII)</b>.</p> <p>TMP-SMX should be permanently discontinued in patients with possible or definite Stevens-Johnson Syndrome or toxic epidermal necrosis <b>(AII)</b>.</p>

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
<p><b><i>Toxoplasma gondii</i> Encephalitis</b></p>	<p><u>Treatment of Acute Infection (AI):</u></p> <ul style="list-style-type: none"> <li>Pyrimethamine<sup>a</sup> 200 mg PO 1 time, followed by weight-based therapy: <ul style="list-style-type: none"> <li>If &lt;60 kg, pyrimethamine<sup>a</sup> 50 mg PO once daily + sulfadiazine 1000 mg PO q6h + leucovorin 10–25 mg PO once daily</li> <li>If ≥60 kg, pyrimethamine<sup>a</sup> 75 mg PO once daily + sulfadiazine 1500 mg PO q6h + leucovorin 10–25 mg PO once daily</li> </ul> </li> <li>Leucovorin dose can be increased to 50 mg daily or BID.</li> </ul> <p><u>Duration for Acute Therapy:</u></p> <ul style="list-style-type: none"> <li>At least 6 weeks (BII); longer duration if clinical or radiologic disease is extensive or response is incomplete at 6 weeks</li> <li>After completion of acute therapy, all patients should be initiated on chronic maintenance therapy</li> </ul> <p><u>Chronic Maintenance Therapy:</u></p> <ul style="list-style-type: none"> <li>Pyrimethamine<sup>a</sup> 25–50 mg PO daily + sulfadiazine 2000–4000 mg PO daily (in 2–4 divided doses) + leucovorin 10–25 mg PO daily (AI)</li> </ul>	<p><u>Treatment of Acute Infection:</u></p> <ul style="list-style-type: none"> <li>Pyrimethamine<sup>a</sup> (leucovorin)* + clindamycin 600 mg IV or PO q6h (AI), <i>or</i></li> <li>TMP-SMX (TMP 5 mg/kg and SMX 25 mg/kg ) IV or PO BID (BI), <i>or</i></li> <li>Atovaquone 1500 mg PO BID with food + pyrimethamine<sup>a</sup> (leucovorin)* (BII), <i>or</i></li> <li>Atovaquone 1500 mg PO BID with food + sulfadiazine 1000–1500 mg PO q6h (weight-based dosing, as in preferred therapy) (BII), <i>or</i></li> <li>Atovaquone 1500 mg PO BID with food (BII)</li> </ul> <p><u>Chronic Maintenance Therapy:</u></p> <ul style="list-style-type: none"> <li>Clindamycin 600 mg PO q8h + (pyrimethamine<sup>a</sup> 25–50 mg + leucovorin 10–25 mg) PO daily (BI), <i>or</i></li> <li>TMP-SMX DS 1 tablet BID (BII), <i>or</i></li> <li>TMP-SMX DS 1 tablet once daily (BII); <i>or</i></li> <li>Atovaquone 750–1500 mg PO BID + (pyrimethamine<sup>a</sup> 25 mg + leucovorin 10 mg) PO daily (BII), <i>or</i></li> <li>Atovaquone 750–1500 mg PO BID + sulfadiazine 2000–4000 mg PO daily (in 2–4 divided doses (BII)), <i>or</i></li> <li>Atovaquone 750–1500 mg PO BID with food (BII)</li> </ul> <p>* Pyrimethamine<sup>a</sup> and leucovorin doses are the same as for preferred therapy.</p>	<p>Refer to <a href="http://www.daraprimdirect.com">http://www.daraprimdirect.com</a> for information regarding how to access pyrimethamine</p> <p>If pyrimethamine is unavailable or there is a delay in obtaining it, TMP-SMX should be utilized in place of pyrimethamine-sulfadiazine (BI).</p> <p>For patients with a history of sulfa allergy, sulfa desensitization should be attempted using one of several published strategies (BI).</p> <p>Atovaquone should be administered until therapeutic doses of TMP-SMX are achieved (CIII).</p> <p>Adjunctive corticosteroids (e.g., dexamethasone) should only be administered when clinically indicated to treat mass effect associated with focal lesions or associated edema (BIII); discontinue as soon as clinically feasible.</p> <p>Anticonvulsants should be administered to patients with a history of seizures (AIII) and continued through acute treatment, but should not be used as seizure prophylaxis (AIII).</p> <p>If clindamycin is used in place of sulfadiazine, additional therapy must be added to prevent PCP (AII).</p>
<p><b>Cryptosporidiosis</b></p>	<ul style="list-style-type: none"> <li>Initiate or optimize ART for immune restoration to CD4 count &gt;100 cells/μL (AII), <i>and</i></li> <li>Aggressive oral or IV rehydration and replacement of electrolyte loss (AIII), <i>and</i></li> <li>Symptomatic treatment of diarrhea with anti-motility agents (AII).</li> </ul>	<p>No therapy has been shown to be effective without ART. Trial of these agents may be used in conjunction with, but not instead of, ART:</p> <ul style="list-style-type: none"> <li>Nitazoxanide 500–1000 mg PO BID for 14 days (CIII), <i>or</i></li> <li>Paromomycin 500 mg PO QID for 14–21 days (CIII)</li> </ul> <p>• With optimized ART, symptomatic treatment and rehydration and electrolyte replacement</p>	<p>Tincture of opium may be more effective than loperamide in management of diarrhea (CII).</p>

**Table 2. Treatment of AIDS-Associated Opportunistic Infections (Includes Recommendations for Acute Treatment and Secondary Prophylaxis/Chronic Suppressive/Maintenance Therapy)** (page 3 of 22)

<b>Opportunistic Infection</b>	<b>Preferred Therapy</b>	<b>Alternative Therapy</b>	<b>Other Comments</b>
<b>Microsporidiosis</b>	<p><u>For GI Infections Caused by <i>Enterocytozoon bienuesi</i>:</u></p> <ul style="list-style-type: none"> <li>• Initiate or optimize ART as immune restoration to CD4 count &gt;100 cells/<math>\mu</math>L (<b>AII</b>); <i>plus</i></li> <li>• Manage severe dehydration, malnutrition, and wasting by fluid support (<b>AII</b>) and nutritional supplement (<b>AIII</b>)</li> </ul> <p><u>For Intestinal and Disseminated (Not Ocular) Infections Caused by Microsporidia Other Than <i>E. bienuesi</i> and <i>Vittaforma corneae</i>:</u></p> <ul style="list-style-type: none"> <li>• Albendazole 400 mg PO BID (<b>AII</b>), continue until CD4 count &gt;200 cells/<math>\mu</math>L for &gt;6 months after initiation of ART (<b>BIII</b>)</li> </ul> <p><u>For Ocular Infection:</u></p> <ul style="list-style-type: none"> <li>• Topical fumagillin bicyclohexylammonium (Fumidil B) eye drops: 3 mg/mL in saline (fumagillin 70 <math>\mu</math>g/mL)—2 drops q2h for 4 days, then 2 drops QID (investigational use only in United States) (<b>BII</b>) + albendazole 400 mg PO BID, for management of systemic infection (<b>BIII</b>)</li> <li>• Therapy should be continued until resolution of ocular symptoms and CD4 count increase to &gt;200 cells/<math>\mu</math>L for &gt;6 months in response to ART (<b>CIII</b>).</li> </ul>	<p><u>For GI Infections Caused by <i>E. bienuesi</i>:</u></p> <ul style="list-style-type: none"> <li>• Fumagillin 60 mg/day (<b>BII</b>) and TNP-470 (a synthetic analog of fumagillin) (<b>BIII</b>) may be effective, but neither is available in the United States.</li> <li>• Nitazoxanide (1000 mg BID) may have some effect but response may be minimal in patients with low CD4 cell counts (<b>CIII</b>).</li> </ul> <p><u>For Disseminated Disease Attributed to <i>Trachipleistophora</i> or <i>Anncalia</i>:</u></p> <ul style="list-style-type: none"> <li>• Itraconazole 400 mg PO daily + albendazole 400 mg PO BID (<b>CIII</b>)</li> </ul>	<p>Anti-motility agents can be used for diarrhea control if required (<b>BIII</b>).</p>

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

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

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

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



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

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

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

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



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

<b>Opportunistic Infection</b>	<b>Preferred Therapy</b>	<b>Alternative Therapy</b>	<b>Other Comments</b>
<p><b>Salmonellosis</b>, continued</p>	<p><u>Secondary Prophylaxis Should Be Considered For:</u></p> <ul style="list-style-type: none"> <li>• Patients with recurrent <i>Salmonella</i> gastroenteritis +/- bacteremia (<b>CIII</b>), or</li> <li>• Patients with CD4 &lt;200 cells/<math>\mu</math>L with severe diarrhea (<b>CIII</b>)</li> </ul>		
<p><b>Shigellosis</b></p>	<ul style="list-style-type: none"> <li>• Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (<b>AIII</b>)</li> </ul> <p><u>Duration of Therapy:</u></p> <ul style="list-style-type: none"> <li>• <i>Gastroenteritis</i>: 7–10 days (<b>AIII</b>) (if azithromycin is used, treat for 5 days)</li> <li>• <i>Bacteremia</i>: <math>\geq</math>14 days (<b>BIII</b>)</li> <li>• <i>Recurrent Infections</i>: up to 6 weeks (<b>BIII</b>)</li> </ul> <p><b>Note:</b> Increased resistance of <i>Shigella</i> to fluoroquinolones is occurring in the United States. Avoid fluoroquinolones if ciprofloxacin MIC is <math>\geq</math>0.12 ug/ml even if the laboratory identifies the isolate as sensitive. Many <i>Shigella</i> strains resistant to fluoroquinolones exhibit resistance to other commonly used antibiotics. Thus, antibiotic sensitivity testing of <i>Shigella</i> isolates from HIV-infected individuals should be performed routinely.</p>	<ul style="list-style-type: none"> <li>• Levofloxacin 750 mg (PO or IV) q24h (<b>BIII</b>), or</li> <li>• Moxifloxacin 400 mg (PO or IV) q24h (<b>BIII</b>), or</li> <li>• TMP 160 mg-SMX 800 mg (PO or IV) q12h (<b>BIII</b>) (<b>Note:</b> <i>Shigella</i> infections acquired outside of the United States have high rates of TMP-SMX resistance), or</li> <li>• Azithromycin 500 mg PO daily for 5 days (<b>BIII</b>) (<b>Note:</b> azithromycin is not recommended for patients with bacteremia [<b>AIII</b>])</li> </ul> <p><b>Note:</b> Azithromycin-resistant <i>Shigella</i> spp has been reported in HIV-infected MSM.</p>	<p>Therapy is indicated both to shorten duration of illness and prevent spread of infection (<b>AIII</b>).</p> <p>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/mm<sup>3</sup> whose diarrhea resolves prior to culture confirmation of <i>Shigella</i> infection (<b>CIII</b>).</p> <p>Oral or IV rehydration if indicated (<b>AIII</b>).</p> <p>Antimotility agents should be avoided (<b>BIII</b>).</p> <p>If no clinical response after 5–7 days, consider follow-up stool culture, alternative diagnosis, or antibiotic resistance.</p> <p>Effective ART may decrease the risk of recurrence of <i>Shigella</i> infections.</p>
<p><b>Campylobacteriosis</b></p>	<p><u>For Mild Disease and If CD4 Count &gt;200 cells/<math>\mu</math>L:</u></p> <ul style="list-style-type: none"> <li>• No therapy unless symptoms persist for more than several days (<b>CIII</b>)</li> </ul> <p><u>For Mild-to-Moderate Disease (If Susceptible):</u></p> <ul style="list-style-type: none"> <li>• Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (<b>BIII</b>), or</li> <li>• Azithromycin 500 mg PO daily (<b>BIII</b>) (<b>Note:</b> Not for patients with bacteremia [<b>AIII</b>])</li> </ul> <p><u>For <i>Campylobacter</i> Bacteremia:</u></p> <ul style="list-style-type: none"> <li>• Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (<b>BIII</b>) + an aminoglycoside (<b>BIII</b>)</li> </ul>	<p><u>For Mild-to-Moderate Disease (If Susceptible):</u></p> <ul style="list-style-type: none"> <li>• Levofloxacin 750 mg (PO or IV) q24h (<b>BIII</b>), or</li> <li>• Moxifloxacin 400 mg (PO or IV) q24h (<b>BIII</b>)</li> </ul> <p>Add an aminoglycoside to fluoroquinolone in bacteremic patients (<b>BIII</b>).</p>	<p>Oral or IV rehydration if indicated (<b>AIII</b>).</p> <p>Antimotility agents should be avoided (<b>BIII</b>).</p> <p>If no clinical response after 5–7 days, consider follow-up stool culture, alternative diagnosis, or antibiotic resistance.</p> <p>There is an increasing rate of fluoroquinolone resistance in the United States (24% resistance in 2011).</p> <p>The rationale of addition of an aminoglycoside to a fluoroquinolone in bacteremic patients is to prevent emergence of quinolone resistance.</p>

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

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

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

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

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

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

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

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

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

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



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

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

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
<p><b>Cytomegalovirus (CMV) Disease</b></p>	<p><u>CMV Retinitis Induction Therapy (followed by Chronic Maintenance Therapy):</u></p> <p><i>For Immediate Sight-Threatening Lesions (within 1500 microns of the fovea):</i></p> <ul style="list-style-type: none"> <li>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 <b>(AIII)</b>; plus</li> <li>Valganciclovir 900 mg PO BID for 14–21 days, then 900mg once daily <b>(AI)</b>:</li> </ul> <p><u>For Peripheral Lesions:</u></p> <ul style="list-style-type: none"> <li>Valganciclovir 900 mg PO BID for 14–21 days, then 900 mg once daily <b>(AI)</b></li> </ul> <p><u>Chronic Maintenance:</u></p> <ul style="list-style-type: none"> <li>Valganciclovir 900 mg PO daily <b>(AI)</b> for 3-6 months until ART induced immune recovery (see Table 4)</li> </ul> <p><u>CMV Esophagitis or Colitis:</u></p> <ul style="list-style-type: none"> <li>Ganciclovir 5 mg/kg IV q12h; may switch to valganciclovir 900 mg PO q12h once the patient can tolerate oral therapy <b>(BI)</b></li> <li>Duration: 21–42 days or until symptoms have resolved <b>(CII)</b></li> <li>Maintenance therapy is usually not necessary, but should be considered after relapses <b>(BII)</b>.</li> </ul> <p><u>Well-Documented, Histologically Confirmed CMV Pneumonia:</u></p> <ul style="list-style-type: none"> <li>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) <b>(CIII)</b>.</li> <li>The optimal duration of therapy and the role of oral valganciclovir have not been established.</li> </ul> <p><u>CMV Neurological Disease</u></p> <p><b>Note: Treatment should be initiated promptly.</b></p> <ul style="list-style-type: none"> <li>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 <b>(CIII)</b></li> </ul>	<p><u>CMV Retinitis</u></p> <p><i>For Immediate Sight-Threatening Lesions (within 1500 microns of the fovea): Intravitreal therapy as listed in the Preferred section, plus one of the following:</i></p> <p><u>Alternative Systemic Induction Therapy (followed by Chronic Maintenance Therapy):</u></p> <ul style="list-style-type: none"> <li>Ganciclovir 5 mg/kg IV q12h for 14–21 days <b>(AI)</b>, or</li> <li>Foscarnet 90 mg/kg IV q12h or 60 mg/kg q8h for 14–21 days <b>(AI)</b>, or</li> <li>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) <b>(BI)</b>. (Note: This regimen should be avoided in patients with sulfa allergy because of cross hypersensitivity with probenecid.)</li> </ul> <p><u>Chronic Maintenance (for 3-6 months until ART induced immune recovery (see Table 4):</u></p> <ul style="list-style-type: none"> <li>Ganciclovir 5 mg/kg IV 5–7 times weekly <b>(AI)</b>, or</li> <li>Foscarnet 90–120 mg/kg IV once daily <b>(AI)</b>, or</li> <li>Cidofovir 5 mg/kg IV every other week with saline hydration and probenecid as above <b>(BI)</b></li> </ul> <p><u>CMV Esophagitis or Colitis:</u></p> <ul style="list-style-type: none"> <li>Foscarnet 90 mg/kg IV q12h or 60 mg/kg q8h <b>(BI)</b> for patients with treatment-limiting toxicities to ganciclovir or with ganciclovir resistance, or</li> <li>Valganciclovir 900 mg PO q12h in milder disease and if able to tolerate PO therapy <b>(BII)</b>, or</li> <li>Duration: 21–42 days or until symptoms have resolved <b>(CII)</b></li> <li>For mild disease, if ART can be initiated without delay, consider withholding CMV therapy <b>(CIII)</b>.</li> </ul>	<p>The choice of therapy for CMV retinitis should be individualized, based on location and severity of the lesions, level of immunosuppression, and other factors (e.g., concomitant medications and ability to adhere to treatment) <b>(AIII)</b>.</p> <p>Given the evident benefits of systemic therapy in preventing contralateral eye involvement, reduce CMV visceral disease and improve survival. Whenever feasible, treatment should include systemic therapy.</p> <p>The ganciclovir ocular implant, which is effective for treatment of CMV retinitis is no longer available. For sight threatening retinitis, intravitreal injections of ganciclovir or foscarnet can be given to achieve higher ocular concentration faster.</p> <p>Routine (i.e., every 3 months) ophthalmologic follow-up is recommended after stopping chronic maintenance therapy for early detection of relapse or IRU, and then periodically after sustained immune reconstitution <b>(AIII)</b>.</p> <p>IRU may develop in the setting of immune reconstitution.</p> <p><u>Treatment of IRU</u></p> <ul style="list-style-type: none"> <li>Periocular corticosteroid or short courses of systemic steroid <b>(BIII)</b>.</li> </ul> <p>Initial therapy in patients with CMV retinitis, esophagitis, colitis, and pneumonitis should include initiation or optimization of ART <b>(BIII)</b>.</p>

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

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

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

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

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
<p><b>HHV-8 Diseases</b> (Kaposi Sarcoma [KS], Primary Effusion Lymphoma [PEL], Multicentric Castleman's Disease [MCD])</p>	<p><u>Mild To Moderate KS (localized involvement of skin and/or lymph nodes):</u></p> <ul style="list-style-type: none"> <li>Initiate or optimize ART (<b>AII</b>)</li> </ul> <p><u>Advanced KS [visceral (<b>AI</b>) or disseminated cutaneous KS (<b>BIII</b>):</u></p> <ul style="list-style-type: none"> <li>Chemotherapy (per oncology consult) + ART</li> <li>Liposomal doxorubicin first line chemotherapy (<b>AI</b>)</li> </ul> <p><u>Primary Effusion Lymphoma:</u></p> <ul style="list-style-type: none"> <li>Chemotherapy (per oncology consult) + ART (<b>AIII</b>)</li> <li>PO valganciclovir or IV ganciclovir can be used as adjunctive therapy (<b>CIII</b>).</li> </ul> <p><u>MCD Therapy Options (in consultation with specialist, depending on HIV/HHV-8 status, presence of organ failure, and refractory nature of disease):</u></p> <p>ART (<b>AIII</b>) along with one of the following</p> <ul style="list-style-type: none"> <li>Valganciclovir 900 mg PO BID for 3 weeks (<b>CII</b>), or</li> <li>Ganciclovir 5 mg/kg IV q12h for 3 weeks (<b>CII</b>), or</li> <li>Valganciclovir PO or Ganciclovir IV + zidovudine 600 mg PO q6h for 7–21 days (<b>CII</b>)</li> <li>Rituximab +/- Prednisone (<b>CII</b>)</li> <li>Monoclonal antibody targeting IL-6 or IL-6 receptor (<b>BII</b>)</li> </ul> <p><u>Concurrent KS and MCD</u></p> <ul style="list-style-type: none"> <li>Rituximab + liposomal doxorubicin (<b>BII</b>)</li> </ul>	<p><u>MCD</u></p> <ul style="list-style-type: none"> <li>Rituximab (375 mg/m<sup>2</sup> given weekly for 4–8 weeks) may be an alternative to or used adjunctively with antiviral therapy (<b>CII</b>).</li> </ul>	<ul style="list-style-type: none"> <li>Corticosteroids should be avoided in patients with KS, including those with KS-IRis (<b>AIII</b>)</li> <li>Corticosteroids are potentially effective as adjunctive therapy for MCD, but should be used with caution, esp. in patients with concurrent KS.</li> <li>Patients who received rituximab for MCD may experience subsequent exacerbation or emergence of KS.</li> </ul>
<p><b>Human Papillomavirus (HPV) Disease</b></p>	<p><b>Treatment of Condyloma Acuminata (Genital Warts)</b></p> <p><u>Patient-Applied Therapy for Uncomplicated External Warts That Can Be Easily Identified by Patients:</u></p> <ul style="list-style-type: none"> <li>Podophylotoxin (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 (<b>BIII</b>), or</li> <li>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 (<b>BII</b>), or</li> <li>Sinecatechins 15% ointment: Apply to affected areas TID for up to 16 weeks, until warts are completely cleared and not visible (<b>BIII</b>).</li> </ul>	<p><u>Provider-Applied Therapy for Complex or Multicentric Lesions, or Lesions Inaccessible to Patient</u></p> <p><u>Applied Therapy:</u></p> <ul style="list-style-type: none"> <li>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 (<b>BIII</b>). Some providers allow the lesion to thaw, then freeze a second time in each session (<b>BIII</b>), or</li> <li>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 (<b>BIII</b>), or</li> <li>Surgical excision (<b>BIII</b>) or laser surgery (<b>CIII</b>) to external or anal warts, or</li> </ul>	<p>HIV-infected patients may have larger or more numerous warts and may not respond as well to therapy for genital warts when compared to HIV-uninfected individuals.</p> <p>Topical cidofovir has activity against genital warts, but the product is not commercially available (<b>CIII</b>).</p> <p>Intralesional interferon-alpha is usually not recommended because of high cost, difficult administration, and potential for systemic side effects (<b>CIII</b>).</p> <p>The rate of recurrence of genital warts is high despite treatment in HIV-infected patients.</p> <p>There is no consensus on the treatment of oral</p>



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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
<p><b>Human Papillomavirus (HPV) Disease,</b> continued</p>		<ul style="list-style-type: none"> <li>Podophyllin resin 10%–25% in tincture of benzoin: Apply to all lesions (up to 10 cm<sup>2</sup>), then wash off a few hours later, repeat weekly for up to 6 weeks until lesions are no longer visible (<b>CIII</b>).</li> </ul>	<p>warts. Many treatments for anogenital warts cannot be used in the oral mucosa. Surgery is the most common treatment for oral warts that interfere with function or for aesthetic reasons.</p>
<p><b>Hepatitis B Virus (HBV) Disease</b></p>	<p>ART regimen which includes 2 drugs that are active against both HBV and HIV is recommended for all HIV/HBV-co-infected patients regardless of CD4 cell count and HBV DNA level (<b>AII</b>).</p> <p>Tenofovir alafenamide (TAF)/emtricitabine or tenofovir disoproxil fumarate (TDF)/emtricitabine PO once daily (+ additional drug (s) for HIV) (<b>AIII</b>).</p> <p>The choice of TAF vs. TDF should be based on renal function and risk of renal or bone toxicities.</p> <p><u>CrCl &gt;60 mL/min</u> TDF 300 mg plus (FTC 200 mg or 3TC 300 mg) or [TAF (10 or 25 mg)<sup>a</sup> plus FTC 200 mg] PO once daily (<b>AIII</b>).</p> <p><u>CrCl 30-59 mL/min</u> TAF (10 or 25 mg)<sup>a</sup> + FTC 200 mg PO once daily (<b>AIII</b>)</p> <p><u>CrCl &lt;30 mL/min</u> A fully suppressive ART regimen without tenofovir should be used, with the addition of renally dosed entecavir to the regimen</p> <p><u>Duration:</u> Continue treatment indefinitely (<b>AIII</b>)</p>	<p><u>If TAF or TDF Cannot Be Used as Part of HIV/HBV Therapy:</u> Use entecavir (dose adjustment according to renal function) plus a fully suppressive ART regimen without TAF or TDF (<b>BIII</b>).</p> <p><u>CrCl &lt; 30 mL/min</u> ART with renally dose adjusted TDF and FTC can be used (<b>BIII</b>) if recovery of renal function is unlikely (See <a href="#">Table 7</a> for dosage recommendation)</p> <p><u>If patient is not receiving ART:</u></p> <ul style="list-style-type: none"> <li>HBV treatment is indicated for elevated ALT, HBV DNA &gt;2000mIU/mL, significant liver fibrosies, advanced liver disease or cirrhosis (<b>AI</b>)</li> <li>Peginterferon alfa-2a 180 µg SQ once weekly for 48 weeks (<b>CIII</b>), or</li> <li>Peginterferon alfa 2b 1.5 µg/kg SQ once weekly for 48 weeks (<b>CIII</b>)</li> </ul>	<p>Chronic administration of lamivudine or emtricitabine as the only active drug against HBV should be avoided because of high rate of selection of HBV resistance (<b>AI</b>).</p> <p>Directly acting HBV drugs such as adefovir, emtricitabine, entecavir, lamivudine, telbivudine, or tenofovir <b>must not be given</b> in the absence of a fully suppressive ART regimen to avoid selection of drug resistance HIV (<b>AI</b>).</p> <p>When changing ART regimens, continue agents with anti-HBV activity (<b>BIII</b>).</p> <p>If anti-HBV therapy is discontinued and a flare occurs, therapy should be re-instituted because it can be potentially life-saving (<b>AIII</b>).</p> <p>As HBV reactivation can occur during treatment for HCV with directly active agents (DAAs) in the absence of HBV-active drugs, all HIV-HBV-coinfected patients who will be treated for HCV should be on HBV-active ART at the time of HCV treatment initiation (<b>AI</b>)</p>
<p><b>Hepatitis C Virus (HCV) Disease</b></p>	<p>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.</p>		
<p><b>Progressive Multifocal Leukoencephalopathy (PML) (JC Virus Infections)</b></p>	<p>There is no specific antiviral therapy for JC virus infection. The main treatment approach is to reverse the immunosuppression caused by HIV.</p> <p>Initiate ART immediately in ART-naïve patients (<b>AII</b>).</p> <p>Optimize ART in patients who develop PML in phase of HIV viremia on ART (<b>AIII</b>)</p>	<p>None.</p>	<p>Corticosteroids may be used for PML-IRIS characterized by contrast enhancement, edema or mass effect, and with clinical deterioration (<b>BIII</b>) (see text for further discussion).</p>



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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
<p><b>Malaria</b></p>	<p>Because <i>Plasmodium falciparum</i> malaria can progress within hours from mild symptoms or low-grade fever to severe disease or death, all HIV-infected patients with confirmed or suspected <i>P. falciparum</i> infection should be hospitalized for evaluation, initiation of treatment, and observation <b>(AIII)</b>.</p> <p>Treatment recommendations for HIV-infected patients are the same as HIV-uninfected patients <b>(AIII)</b>.</p> <p>Choice of therapy is guided by the degree of parasitemia, the species of <i>Plasmodium</i>, the patient's clinical status, region of infection, and the likely drug susceptibility of the infected species, and can be found at <a href="http://www.cdc.gov/malaria">http://www.cdc.gov/malaria</a>.</p>	<p>When suspicion for malaria is low, antimalarial treatment should not be initiated until the diagnosis is confirmed.</p>	<p>For treatment recommendations for specific regions, clinicians should refer to the following web link:  <a href="http://www.cdc.gov/malaria/">http://www.cdc.gov/malaria/</a>                      or call the CDC Malaria Hotline: (770) 488-7788: M–F 8 AM–4:30 PM ET, or (770) 488-7100 after hours</p>
<p><b>Leishmaniasis, visceral</b></p>	<p><u>For Initial Infection:</u></p> <ul style="list-style-type: none"> <li>• Liposomal amphotericin B 2–4 mg/kg IV daily <b>(AII)</b>, <i>or</i></li> <li>• Liposomal amphotericin B interrupted schedule (e.g., 4 mg/kg on days 1–5, 10, 17, 24, 31, 38) <b>(AII)</b></li> <li>• To achieve total dose of 20–60 mg/kg <b>(AII)</b></li> </ul> <p><u>Chronic Maintenance Therapy (Secondary Prophylaxis); Especially in Patients with CD4 Count &lt;200 cells/μL:</u></p> <ul style="list-style-type: none"> <li>• Liposomal amphotericin B 4 mg/kg every 2–4 weeks <b>(AII)</b>, <i>or</i></li> <li>• Amphotericin B lipid complex <b>(AII)</b> 3 mg/kg every 21 days <b>(AII)</b></li> </ul>	<p><u>For Initial Infection:</u></p> <ul style="list-style-type: none"> <li>• Other lipid formulation of amphotericin B, dose and schedule as in Preferred Therapy, <i>or</i></li> <li>• Amphotericin B deoxycholate 0.5–1.0 mg/kg IV daily for total dose of 1.5–2.0 g <b>(BII)</b>, <i>or</i></li> <li>• Sodium stibogluconate (pentavalent antimony) <b>(BII)</b> 20 mg/kg IV or IM daily for 28 days.</li> </ul> <p><u>Another Option:</u></p> <ul style="list-style-type: none"> <li>• Miltefosine 100 mg PO daily for 4 weeks (available in the United States under a treatment IND) <b>(CIII)</b></li> </ul> <p><u>Chronic Maintenance Therapy (Secondary Prophylaxis):</u></p> <ul style="list-style-type: none"> <li>• Sodium stibogluconate 20 mg/kg IV or IM every 4 weeks <b>(BII)</b></li> </ul>	<p>ART should be initiated or optimized <b>(AIII)</b>.</p> <p>For sodium stibogluconate, contact the CDC Drug Service at (404) 639-3670 or <a href="mailto:drugservice@cdc.gov">drugservice@cdc.gov</a>.</p>

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

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

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

Opportunistic Infection	Preferred Therapy	Alternative Therapy	Other Comments
<b>Isosporiasis</b>	<p>For Acute Infection:</p> <ul style="list-style-type: none"> <li>• TMP-SMX (160 mg/800 mg) PO (or IV) QID for 10 days <b>(AII)</b>, <i>or</i></li> <li>• TMP-SMX (160 mg/800 mg) PO (or IV) BID for 7–10 days <b>(BI)</b></li> <li>• Can start with BID dosing first and increase daily dose and/or duration (up to 3–4 weeks) if symptoms worsen or persist <b>(BIII)</b></li> <li>• IV therapy may be used for patients with potential or documented mal-absorption.</li> </ul> <p><u>Chronic Maintenance Therapy (Secondary Prophylaxis):</u></p> <ul style="list-style-type: none"> <li>• In patients with CD4 count &lt;200/<math>\mu</math>L, TMP-SMX (160 mg/800 mg) PO TIW <b>(AI)</b></li> </ul>	<p>For Acute Infection:</p> <ul style="list-style-type: none"> <li>• Pyrimethamine 50–75 mg PO daily + leucovorin 10–25 mg PO daily <b>(BIII)</b>, <i>or</i></li> <li>• Ciprofloxacin 500 mg PO BID for 7 days <b>(CI)</b> as a second line alternative</li> </ul> <p><u>Chronic Maintenance Therapy (Secondary Prophylaxis):</u></p> <ul style="list-style-type: none"> <li>• TMP-SMX (160 mg/800 mg) PO daily or (320 mg/1600 mg) three times weekly <b>(BIII)</b></li> <li>• Pyrimethamine 25 mg PO daily + leucovorin 5–10 mg PO daily <b>(BIII)</b></li> <li>• Ciprofloxacin 500 mg three times weekly <b>(CI)</b> as a second-line alternative</li> </ul>	<p>Fluid and electrolyte management in patients with dehydration <b>(AIII)</b>.</p> <p>Nutritional supplementation for malnourished patients <b>(AIII)</b>.</p> <p>Immune reconstitution with ART may result in fewer relapses <b>(AIII)</b>.</p>

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

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

**Evidence Rating:**

*Strength of Recommendation:*

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

*Quality of Evidence for the Recommendation:*

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

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