Guidelines for the Prevention and Treatment of Opportunistic Infections Among HIV-Exposed and HIV-Infected Children

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<table>
<thead>
<tr>
<th>Indication:</th>
<th>First Choice</th>
<th>Alternative</th>
<th>Comments/Special Issues</th>
<th>Last Reviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacterial Infections</strong>&lt;br&gt; <em>S. pneumoniae</em> and other invasive bacteria</td>
<td>• Pneumococcal, meningococcal, and Hib vaccines&lt;br&gt;• Intravenous immune globulin (400 mg/kg body weight every 2 to 4 weeks)</td>
<td>• TMP-SMX 75/375 mg/m² body surface area per dose by mouth twice daily</td>
<td>See Figures 1 and 2 for detailed vaccines recommendations. Vaccines Routinely Recommended for Primary Prophylaxis, Additional Primary Prophylaxis Indicated For:&lt;br&gt;• Hypogammaglobulinemia (that is, IgG &lt; 400mg/dL) Criteria for discontinuing primary prophylaxis:&lt;br&gt;• Resolution of hypogammaglobulinemia Criteria for restarting primary prophylaxis:&lt;br&gt;• Relapse of hypogammaglobulinemia</td>
<td>November 6, 2013</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>Not routinely recommended</td>
<td>N/A</td>
<td>N/A</td>
<td>January 31, 2019</td>
</tr>
<tr>
<td>Coccidioidomycosis</td>
<td>N/A</td>
<td>N/A</td>
<td>Primary prophylaxis not routinely indicated in children.</td>
<td>November 6, 2013</td>
</tr>
<tr>
<td>Cryptococcosis</td>
<td>Not recommended</td>
<td>Not recommended</td>
<td>N/A</td>
<td>November 6, 2013</td>
</tr>
<tr>
<td>Cryptosporidiosis</td>
<td>ARV therapy to avoid advanced immune deficiency</td>
<td>N/A</td>
<td>N/A</td>
<td>August 29, 2019</td>
</tr>
<tr>
<td>Cytomegalovirus (CMV)</td>
<td>• For older children who can receive adult dose (based on their BSA), valganciclovir tablets 900 mg orally once daily with food&lt;br&gt;• For children aged 4 months–16 years, valganciclovir oral solution 50 mg/mL at dose in milligrams = 7 x BSA x CrCl (up to maximum CrCl of 150 mL/min/1.73 m²) orally once daily with food (maximum dose 900 mg/day)</td>
<td>N/A</td>
<td>Primary Prophylaxis Can Be Considered for:&lt;br&gt;• CMV antibody positivity and severe immunosuppression (i.e., CD4 cell count &lt;50 cells/mm³ in children ≥6 years; CD4 percentage &lt;5% in children &lt;6 years)&lt;br&gt;Criteria for Discontinuing Primary Prophylaxis:&lt;br&gt;• CD4 cell count &gt;100 cells/mm³ for children ≥6 years; CD4 percentage &gt;10% in children &lt;6 years Criteria for Considering Restarting Primary Prophylaxis:&lt;br&gt;• CD4 cell count &lt;50 cells/mm³ in children ≥6 years; CD4 percentage &lt;5% in children &lt;6 years</td>
<td>November 6, 2013</td>
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<tr>
<td>Giardiasis</td>
<td>ART to avoid advanced immunodeficiency</td>
<td>N/A</td>
<td>N/A</td>
<td>August 22, 2019</td>
</tr>
<tr>
<td>Hepatitis B Virus (HBV)</td>
<td>• Hepatitis B vaccine&lt;br&gt;• Combination of hepatitis B immunoglobulin and hepatitis B vaccine for infants born to mothers with hepatitis B infection</td>
<td>Hepatitis B immunoglobulin following exposure</td>
<td>See Figures 1 and 2 for detailed vaccine recommendations. Primary Prophylaxis Indicated for:&lt;br&gt;• All individuals who are not HBV infected Criteria for Discontinuing Primary Prophylaxis:&lt;br&gt;• N/A Criteria for Restarting Primary Prophylaxis&lt;br&gt;• N/A</td>
<td>November 6, 2013</td>
</tr>
<tr>
<td>Hepatitis C Virus (HCV)</td>
<td>None</td>
<td>N/A</td>
<td>N/A</td>
<td>November 6, 2013</td>
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</tbody>
</table>
### Table 1: Primary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 2 of 9)

<table>
<thead>
<tr>
<th>Indication</th>
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<tbody>
<tr>
<td>Herpes Simplex Virus Infections (HSV)</td>
<td>None</td>
<td>None</td>
<td>Primary prophylaxis is not indicated.</td>
<td>November 6, 2013</td>
</tr>
<tr>
<td>Histoplasmosis</td>
<td>N/A</td>
<td>N/A</td>
<td>Primary Prophylaxis indicated for selected HIV-infected adults but not children.</td>
<td>November 6, 2013</td>
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<td></td>
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<td>Criteria for Discontinuing Primary Prophylaxis:</td>
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<td></td>
<td>• N/A</td>
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<td>Criteria for Restarting Primary Prophylaxis:</td>
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<td></td>
<td>• N/A</td>
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<tr>
<td>Human Papillomavirus (HPV)</td>
<td>HPV vaccine</td>
<td>N/A</td>
<td>See Figure 2 for detailed vaccine recommendations.</td>
<td>November 6, 2013</td>
</tr>
<tr>
<td>Influenza A and B</td>
<td>Oseltamivir</td>
<td>None</td>
<td>Pre-Exposure Chemoprophylaxis</td>
<td>July 17, 2018</td>
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<td><strong>Indications:</strong></td>
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<td>• After careful consideration of risks and benefits, pre-exposure antiviral chemoprophylaxis may be considered for children with HIV with severe immunosuppression while influenza virus is circulating in the community.</td>
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<td><strong>Duration:</strong></td>
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<td></td>
<td>• When employed, pre-exposure antiviral chemoprophylaxis should continue for the duration of influenza virus circulation in the community.</td>
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<td></td>
<td>Zanamivir (Aged ≥5 Years):</td>
<td>None</td>
<td>Post-Exposure Chemoprophylaxis</td>
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<td><strong>Indications Recommended For:</strong></td>
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<tr>
<td></td>
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<td></td>
<td>• Children with HIV with severe immunosuppression regardless of influenza vaccination status.</td>
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<td>• Children with HIV with moderate to no immunosuppression if</td>
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<td>• Influenza vaccination is contraindicated or unavailable; or</td>
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<td>• Low influenza vaccine effectiveness is documented in the current influenza season; and</td>
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<td>• Antiviral chemoprophylaxis can be started within 48 hours of exposure to an ill person with confirmed or suspected influenza.</td>
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<td><strong>Duration:</strong></td>
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<td></td>
<td>• Duration of chemoprophylaxis depends on the type of exposure, whether influenza vaccination was provided after the exposure, and whether influenza vaccine is anticipated to be effective based on the child’s degree of immunosuppression and the degree of match with circulating influenza viruses.</td>
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<td>• If influenza vaccination is provided after contact, chemoprophylaxis duration should be 2 weeks after vaccination.</td>
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Table 1: Primary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 3 of 9)

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<tr>
<td>Influenza A and B, continued</td>
<td></td>
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<td>• If exposure is to a household contact, chemoprophylaxis duration should be 7 days.</td>
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<td></td>
<td>• If chemoprophylaxis is provided in setting of an institutional outbreak, the duration is either 14 days or 7 days after onset of symptoms in the last person infected, whichever is longer.</td>
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<tr>
<td>Oseltamivir Dosing Adjustments</td>
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<td>Premature Infants:</td>
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<tr>
<td></td>
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<td>• Current weight-based dosing recommendations for oseltamivir are not appropriate for premature infants (i.e., gestational age at delivery &lt;38 weeks).</td>
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<td>Renal Insufficiency:</td>
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<td>• A reduction in dose of oseltamivir is recommended for patients with CrCl &lt;30 mL/min. For patients with CrCl 10–30 mL/min, a reduction in chemoprophylaxis dosing frequency to every other day is recommended. PK data are limited for dosing recommendations for patients with severe renal insufficiency on dialysis.</td>
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<td></td>
<td>• Oseltamivir is FDA-approved for prophylaxis of influenza in children aged ≥1 year. It is not approved for prophylaxis in children aged &lt;1 year. However, CDC recommends that health care providers who treat children aged ≥3 months to &lt;1 year administer a chemoprophylaxis dose of oseltamivir 3 mg/kg body weight/dose once daily. Chemoprophylaxis for infants aged &lt;3 months is not recommended unless the exposure situation is judged to be critical.</td>
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<td></td>
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<td></td>
<td>• Zanamivir is not recommended for chemoprophylaxis in children aged &lt;5 years or for children with underlying respiratory disease.</td>
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<td></td>
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<td></td>
<td>• See Fiore 2011 and Influenza Antiviral Medications: Summary for Clinicians for further details.</td>
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</tr>
<tr>
<td>Isosporiasis (Cystoisosporiasis)</td>
<td>There are no U.S. recommendations for primary prophylaxis of isosporiasis.</td>
<td>N/A</td>
<td>Initiation of ART to avoid severe immunodeficiency may reduce incidence; TMP-SMX prophylaxis may reduce incidence.</td>
<td>February 8, 2019</td>
</tr>
</tbody>
</table>
### Table 1: Primary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 4 of 9)

<table>
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<tr>
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</thead>
<tbody>
<tr>
<td><strong>Malaria</strong></td>
<td>For Travel To Chloroquine-Sensitive Areas:</td>
<td>N/A</td>
<td>Recommendations are the same for HIV-infected and HIV-uninfected children. Please 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>November 6, 2013</td>
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<tr>
<td></td>
<td>• Chloroquine base 5 mg/kg body weight base by mouth, up to 300 mg once weekly (equivalent to 7.5 mg/kg body weight chloroquine phosphate). Start 1–2 weeks before leaving, take weekly while away, and then take once weekly for 4 weeks after returning home</td>
<td></td>
<td>For travel to chloroquine-sensitive areas. Equally recommended options include chloroquine, atovaquone/proguanil, doxycycline (for children aged ≥8 years), and mefloquine; primaquine is recommended for areas with mainly P. vivax.</td>
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<td></td>
<td>• Atovaquone/proguanil once daily started 1–2 days before travel, for duration of stay, and then for 1 week after returning home</td>
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<td>G6PD screening must be performed prior to primaquine use.</td>
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<td></td>
<td>• 11–20 kg; 1 pediatric tablet (62.5 mg/25 mg)</td>
<td></td>
<td>Chloroquine phosphate is the only formulation of chloroquine available in the United States; 10 mg of chloroquine phosphate = 6 mg of chloroquine base.</td>
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<td></td>
<td>• 21–30 kg; 2 pediatric tablets (125 mg/50 mg)</td>
<td></td>
<td>For travel to chloroquine-resistant areas, preferred drugs are atovaquone/proguanil, doxycycline (for children aged ≥8 years) or mefloquine.</td>
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<td>• 31–40 kg; 3 pediatric tablets (187.5 mg/75 mg)</td>
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<td></td>
<td>• &gt;40 kg; 1 adult tablet (250 mg/100 mg)</td>
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<td></td>
<td>• Doxycycline 2.2 mg/kg body weight (maximum 100 mg) by mouth once daily for children aged ≥8 years. Must be taken 1–2 days before travel, daily while away, and then up to 4 weeks after returning</td>
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<td>• Mefloquine 5 mg/kg body weight orally given once weekly (max 250 mg)</td>
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<td>For Areas with Mainly P. Vivax:</td>
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<td>• Primaquine phosphate 0.6 mg/kg body weight base once daily by mouth, up to a maximum of 30 mg base/day. Starting 1 day before leaving, taken daily, and for 3–7 days after return</td>
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<td></td>
<td>For Travel to Chloroquine-Resistant Areas:</td>
<td>N/A</td>
<td></td>
<td>December 15, 2016</td>
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<tr>
<td></td>
<td>• Atovaquone/proguanil once daily started 1–2 days before travel, for duration of stay, and then for 1 week after returning home</td>
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<tr>
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<td>• 11–20 kg; 1 pediatric tablet (62.5 mg/25 mg)</td>
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<td>• &gt;40 kg; 1 adult tablet (250 mg/100 mg)</td>
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<td>• Doxycycline 2.2 mg/kg body weight (maximum 100 mg) by mouth once daily for children aged ≥8 years. Must be taken 1–2 days before travel, daily while away, and then up to 4 weeks after returning</td>
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<tr>
<td></td>
<td>• Mefloquine 5 mg/kg body weight orally given once weekly (max 250 mg)</td>
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<tr>
<td><strong>Microsporidiosis</strong></td>
<td>N/A</td>
<td>N/A</td>
<td>Not recommended</td>
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<td></td>
<td>N/A</td>
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<tr>
<td><em>Mycobacterium avium</em> Complex (MAC)</td>
<td>• Clarithromycin 7.5 mg/kg body weight (maximum 500 mg) orally twice daily, or • Azithromycin 20 mg/kg body weight (maximum 1200 mg) orally once weekly</td>
<td>• Azithromycin 5 mg/kg body weight (maximum 250 mg) orally once daily • Children aged &gt;5 years: rifabutin 300 mg orally once daily with food</td>
<td>Primary Prophylaxis Indicated for Children: • Age &lt;1 year: CD4 count &lt;750 cells/mm³; • Age 1 to &lt;2 years: CD4 count &lt;500 cells/mm³; • Age 2 to &lt;6 years: CD4 count &lt;75 cells/mm³; • Age ≥6 years: CD4 count &lt;50 cells/mm³ Criteria for Discontinuing Primary Prophylaxis: • Do not discontinue in children age &lt;2 years. • After ≥6 months of ART, and: • Age 2 to &lt;6 years: CD4 count &gt;200 cells/mm³ for &gt;3 consecutive months • Age ≥6 years: CD4 count &gt;100 cells/mm³ for &gt;3 consecutive months Criteria for Restarting Primary Prophylaxis: • Age 2 to &lt;6 years: CD4 count &lt;200 cells/mm³ • Age ≥6 years: CD4 count &lt;100 cells/mm³</td>
<td>January 8, 2019</td>
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</table>
### Table 1: Primary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 6 of 9)

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<thead>
<tr>
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</table>
| **Mycobacterium Tuberculosis**<br>(post-exposure) | Source Case Drug Susceptible:  
• Isoniazid 10–15 mg/kg body weight (maximum 300 mg/day) by mouth daily for 9 months |  
• If adherence with daily isoniazid cannot be ensured, consider isoniazid 20–30 mg/kg body weight (maximum 900 mg/day) by mouth 2 times a week by DOT for 9 months | Drug-drug interactions with cART should be considered for all rifamycin containing alternatives. |
| | Source Case Drug Resistant:  
• Consult expert and local public health authorities. |  
• Isoniazid 10–15 mg/kg body weight (maximum 300 mg/day) and rifampin 10–20 mg/kg/body weight (maximum 600 mg/day) by mouth daily for 3–4 months |  |
| | |  
• Rifampin 10–20 mg/kg body weight (maximum 600 mg/day) by mouth daily for 4–6 months |  |
| | |  
Criteria for Discontinuing Prophylaxis:  
• Only with documented severe adverse event, which is exceedingly rare. |  |
| | |  
Adjunctive Treatment:  
• Pyridoxine 1–2 mg/kg body weight once daily (maximum 25–50 mg/day) with isoniazid; pyridoxine supplementation is recommended for exclusively breastfed infants and for children and adolescents on meat- and milk-deficient diets; children with nutritional deficiencies, including all symptomatic HIV-infected children; and pregnant adolescents and women. | November 6, 2013 |

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**Indication:**  
• Positive TST (TST ≥5 mm) or IGRA without previous TB treatment  
• Close contact with any infectious TB case (repeated exposures warrant repeated post-exposure prophylaxis)  
• TB disease must be excluded before starting treatment.  
• No indication for pre-exposure and post-treatment prophylaxis.  

**Criteria for Discontinuing Prophylaxis:**  
• Only with documented severe adverse event, which is exceedingly rare.  

**Adjunctive Treatment:**  
• Pyridoxine 1–2 mg/kg body weight once daily (maximum 25–50 mg/day) with isoniazid; pyridoxine supplementation is recommended for exclusively breastfed infants and for children and adolescents on meat- and milk-deficient diets; children with nutritional deficiencies, including all symptomatic HIV-infected children; and pregnant adolescents and women.  

**Last Reviewed:** November 6, 2013
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</table>
| Pneumocystis jirovecii Pneumonia | • TMP-SMX (Cotrimoxazole): TMP 2.5–5 mg/kg body weight/dose with SMX 12.5–25 mg/kg body weight/dose twice per day. Dosing based on TMP component.  
• The total daily dose should not exceed 320 mg TMP and 1600 mg SMX. Several dosing schemes have been used successfully—  
• Given 3 days per week on consecutive days or on alternate days  
• Given 2 days per week on consecutive days or on alternate days  
• Given every day (total daily dose of TMP 5–10 mg/kg body weight given as a single dose each day) | Dapsone  
Children aged ≥1 months:  
• 2 mg/kg body weight (maximum 100 mg) by mouth once daily or 4 mg/kg body weight (maximum 200 mg) by mouth once weekly  
Atovaquone  
Children Aged 1–3 Months and ≥24 Months–12 Years:  
• 30-40 mg/kg body weight/dose by mouth once daily with food  
Children Aged 4–24 Months:  
• 45 mg/kg body weight/dose by mouth once daily with food  
Children Aged ≥13 Years:  
• 1500 mg (10 cc oral yellow suspension) per dose by mouth once daily  
Aerosolized Pentamidine  
Children Aged ≥5 Years:  
• 300 mg every month via Respirgard II™ nebulizer (manufactured by Marquest; Englewood, Colorado) | Primary Prophylaxis Indicated For:  
• All HIV-infected or HIV-indeterminate infants from aged 4–6 weeks to 12 months. regardless of CD4 cell count/ percentage  
• HIV-infected children aged 1 to <6 years with CD4 count <500 cells/mm³ or CD4 percentage <15%, HIV-infected children aged 6–12 years with CD4 count <200 cells/mm³ or CD4 percentage <15%  
Criteria for Discontinuing Primary Prophylaxis:  
Note: Do not discontinue in HIV-infected children aged <1 year  
After ≥6 Months of cART:  
• Aged 1 to <6 years; CD4 percentage ≥15% or CD4 count is ≥500 cells/mm³ for >3 consecutive months, or  
• Aged ≥6 years, CD4 percentage ≥15% or CD4 count is ≥200 cells/mm³ for >3 consecutive months  
Criteria for Restarting Primary Prophylaxis:  
• Aged 1 to < 6 years with CD4 percentage <15 or CD4 count <500 cells/mm³  
• Aged ≥6 years with CD4 percentage <15% or CD4 count <200 cells/mm³ | November 6, 2013 |
| Syphilis                   | N/A                                               | N/A         | Primary Prophylaxis Indicated for:  
• N/A  
Criteria for Discontinuing Primary Prophylaxis:  
• N/A  
Criteria for Restarting Primary Prophylaxis:  
• N/A | November 6, 2013 |
Table 1: Primary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 8 of 9)

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</table>
| Toxoplasmosis     | TMP-SMX 150/750 mg/m² body surface area once daily by mouth | For Children Aged ≥1 Month:  
• Dapsone 2 mg/kg body weight or 15 mg/m² body surface area (maximum 25 mg) by mouth once daily, plus  
• Pyrimethamine 1 mg/kg body weight (maximum 25 mg) by mouth once daily, plus  
• Leucovorin 5 mg by mouth every 3 days  
For Children Aged 1–3 Months, and those >24 Months:  
• Atovaquone 30 mg/kg body weight by mouth once daily  
Children Aged 4–24 Months:  
• Atovaquone 45 mg/kg body weight by mouth once daily, with or without pyrimethamine 1 mg/kg body weight or 15 mg/m² body surface area (maximum 25 mg) by mouth once daily, plus  
• Leucovorin 5 mg by mouth every 3 days  
|                   | Acceptable Alternative Dosage Schedules for TMP-SMX:  
• TMP-SMX 150/750 mg/m² body surface area per dose once daily by mouth 3 times weekly on 3 consecutive days per week  
• TMP-SMX 75/375 mg/m² body surface area per dose twice daily by mouth every day  
• TMP-SMX 75/375 mg/m² body surface area per dose twice daily by mouth 3 times weekly on alternate days  
|                   | Primary Prophylaxis Indicated For: IgG Antibody to Toxoplasma and Severe Immunosuppression:  
• HIV-infected children aged <6 years with CD4 percentage <15%; HIV-infected children aged ≥6 years with CD4 count <100 cells/mm³  
Criteria for Discontinuing Primary Prophylaxis:  
Note: Do not discontinue in children aged <1 year  
• After ≥6 months of cART, and  
• Aged 1 to <6 years; CD4 percentage is ≥15% for >3 consecutive months  
• Aged ≥6 years; CD4 count >200 cells/mm³ for >3 consecutive months  
Criteria for Restarting Primary Prophylaxis:  
• Aged 1 to <6 years with CD4 percentage <15%  
• Aged ≥6 years with CD4 count <100 to 200 cells/mm³  
| November 6, 2013  |
### Table 1: Primary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 9 of 9)

<table>
<thead>
<tr>
<th>Indication</th>
<th>First Choice</th>
<th>Alternative</th>
<th>Comments/Special Issues</th>
<th>Last Reviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varicella-Zoster Virus (VZV)</td>
<td>Varicella vaccine</td>
<td>N/A</td>
<td>See Figures 1 and 2 for detailed vaccine recommendations.</td>
<td>November 6, 2013</td>
</tr>
<tr>
<td>Pre-Exposure Prophylaxis</td>
<td></td>
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</tbody>
</table>
| Varicella-Zoster Virus (VZV)        | VariZIG 125 IU/10 kg body weight IM (maximum 625 IU), administered ideally within 96 hours (potentially beneficial up to 10 days) after exposure | If VariZIG cannot be administered within 96 hours (up to 10 days), IVIG 400 mg/kg body weight, administered once should be considered. IVIG should ideally be administered within 96 hours of exposure When passive immunization is not possible, some experts recommend prophylaxis with acyclovir 20 mg/kg body weight/dose (maximum dose 800 mg), administered QID for 7 days, beginning 7–10 days after exposure | Primary Post-Exposure Prophylaxis Indicated for:  
  • Patients with substantial exposure to varicella or zoster with no verified history of varicella or zoster or who are seronegative for VZV on a sensitive, specific antibody assay or who lack evidence of vaccination. Many experts limit this recommendation to varicella or zoster-exposed HIV-infected children who are considered to be severely immunocompromised, (i.e., in CDC Immunologic Category 3), especially if also classified as CDC Clinical Category Ca and experiencing a high HIV RNA plasma viral load (Bill).  
  • Some experts start acyclovir at first appearance of rash.  
Note: To obtain VariZIG, contact FFF Enterprises at 1-800-843-7477 or [http://www.fffenterprises.com](http://www.fffenterprises.com). | November 6, 2013 |
| Primary (Post-Exposure) Prophylaxis |                       |             |                                                              |               |

**Key to Acronyms:** ARV = antiretroviral; BSA = body surface area; cART = combination antiretroviral therapy; CrCl= (estimated) creatinine clearance; DOT = directly observed therapy; HBV = hepatitis B virus; IGRA = interferon-gamma release assay; QID = four times daily; TB = tuberculosis; TMP-SMX = trimethoprim-sulfamethoxazole
### Table 2: Secondary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations  (Last updated August 29, 2019; last reviewed August 29, 2019)  (page 1 of 6)

<table>
<thead>
<tr>
<th>Indication</th>
<th>First Choice</th>
<th>Alternative</th>
<th>Comments/Special Issues</th>
<th>Last Reviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacterial Infections</strong></td>
<td>• TMP-SMX 75/375 mg/m² body surface area per dose by mouth twice daily</td>
<td>• IVIG 400 mg/kg body weight every 2–4 weeks</td>
<td>Secondary Prophylaxis Indicated:</td>
<td>November 6, 2013</td>
</tr>
<tr>
<td><em>S. pneumoniae</em> and other invasive bacteria.</td>
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<td></td>
<td>• &gt;2 serious bacterial infections in a 1-year period in children who are unable to take cART</td>
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<td>Criteria for Discontinuing Secondary Prophylaxis:</td>
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<td></td>
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<td></td>
<td>• Sustained (≥ 3 months) immune reconstitution (CD4 percentage ≥25% if ≤6 years old; CD4 percentage ≥20% or CD4 count &gt;350 cells/mm³ if &gt;6 years old)</td>
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<td>Criteria for Restarting Secondary Prophylaxis:</td>
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<td></td>
<td>• &gt;2 serious bacterial infections in a 1-year period despite cART</td>
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<tr>
<td><strong>Candidiasis</strong></td>
<td>Not routinely recommended, but can be considered for frequent severe recurrences. Fluconazole:</td>
<td>N/A</td>
<td>Secondary Prophylaxis Indicated:</td>
<td>January 31, 2019</td>
</tr>
<tr>
<td></td>
<td>• Fluconazole 3–6 mg/kg body weight daily (maximum 200 mg) by mouth, or itraconazole oral solution, 2.5 mg/kg body weight/dose twice daily</td>
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<td>• Frequent or severe recurrences</td>
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<td>Criteria for Discontinuing Secondary Prophylaxis:</td>
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<td></td>
<td></td>
<td>• When CD4 count or percentage has risen to CDC immunologic Category 2 or 1</td>
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<td>Criteria for Restarting Secondary Prophylaxis:</td>
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<td></td>
<td></td>
<td></td>
<td>• Frequent severe recurrences</td>
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<tr>
<td><strong>Coccidioidomycosis</strong></td>
<td>Fluconazole 6 mg/kg body weight (maximum 400 mg) by mouth once daily</td>
<td>Itraconazole 2–5 mg/kg body weight (maximum 200 mg) by mouth per dose twice daily</td>
<td>Lifelong secondary prophylaxis with fluconazole for patients with meningitis or disseminated disease in the immunocompromised patient is recommended. Secondary prophylaxis should be considered after treatment of milder disease if CD4 count remains &lt;250 cells/mm³ or CD4 percentage &lt;15%.</td>
<td>November 6, 2013</td>
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<tr>
<td><strong>Cryptococcosis</strong></td>
<td>Fluconazole 6 mg/kg body weight (maximum 200 mg) by mouth once daily</td>
<td>Itraconazole oral solution 5 mg/kg body weight (maximum 200 mg) by mouth once daily</td>
<td>Secondary Prophylaxis Indicated:</td>
<td>November 6, 2013</td>
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<tr>
<td>a Secondary prophylaxis is also referred to as maintenance therapy or suppressive therapy</td>
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<td></td>
<td>• Documented disease</td>
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<td>Criteria for Discontinuing Secondary Prophylaxis</td>
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<td>If All of the Following Criteria are Fulfilled:</td>
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<td></td>
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<td>• Age ≥6 years</td>
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<td></td>
<td>• Asymptomatic on ≥12 months of secondary prophylaxis</td>
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<td></td>
<td>• CD4 count ≥100 cells/mm³ with undetectable HIV viral load on cART for &gt;3 months</td>
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<td>Criteria for Restarting Secondary Prophylaxis:</td>
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<td></td>
<td></td>
<td></td>
<td>• CD4 count &lt;100/mm³</td>
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<tr>
<td><strong>Cryptosporidiosis</strong></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>August 29, 2019</td>
</tr>
</tbody>
</table>
# Table 2: Secondary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations

<table>
<thead>
<tr>
<th>Indication</th>
<th>First Choice</th>
<th>Alternative</th>
<th>Comments/Special Issues</th>
<th>Last Reviewed</th>
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</thead>
<tbody>
<tr>
<td><strong>Cytomegalovirus (CMV)</strong></td>
<td>• Ganciclovir 5 mg/kg body weight IV once daily, or&lt;br&gt;• For older children who can receive adult dose (based on their BSA), valganciclovir tablets 900 mg orally once daily with food, or&lt;br&gt;• For children age 4 months–16 years, valganciclovir oral solution 50 mg/mL (at dose in milligrams = 7 x BSA x CrCl up to maximum CrCl of 150 mL/min/1.73 m²) orally once daily with food, or&lt;br&gt;• Foscarnet 90–120 mg/kg body weight IV once daily</td>
<td>• Cidofovir 5 mg/kg body weight per dose IV every other week. Must be given with probenecid and IV hydration.</td>
<td><strong>Secondary Prophylaxis Indicated For:</strong>&lt;br&gt;• Prior disseminated disease, retinitis, neurologic disease, or GI disease with relapse&lt;br&gt;<strong>Criteria for Discontinuing Secondary Prophylaxis If All of the Following Criteria Are Fulfilled:</strong>&lt;br&gt;• Completed ≥6 months of cART&lt;br&gt;• Consultation with ophthalmologist (if retinitis)&lt;br&gt;• Age &lt;6 years with CD4 percentage ≥15% for &gt;6 consecutive months&lt;br&gt;• Age ≥6 years with CD4 cell count &gt;100 cells/mm³ for &gt;6 consecutive months&lt;br&gt;• For retinitis, routine (i.e., every 3–6 months) ophtalmological follow-up is recommended for early detection of relapse or immune restoration uveitis.&lt;br&gt;<strong>Criteria for Restarting Secondary Prophylaxis:</strong>&lt;br&gt;• Age &lt;6 years with CD4 percentage &lt;15%&lt;br&gt;• Age ≥6 years with CD4 cell count &lt;100 cells/mm³</td>
<td>November 6, 2013</td>
</tr>
<tr>
<td><strong>Giardiasis</strong></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>August 22, 2019</td>
</tr>
<tr>
<td><strong>Hepatitis B Virus (HBV)</strong></td>
<td>Hepatitis A Vaccine</td>
<td>N/A</td>
<td><strong>Secondary Prophylaxis Indicated for:</strong>&lt;br&gt;• Chronically HBV-infected individuals to prevent further liver injury&lt;br&gt;<strong>Criteria for Discontinuing Secondary Prophylaxis:</strong>&lt;br&gt;• N/A&lt;br&gt;<strong>Criteria for Restarting Secondary Prophylaxis:</strong>&lt;br&gt;• N/A</td>
<td>November 6, 2013</td>
</tr>
<tr>
<td><strong>Hepatitis C Virus (HCV)</strong></td>
<td>None</td>
<td>N/A</td>
<td>N/A</td>
<td>November 6, 2013</td>
</tr>
</tbody>
</table>
### Table 2: Secondary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 3 of 6)

<table>
<thead>
<tr>
<th>Indication</th>
<th>First Choice</th>
<th>Alternative</th>
<th>Comments/Special Issues</th>
<th>Last Reviewed</th>
</tr>
</thead>
</table>
| **Herpes Simplex Virus (HSV) Infections** |                                |                                                  | **Secondary Prophylaxis Indicated:**  
  • Suppressive secondary prophylaxis can be considered for children with severe and recurrent mucocutaneous (oral or genital) disease  
  **Criteria for Discontinuing Secondary Prophylaxis:**  
  • After a prolonged period (e.g., 1 year) of prophylaxis, consider suspending prophylaxis and determine with the patient whether additional prophylaxis is necessary. Although level of immune reconstitution is a consideration, no specific CD4 threshold has been established.  | June 27, 2018 |
| Mucocutaneous Disease:            |                                |                                                  | **Secondary Prophylaxis Indicated:**  
  • Suppressive secondary prophylaxis can be considered for children with severe and recurrent mucocutaneous (oral or genital) disease  
  **Criteria for Discontinuing Secondary Prophylaxis:**  
  • After a prolonged period (e.g., 1 year) of prophylaxis, consider suspending prophylaxis and determine with the patient whether additional prophylaxis is necessary. Although level of immune reconstitution is a consideration, no specific CD4 threshold has been established.  |                                |
| Mucocutaneous Disease, For Adolescents Old Enough to Receive Adult Dosing: |                                |                                                  | **Secondary Prophylaxis Indicated:**  
  • Suppressive secondary prophylaxis can be considered for children with severe and recurrent mucocutaneous (oral or genital) disease  
  **Criteria for Discontinuing Secondary Prophylaxis:**  
  • After a prolonged period (e.g., 1 year) of prophylaxis, consider suspending prophylaxis and determine with the patient whether additional prophylaxis is necessary. Although level of immune reconstitution is a consideration, no specific CD4 threshold has been established.  |                                |
| Acyclovir 20 mg/kg body weight/dose (maximum 800 mg/dose) by mouth BID |                                |                                                  | **Secondary Prophylaxis Indicated:**  
  • Suppressive secondary prophylaxis can be considered for children with severe and recurrent mucocutaneous (oral or genital) disease  
  **Criteria for Discontinuing Secondary Prophylaxis:**  
  • After a prolonged period (e.g., 1 year) of prophylaxis, consider suspending prophylaxis and determine with the patient whether additional prophylaxis is necessary. Although level of immune reconstitution is a consideration, no specific CD4 threshold has been established.  |                                |
| Acyclovir 300 mg/m² body surface area/dose by mouth TID for 6 months |                                |                                                  | **Secondary Prophylaxis Indicated:**  
  • Suppressive secondary prophylaxis can be considered for children with severe and recurrent mucocutaneous (oral or genital) disease  
  **Criteria for Discontinuing Secondary Prophylaxis:**  
  • After a prolonged period (e.g., 1 year) of prophylaxis, consider suspending prophylaxis and determine with the patient whether additional prophylaxis is necessary. Although level of immune reconstitution is a consideration, no specific CD4 threshold has been established.  |                                |
| Valacyclovir 500 mg by mouth BID |                                |                                                  | **Secondary Prophylaxis Indicated:**  
  • Suppressive secondary prophylaxis can be considered for children with severe and recurrent mucocutaneous (oral or genital) disease  
  **Criteria for Discontinuing Secondary Prophylaxis:**  
  • After a prolonged period (e.g., 1 year) of prophylaxis, consider suspending prophylaxis and determine with the patient whether additional prophylaxis is necessary. Although level of immune reconstitution is a consideration, no specific CD4 threshold has been established.  |                                |
| Famciclovir 500 mg by mouth BID |                                |                                                  | **Secondary Prophylaxis Indicated:**  
  • Suppressive secondary prophylaxis can be considered for children with severe and recurrent mucocutaneous (oral or genital) disease  
  **Criteria for Discontinuing Secondary Prophylaxis:**  
  • After a prolonged period (e.g., 1 year) of prophylaxis, consider suspending prophylaxis and determine with the patient whether additional prophylaxis is necessary. Although level of immune reconstitution is a consideration, no specific CD4 threshold has been established.  |                                |
| **Histoplasmosis (Suppressive Therapy)** | Itraconazole oral solution 5–10 mg/kg body weight (maximum 200 mg) per dose by mouth daily | Fluconazole 3–6 mg/kg body weight (maximum 200 mg) by mouth once daily | Use same initial itraconazole dosing for capsules as for solution. Itraconazole solution is preferred to the capsule formulation because it is better absorbed; solution can achieve serum concentrations 30% higher than those achieved with the capsules.  | November 6, 2013 |
| **Influenza**                      | N/A                           | N/A                                             | **Secondary Prophylaxis Indicated:**  
  • Suppressive secondary prophylaxis can be considered for children with severe and recurrent mucocutaneous (oral or genital) disease  
  **Criteria for Discontinuing Secondary Prophylaxis:**  
  • After a prolonged period (e.g., 1 year) of prophylaxis, consider suspending prophylaxis and determine with the patient whether additional prophylaxis is necessary. Although level of immune reconstitution is a consideration, no specific CD4 threshold has been established.  | July 17, 2018 |
| **Human Papillomavirus (HPV)**    | N/A                           | N/A                                             |                                                  | November 6, 2013 |
| **Influenza**                      | N/A                           | N/A                                             | No role for secondary chemoprophylaxis |
Table 2: Secondary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 4 of 6)

<table>
<thead>
<tr>
<th>Indication</th>
<th>First Choice</th>
<th>Alternative</th>
<th>Comments/Special Issues</th>
<th>Last Reviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Isosporiasis (Cystoisosporiasis)</strong></td>
<td>If Severe Immunosuppression: • TMP-SMX 2.5 mg/kg body weight of the TMP component (maximum 80 mg TMP) twice daily by mouth 3 times per week</td>
<td>Pyrimethamine 1 mg/kg body weight (maximum 25 mg) plus folinic acid, 5–15 mg by mouth once daily. <strong>Second-Line Alternative:</strong> • Ciprofloxacin, 10–20 mg/kg body weight (maximum 500 mg) by mouth 3 times per week</td>
<td>Consider discontinuing secondary prophylaxis in patients without evidence of active <em>Isospora</em> infection who have sustained improvement in immunologic status (from CDC immunologic category 3 to CD4 values that fall within category 1 or 2) for &gt;6 months in response to ART. In adults, the dose of pyrimethamine for secondary prophylaxis (25 mg daily) is lower than the dose for treatment (50–75 mg daily), but no data exist for dosing in children. Thus, the recommended dose for secondary prophylaxis in children is pyrimethamine 1 mg/kg (maximum 25 mg) by mouth once daily. Ciprofloxacin is not a drug of choice in children because of increased incidence of adverse events, including events related to joints and/or surrounding tissues.</td>
<td>February 8, 2019</td>
</tr>
<tr>
<td><strong>Malaria</strong></td>
<td>For <em>P. vivax</em> or <em>P. ovale</em>: • Primaquine 0.5 mg/kg base (0.8 mg/kg salt) up to adult dose orally, daily for 14 days after departure from the malarious area</td>
<td>N/A</td>
<td>This regimen, known as PART, is recommended only for individuals who have resided in a malaria-endemic area for an extended period of time. Adult dose: 30 mg base (52.6 mg salt) orally, daily for 14 days after departure from the malarious area. <a href="http://wwwnc.cdc.gov/travel/yellowbook/2012/chapter-3-infectious-diseases-related-to-travel/malaria.htm#1939">http://wwwnc.cdc.gov/travel/yellowbook/2012/chapter-3-infectious-diseases-related-to-travel/malaria.htm#1939</a></td>
<td>November 6, 2013</td>
</tr>
<tr>
<td><strong>Microsporidiosis</strong></td>
<td>Disseminated, Non-Ocular Infection or GI Infection Caused by Microsporidia Other Than <em>E. Bieneusi</em> or <em>V. Corneae</em>: • Albendazole 7.5 mg/kg body weight (maximum 400 mg/dose) by mouth twice daily</td>
<td>N/A</td>
<td>Criteria For Discontinuing Secondary Prophylaxis: • After initiation of ART, resolution of signs and symptoms and sustained immune reconstitution (more than 6 months at CDC immunologic category 1 or 2)</td>
<td>December 15, 2016</td>
</tr>
</tbody>
</table>
Table 2: Secondary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 5 of 6)

<table>
<thead>
<tr>
<th>Indication</th>
<th>First Choice</th>
<th>Alternative</th>
<th>Comments/Special Issues</th>
<th>Last Reviewed</th>
</tr>
</thead>
</table>
| **Mycobacterium avium Complex (MAC) (Chronic Suppressive Therapy)** | • Clarithromycin 7.5 mg/kg body weight (maximum 500 mg) orally twice daily, **plus**
  • Ethambutol 15–25 mg/kg body weight (maximum 2.5 g) orally once daily, with or without food
  • Children aged >5 years who received rifabutin as part of initial treatment: Rifabutin 5 mg/kg body weight (maximum 300 mg) orally once daily with food | • Azithromycin 5 mg/kg body weight (maximum 250 mg) orally once daily, **plus**
  • Ethambutol 15–25 mg/kg body weight (maximum 2.5 g) orally once daily, with or without food
  • Children aged >5 years who received rifabutin as part of initial treatment: Rifabutin 5 mg/kg body weight (maximum 300 mg) orally once daily with food | Secondary Prophylaxis Indicated:
  • Prior disease
  Criteria for Discontinuing Secondary Prophylaxis:
  Fulfillment of All of the Following Criteria:
  • Completed ≥6 months of ART
  • Completed ≥12 months MAC therapy
  • Asymptomatic for signs and symptoms of MAC
  • Aged 2 to <6 years: CD4 count >200 cells/mm³ for ≥6 consecutive months
  • Aged ≥6 years: CD4 count >100 cells/mm³ for ≥6 consecutive months
  Criteria for Restarting Secondary Prophylaxis:
  • Aged 2 to <6 years: CD4 count <200 cells/mm³
  • Aged ≥6 years: CD4 count <100 cells/mm³ | January 8, 2019 |

| **Mycobacterium Tuberculosis** | N/A                                               | N/A                                             | N/A                                                                                                      | November 6, 2013 |
| **Pneumocystis Pneumonia**    | • TMP-SMX (Cotrimoxazole): TMP 2.5–5 mg/kg body weight/ dose with SMX 12.5–25 mg/kg body weight/dose twice per day. Dosing based on TMP component.
  • The total daily dose should not exceed 320 mg TMP and 1600 mg SMX. Several dosing schemes have been used successfully—
    • Given 3 days per week on consecutive days or on alternate days
    • Given 2 days per week on consecutive days or on alternate days
    • Given every day (total daily dose of TMP 5–10 mg/kg body weight given as a single dose each day) | Dapsone
  **Children Aged ≥1 months:**
  • 2 mg/kg body weight (maximum 100 mg) by mouth once daily or 4 mg/kg body weight (maximum 200 mg) by mouth once weekly
  Atovaquone
  **Children Aged 1–3 Months and >24 Months–12 Years:**
  • 30-40 mg/kg body weight/dose by mouth once daily with food
  **Children Aged 4–24 Months:**
  • 45 mg/kg body weight/dose by mouth once daily with food
  **Children Aged ≥13 Years:**
  • 1500 mg (10 cc oral yellow suspension) per dose by mouth once daily
  Aerosolized Pentamidine
  **Children Aged ≥5 Years:**
  • 300 mg every month via Respirgard II™ nebulizer (manufactured by Marquest; Englewood, Colorado) | Secondary Prophylaxis Indicated For:
  • Children with prior episode of PCP
  Criteria for Discontinuing Secondary Prophylaxis:
  • Same as for primary prophylaxis
  Criteria for Restarting Secondary Prophylaxis:
  • Same as for primary prophylaxis | November 6, 2013 |
Table 2: Secondary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 6 of 6)

<table>
<thead>
<tr>
<th>Indication</th>
<th>First Choice</th>
<th>Alternative</th>
<th>Comments/Special Issues</th>
<th>Last Reviewed</th>
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</thead>
<tbody>
<tr>
<td>Syphilis</td>
<td>N/A</td>
<td>N/A</td>
<td>Secondary Prophylaxis Indicated: N/A</td>
<td>November 6, 2013</td>
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<td>Criteria For Discontinuing Secondary Prophylaxis: N/A</td>
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<td></td>
<td>Criteria For Restarting Secondary Prophylaxis: N/A</td>
<td></td>
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<tr>
<td>Toxoplasmosis (Suppressive Therapy)</td>
<td>Sulfadiazine 42.5–60 mg/kg body weight per dose twice daily* (maximum 2–4 g per day) by mouth, <strong>plus</strong></td>
<td>Clindamycin 7–10 mg/kg body weight per dose by mouth 3 times daily, plus</td>
<td>November 6, 2013</td>
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<td>Pyrimethamine 1 mg/kg body weight or 15 mg/m² body surface area (maximum 25 mg) by mouth once daily, <strong>plus</strong></td>
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<td></td>
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<td>Leucovorin 5 mg by mouth once every 3 days</td>
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<td>Secondary Prophylaxis Indicated: Prior toxoplasmic encephalitis</td>
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<td>Criteria For Discontinuing Secondary Prophylaxis:</td>
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<td>If All of the Following Criteria are Fulfilled:</td>
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<td>Completed ≥6 months of cART, completed initial therapy for TE, asymptomatic for TE, and</td>
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<td></td>
<td>Aged 1 to &lt; 6 years; CD4 percentage ≥15% for &gt;6 consecutive months</td>
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<td>Children Aged 1–3 Months and &gt;24 Months:</td>
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<td></td>
<td>Aged ≥6 years; CD4 cell count &gt;200 cells/mm³ for &gt;6 consecutive months</td>
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<tr>
<td></td>
<td>Atovaquone 30 mg/kg body weight by mouth once daily</td>
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<td>Criteria For Restarting Secondary Prophylaxis:</td>
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</tr>
<tr>
<td>Children Aged 4–24 Months:</td>
<td>Atovaquone 45 mg/kg body weight by mouth once daily, with or without pyrimethamine 1 mg/kg body weight or 15 mg/m² body surface area (maximum 25 mg) by mouth once daily, <strong>plus</strong></td>
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<td></td>
<td>Leucovorin, 5 mg by mouth every 3 days</td>
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<td></td>
<td>TMP-SMX, 150/750 mg/m² body surface area once daily by mouth</td>
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<tr>
<td>Varicella-Zoster Virus (VZV)</td>
<td>N/A</td>
<td>N/A</td>
<td>There is no indication for secondary prophylaxis</td>
<td>November 6, 2013</td>
</tr>
</tbody>
</table>

Key to Acronyms: BID = twice daily; BSA = body surface area; cART = combination antiretroviral therapy; CNS = central nervous system; CrCl = (estimated) creatinine clearance, CSF = cerebrospinal fluid; GI = gastrointestinal; HBV = hepatitis B virus; HSV = herpes simplex virus; IV = intravenous; SQ = subcutaneous; TE = toxoplasmic encephalitis; TID = three times daily; TMP-SMX = trimethoprim-sulfamethoxazole

Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children

Downloaded from https://aidsinfo.nih.gov/guidelines on 11/8/2019
### Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations  
(Least updated August 29, 2019; last reviewed August 29, 2019)  
(page 1 of 24)

<table>
<thead>
<tr>
<th>Indication</th>
<th>First Choice</th>
<th>Alternative</th>
<th>Comments/Special Issues</th>
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</tr>
</thead>
</table>
| **Bacterial Infections**  
Bacterial pneumonia  
*Streptococcus pneumoniae*; occasionally  
*Staphylococcus aureus*, *Haemophilus influenzae*,  
*Pseudomonas aeruginosa* | • Ceftriaxone 50–100 mg/kg body weight per dose once daily, or 25–50 mg/kg body weight per dose twice daily IV or IM (max 4 g/day), or  
• Cefotaxime 40–50 mg/kg body weight per dose 4 times daily, or 50–65 mg/kg body weight 3 times daily (max 8–10 g/day) IV | • Cefuroxime, 35–50 mg/kg body weight per dose 3 times daily (max 4–6 g/day) IV | For children who are receiving effective cART, have mild or no immunosuppression, and have mild to moderate community-acquired pneumonia, oral therapy option would be amoxicillin 45 mg/kg body weight per dose twice daily (maximum dose: 4 g per day).  
Add azithromycin for hospitalized patients to treat other common community-acquired pneumonia pathogens (*M. pneumoniae*, *C. pneumoniae*).  
Add clindamycin or vancomycin if methicillin-resistant *S. aureus* is suspected (base the choice on local susceptibility patterns).  
For patients with neutropenia, chronic lung disease other than asthma (e.g., LIP, bronchiectasis) or indwelling venous catheter, consider regimen that includes activity against *P. aeruginosa* (such as ceftazidime or cefepime instead of ceftriaxone).  
Consider PCP in patients with severe pneumonia or more advanced HIV disease.  
Evaluate for tuberculosis, cryptococcosis, and endemic fungi as epidemiology suggests. | November 6, 2013 |
| **Candidiasis**  
Oropharyngeal:  
• Fluconazole 6–12 mg/kg body weight (maximum 400 mg/dose) by mouth once daily  
• Clotrimazole troches, 10-mg troche by mouth 4–5 times daily  
• Nystatin suspension 4–6 mL by mouth 4 times daily, or 1–2, 200,000-unit flavored pastilles by mouth 4–5 times daily  
*Treatment Duration:*  
• 7 to 14 days | Oropharyngeal,  
(Fluconazole-Refractory):  
• Itraconazole oral solution 2.5 mg/kg body weight/dose by mouth twice daily (maximum 200–400 mg/day) | *Itraconazole oral solution should not be used interchangeably with itraconazole capsules.* Itraconazole capsules are generally ineffective for treatment of esophageal disease.  
Central venous catheters should be removed, when feasible, in children with HIV with fungemia.  
In uncomplicated catheter-associated *C. albicans* candidemia, an initial course of amphotericin B followed by fluconazole to complete treatment can be used (use invasive disease dosing).  
Voriconazole has been used to treat esophageal candidiasis in a small number of immunocompromised children without HIV. | January 31, 2019 |
| Esophageal Disease:  
• Fluconazole 6–12 mg/kg body weight by mouth once daily (maximum dose: 600 mg)  
• Itraconazole oral solution, 2.5 mg/kg body weight/dose by mouth twice daily | Esophageal Disease:  
• Amphotericin B (deoxycholate) 0.3–0.7 g/kg body weight IV once daily | | |
Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 2 of 24)

<table>
<thead>
<tr>
<th>Indication</th>
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<th>Comments/Special Issues</th>
<th>Last Reviewed</th>
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<tbody>
<tr>
<td>Candidiasis, continued</td>
<td>Treatment Duration:</td>
<td>Echinocandins Anidulafungin:</td>
<td>Voriconazole Dosing in Pediatric Patients:</td>
<td>January 31, 2019</td>
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<tr>
<td></td>
<td>• Minimum of 3 weeks and for at least 2 weeks following the resolution of symptoms</td>
<td>• Aged 2–17 Years: Loading dose of 3 mg/kg body weight/daily and then maintenance at 1.5 mg/kg body weight/dose daily IV</td>
<td>• Voriconazole 9 mg/kg body weight/dose every 12 hours IV loading for day 1, followed by voriconazole 8 mg/kg body weight/dose IV every 12 hours.</td>
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<td>• Aged ≥18 Years: 200-mg loading dose, then 100 mg/dose daily IV</td>
<td>• Conversion to oral voriconazole should be at 9 mg/kg body weight/dose orally every 12 hours.</td>
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<td>Caspofungin:</td>
<td>• Children aged ≥12 years and weighing at least 40 kg can use adult dosing (load voriconazole 6 mg/kg body weight/dose every 12 hours IV on day 1, followed by 4 mg/kg body weight/dose every 12 hours IV. Conversion to oral therapy at 200 mg every 12 hours by mouth).</td>
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<td></td>
<td></td>
<td>• Infants Aged &lt;3 Months: 25 mg/m² BSA/dose daily IV</td>
<td>Anidulafungin in Children Aged 2–17 Years:</td>
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<td>• Aged 3 Months–17 Years: 70 mg/m²/day IV loading dose followed by 50 mg/m²/day IV (maximum 70 mg). Note: Dosing of caspofungin for children should be based on body surface area.</td>
<td>• Loading dose of 3 mg/kg body weight/once daily followed by 1.5 mg/kg body weight/once daily (100 mg/day maximum).</td>
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<td></td>
<td>• Aged ≥18 Years: 70-mg loading dose IV, then 50 mg/dose daily IV</td>
<td>Fluconazole Dosing Considerations:</td>
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<td>Micafungin:</td>
<td>• If a neonate’s creatinine level is &gt;1.2 mg/dL for &gt;3 consecutive doses, the dosing interval for fluconazole 12 mg/kg body weight may be prolonged to one dose every 48 hours until the serum creatinine level is &lt;1.2 mg/dL</td>
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<td>• Note: In the United States, optimal dosing for children is not yet established, and there is no pediatric indication yet. Studies indicate linear PK; age and clearance are inversely related (see recommended doses below).</td>
<td>• Aged ≥18 Years: 400 mg/dose once daily (6 mg/kg body weight once daily).</td>
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<td>• Neonates: Up to 10–12 mg/kg body weight/dose daily IV may be required to achieve therapeutic concentrations.</td>
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<td>• Infants &lt;15 kg body weight, 5–7 mg/kg body weight/dose daily IV</td>
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<td>• Children ≤40 kg body weight and aged 2–8 years, 3–4 mg/kg body weight/dose daily IV</td>
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<td>• Children ≤40 kg body weight and aged 9–17 years, 2–3 mg/kg body weight/dose daily IV</td>
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<td></td>
<td></td>
<td>• Children &gt;40 kg body weight, 100 mg/dose daily IV</td>
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<td>IV Fluconazole:</td>
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<td>• Children: 6–12 mg/kg body weight/dose daily for infants and children of all ages (maximum dose: 600 mg daily).</td>
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</tbody>
</table>
### Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations

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<tr>
<th>Indication</th>
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<th>Comments/Special Issues</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Candidiasis, continued</strong></td>
<td>Invasive Disease</td>
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<tr>
<td></td>
<td>Critically ill</td>
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<tr>
<td><strong>Echinocandin Recommended</strong></td>
<td>Anidulafungin</td>
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<tr>
<td>• Aged 2–17 Years: Load with 3 mg/kg body weight/daily dose and then maintenance dose at 1.5 mg/kg body weight once daily</td>
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<tr>
<td>• Aged ≥18 Years: 200 mg loading dose, then 100 mg once daily</td>
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<tr>
<td><strong>Caspofungin</strong></td>
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<tr>
<td>• Infants Aged &lt;3 Months: 25 mg/m2 BSA/dose once daily IV</td>
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<tr>
<td>• Aged 3 months-17 years: 70 mg/m2 BSA/day loading dose followed by 50 mg/m2 once daily (maximum, 70 mg) Note: Dosing of caspofungin in children should be based on body surface area.</td>
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<tr>
<td>• Aged ≥18 Years: 70-mg loading dose, then 50 mg once daily</td>
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<tr>
<td><strong>Micafungin</strong></td>
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<td>• Note: In the United States, optimal dosing for children is not yet established, and there is no pediatric indication yet. Studies indicate linear PK; age and clearance are inversely related (see recommended doses below).</td>
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<td>• Neonates: Up to 10–12 mg/kg body weight/dose daily IV may be required to achieve therapeutic concentrations.</td>
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<td>• Infants &lt;15 kg body weight: 5–7 mg/kg/day</td>
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<td>• Children ≤40 kg body weight and aged 2–8 years: 3–4 mg/kg body weight/dose daily IV</td>
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<td>• Children ≤40 kg body weight and aged 9–17 years: 2–3 mg/kg body weight/dose daily</td>
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<td>• Children &gt;40 kg body weight: 100 mg/dose daily IV</td>
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<tr>
<td><strong>Treatment Duration:</strong></td>
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<tr>
<td>• Based on presence of deep-tissue foci and clinical response; in patients with candidemia, treat until 2 weeks after last positive blood culture.</td>
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<td>January 31, 2019</td>
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<tr>
<td></td>
<td>Invasive Disease</td>
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<tr>
<td>• Fluconazole 12 mg/kg body weight IV once daily (maximum 600 mg/day) for minimum 2 weeks after last positive blood culture (if uncomplicated candidemia)</td>
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<tr>
<td>• Lipid formulations of amphotericin B, 5 mg/kg body weight IV once daily</td>
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<tr>
<td>• Amphotericin B deoxycholate, 1 mg/kg body weight IV once daily</td>
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</table>
### Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 4 of 24)

<table>
<thead>
<tr>
<th>Indication</th>
<th>First Choice</th>
<th>Alternative</th>
<th>Comments/Special Issues</th>
<th>Last Reviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Candidiasis</strong></td>
<td><strong>Not critically ill</strong></td>
<td><strong>Fluconazole Recommended:</strong></td>
<td><strong>Treatment Duration:</strong></td>
<td><strong>January 31, 2019</strong></td>
</tr>
<tr>
<td></td>
<td>• 12 mg/kg body weight/dose daily IV (maximum dose: 600 mg) for infants and children of all ages</td>
<td>• Avoid fluconazole for <em>C. krusei</em> and <em>C. glabrata</em>, avoid echinocandin for <em>C. parapsilosis</em>.</td>
<td>• Based on presence of deep-tissue foci and clinical response; in patients with candidemia, treat until 2 weeks after last positive blood culture.</td>
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<tr>
<td><strong>Coccidioidomycosis</strong></td>
<td><strong>Severe Illness with Respiratory Compromise due to Diffuse Pulmonary or Disseminated Non-Meningitic Disease:</strong></td>
<td><strong>Severe Illness with Respiratory Compromise Due to Diffuse Pulmonary or Disseminated Non-Meningitic Disease (If Unable to Use Amphotericin):</strong></td>
<td>• Amphotericin B deoxycholate 0.5–1.0 mg/kg body weight IV once daily, until clinical improvement.</td>
<td><strong>November 6, 2013</strong></td>
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<td></td>
<td>• A lipid amphotericin B preparation can be substituted at a dose of 5 mg/kg body weight IV once daily (dosage of the lipid preparation can be increased to as much as 10 mg/kg body weight IV once daily for life-threatening infection).</td>
<td>• Fluconazole 12mg/kg body weight (maximum 800 mg) per dose IV or by mouth once daily</td>
<td>• Treatment is continued for total of 1 year, followed by secondary prophylaxis.</td>
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<td>• After the patient is stabilized, therapy with an azole (fluconazole or itraconazole) can be substituted and continued to complete a 1-year course of antifungal therapy.</td>
<td>• Amphotericin B plus intrathecal amphotericin B followed by secondary prophylaxis. <strong>Note:</strong> Expert consultation recommended.</td>
<td>Surgical debridement of bone, joint, and/or excision of cavitary lung lesions may be helpful.</td>
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<td></td>
<td>• Treatment is continued for total of 1 year, followed by secondary prophylaxis.</td>
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<td>Itraconazole is the preferred azole for treatment of bone infections.</td>
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<td></td>
<td><strong>Meningeal Infection:</strong></td>
<td><strong>Meningeal Infection (Unresponsive to Fluconazole):</strong></td>
<td>Some experts initiate an azole during amphotericin B therapy; others defer initiation of the azole until after amphotericin B is stopped.</td>
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<td></td>
<td>• Fluconazole 12 mg/kg body weight (maximum 800 mg) IV or by mouth once daily followed by secondary lifelong prophylaxis.</td>
<td>• IV amphotericin B plus intrathecal amphotericin B followed by secondary prophylaxis.</td>
<td>For treatment failure, can consider voriconazole, caspofungin, or posaconazole (or combinations). However, experience is limited and definitive pediatric dosages have not been determined.</td>
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<td>Options should be discussed with an expert in the treatment of coccidioidomycosis.</td>
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<td>Chronic suppressive therapy (secondary prophylaxis) with fluconazole or itraconazole is routinely recommended following initial induction therapy for disseminated disease and is continued lifelong for meningal disease.</td>
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<td>Therapy with amphotericin results in a more rapid clinical response in severe, non-meningal disease.</td>
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<td>Indication</td>
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<td>Alternative</td>
<td>Comments/Special Issues</td>
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<tr>
<td><strong>Coccidioidomycosis</strong></td>
<td>Mild-to-Moderate Non-Meningeal Infection (e.g., Focal Pneumonia):</td>
<td>Mild-to-Moderate Non-Meningeal Infection (e.g., Focal Pneumonia):</td>
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<td></td>
<td>• Fluconazole 6–12 mg/kg body weight (maximum 400 mg) per dose IV or by mouth once daily.</td>
<td>• Itraconazole 2–5 mg/kg body weight per dose (maximum dose 200 mg) per dose IV or by mouth 3 times daily for 3 days, then 2–5 mg/kg body weight (maximum dose 200 mg) by mouth per dose twice daily thereafter.</td>
<td>Duration of treatment determined by rate of clinical response.</td>
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<td><strong>Cryptococcosis</strong></td>
<td>CNS Disease Acute Therapy (Minimum 2-Week Induction Followed by Consolidation Therapy):</td>
<td>CNS Disease Acute Therapy (Minimum 2-Week Induction Followed by Consolidation Therapy):</td>
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<td>• Amphotericin B deoxycholate 1.0 mg/kg body weight (or liposomal amphotericin B 6 mg/kg body weight) IV once daily PLUS flucytosine 25 mg/kg body weight per dose by mouth given 4 times daily</td>
<td>If Flucytosine Not Tolerated or Unavailable:</td>
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<td>Consolidation Therapy (Followed by Secondary Prophylaxis):</td>
<td>• A. Liposomal amphotericin B, 6 mg/kg body weight IV once daily, or Amphotericin B Lipid Complex, 5 mg/kg body weight IV once daily, or Amphotericin B deoxycholate, 1.0–1.5 mg/kg body weight IV once daily alone or B. in combination with high-dose fluconazole (12 mg/kg body weight on day 1 and then 10–12 mg/kg body weight [max 800 mg] IV). Note: Data-driven pediatric dosing guidelines are unavailable for fluconazole with use of such combination therapy.</td>
<td>If Amphotericin B-Based Therapy Not Tolerated:</td>
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<td>• Fluconazole 12 mg/kg body weight on day 1, then 10–12 mg/kg body weight (max 800 mg) once daily IV or by mouth for a minimum of 8 weeks</td>
<td></td>
<td>• Fluconazole, 12 mg/kg body weight on day 1 and then 10–12 mg/kg body weight (maximum 800 mg) IV or by mouth once daily PLUS flucytosine, 25 mg/kg body weight per dose by mouth given 4 times daily</td>
<td>If Amphotericin B-Based Therapy Not Tolerated:</td>
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<td>In patients with meningitis, CSF culture should be negative prior to initiating consolidation therapy.</td>
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<td>Overall, <em>in vitro</em> resistance to antifungal agents used to treat cryptococcosis remains uncommon. Newer azoles (voriconazole, posaconazole, ravuconazole) are all very active in vitro against <em>C. neoformans</em>, but published clinical experience on their use for cryptococcosis is limited.</td>
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<td>Liposomal amphotericin and amphotericin B lipid complex are especially useful for children with renal insufficiency or infusion-related toxicity to amphotericin B deoxycholate.</td>
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<td>Liposomal amphotericin and amphotericin B lipid complex are <strong>significantly more expensive than amphotericin B deoxycholate</strong>.</td>
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<td>Liquid preparation of itraconazole (if tolerated) is preferable to tablet formulation because of better bioavailability, but it is more expensive. Bioavailability of the solution is better than the capsule, but there were no upfront differences in dosing range based on preparation used. Ultimate dosing adjustments should be guided by itraconazole levels.</td>
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<td>Serum itraconazole concentrations should be monitored to optimize drug dosing.</td>
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<td>Amphotericin B may increase toxicity of flucytosine by increasing cellular uptake, or impair its renal excretion, or both.</td>
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Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—
Summary of Recommendations  (page 6 of 24)

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<tbody>
<tr>
<td><strong>Cryptococcus, continued</strong></td>
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<td><strong>Consolidation Therapy (followed by secondary prophylaxis):</strong>&lt;br&gt;• Itraconazole 5–10 mg/kg body weight by mouth given once daily, or 2.5–5 mg/kg body weight given twice daily (maximum 200 mg/dose) for a minimum of 8 weeks. A loading dose (2.5–5 mg/kg body weight per dose 3 times daily) is given for the first 3 days (maximum 200 mg/dose; 600 mg/day). See comment on itraconazole under Other Options/Issues.</td>
<td>Flucytosine dose should be adjusted to keep 2-hour post-dose drug levels at 40–60 μg/mL. Oral acetazolamide should not be used for reduction of ICP in cryptococcal meningitis. Corticosteroids and mannitol have been shown to be ineffective in managing ICP in adults with cryptococcal meningitis. Secondary prophylaxis is recommended following completion of initial therapy (induction plus consolidation)—drugs and dosing listed above.</td>
<td>November 6, 2013</td>
</tr>
<tr>
<td><strong>Localized Disease, Including Isolated Pulmonary Disease (CNS Not Involved)b:</strong>&lt;br&gt;• Fluconazole 12 mg/kg body weight on day 1 and then 6–12 mg/kg body weight (maximum 600 mg) IV or by mouth once daily</td>
<td><strong>Localized Disease, Including Isolated Pulmonary Disease (CNS Not Involved)b:</strong>&lt;br&gt;• Amphotericin B, 0.7–1.0 mg/kg body weight, or&lt;br&gt;• Amphotericin liposomal 3–5 mg/kg body weight, or&lt;br&gt;• Amphotericin lipid complex, 5 mg/kg body weight IV once daily</td>
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<tr>
<td><strong>Disseminated Disease (CNS not involved) or Severe, Pulmonary Diseaseb:</strong>&lt;br&gt;• Amphotericin B 0.7–1.0 mg/kg body weight, or&lt;br&gt;• Liposomal amphotericin, 3–5 mg/kg body weight, or&lt;br&gt;• Amphotericin B lipid complex 5 mg/kg body weight IV once daily (± flucytosine)</td>
<td><strong>Disseminated disease (CNS not involved) or severe, pulmonary diseaseb:</strong>&lt;br&gt;• Fluconazole, 12 mg/kg body weight on day 1 and then 6–12 mg/kg body weight (maximum 600 mg) IV or by mouth once daily</td>
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<tr>
<td><strong>Cryptosporidiosis</strong></td>
<td><strong>Effective ART:</strong>&lt;br&gt;• Immune reconstitution might lead to parasitologic and clinical response</td>
<td>There is no consistently effective therapy for cryptosporidiosis in patients with HIV infection; optimized ART and a trial of nitazoxanide should be considered. &lt;br&gt;&lt;br&gt;<strong>Nitazoxanide</strong>&lt;br&gt;• 1–3 years of age: Nitazoxanide (20 mg/mL oral solution) 100 mg orally twice daily with food&lt;br&gt;• 4–11 years of age: Nitazoxanide (20 mg/mL oral solution) 200 mg orally twice daily with food</td>
<td><strong>Supportive Care:</strong>&lt;br&gt;• Hydration, correct electrolyte abnormalities, nutritional support&lt;br&gt;Antimotility agents (such as loperamide) should be used with caution in young children.</td>
<td>August 29, 2019</td>
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<td>Indication</td>
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<td>Cryptosporidiosis, continued</td>
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<td>• ≥12 years of age: Nitazoxanide tablet 500 mg orally twice daily with food.</td>
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<td>Treatment Duration: • 3–14 days</td>
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<td>Cytomegalovirus (CMV)</td>
<td>Symptomatic Congenital Infection with Neurologic Involvement: • Ganciclovir 6 mg/kg body weight per dose IV every 12 hours for 6 weeks</td>
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<td>November 6, 2013</td>
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<td>Disseminated Disease and Retinitis: Induction Therapy (Followed by Chronic Suppressive Therapy): • Ganciclovir 5 mg/kg body weight per dose IV every 12 hours for 14–21 days (may be increased to 7.5 mg/kg body weight per dose IV twice daily), then 5 mg/kg body weight once daily for 5–7 days per week for chronic suppression</td>
<td>Disseminated Disease and Retinitis: Induction Therapy (Followed by Chronic Suppressive Therapy): • Foscarnet, 60 mg/kg body weight per dose IV every 8 hours or 90 mg/kg body weight per dose IV every 12 hours x 14 to 21 days, then 90–120 mg/kg body weight IV once daily for chronic suppression</td>
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<td>Central Nervous System Disease (Followed by Chronic Suppressive Therapy; See Secondary Prophylaxis): • Ganciclovir 5 mg/kg body weight per dose IV every 12 hours PLUS foscarnet 60 mg/kg body weight per dose IV every 8 hours (or 90 mg/kg body weight per dose IV every 12 hours) continued until symptomatic improvement, followed by chronic suppression</td>
<td>Alternatives for Retinitis (Followed by Chronic Suppressive Therapy; See Secondary Prophylaxis): • Valganciclovir tablets 900 mg per dose orally twice daily for 14–21 days, followed by chronic suppressive therapy (see above). Note: This is an option in older children who can receive the adult dose (based on their BSA). • IV ganciclovir plus IV foscarnet (at above induction doses) may be considered as initial induction therapy in children with sight-threatening disease or for treatment following failure/relapse on monotherapy.</td>
<td>• Data on valganciclovir dosing in young children for treatment of retinitis are unavailable, but consideration can be given to transitioning from IV ganciclovir to oral valganciclovir after improvement of retinitis is noted. • Intravitreal injections of ganciclovir, foscarnet, or cidofovir are used in adults for retinitis but are not practical for most children. • Combination ganciclovir and foscarnet is associated with substantial rates of adverse effects, and optimal treatment for neurologic disease in children is unknown, particularly if receiving optimized cART.</td>
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<td>Cytomegalo-&lt;br&gt;lovirus (CMV), continued</td>
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<td>• Cidofovir is also used to treat CMV retinitis in adults intolerant to other therapies. Induction dosing in adults is 5 mg/kg body weight IV once weekly for 2 weeks, followed by chronic suppressive therapy (see secondary prophylaxis); however, data on dosing in children are unavailable. Must be given with probenecid and IV hydration.</td>
<td>• Chronic suppressive therapy (secondary prophylaxis) is recommended in adults and children following initial therapy of disseminated disease, retinitis, neurologic disease, or GI disease with relapse.</td>
<td>November 6, 2013</td>
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<td>Giardiasis</td>
<td>• Tinidazole, 50 mg/kg by mouth, administered as 1 dose given with food (maximum 2 g).&lt;br&gt;Note: Based on data from children who are HIV-negative&lt;br&gt;• Nitazoxanide:&lt;br&gt;  • 1–3 years: 100 mg by mouth every 12 hours with food for 3 days&lt;br&gt;  • 4–11 years: 200 mg by mouth every 12 hours with food for 3 days&lt;br&gt;  • ≥12 years: 500 mg by mouth every 12 hours with food for 3 days&lt;br&gt;Note: Based on data from children who are HIV-negative</td>
<td>Metronidazole 5 mg/kg by mouth every 8 hours for 5-7 days.&lt;br&gt;Note: Based on data from children who are HIV-negative</td>
<td>Tinidazole is FDA-approved in the United States for children aged ≥3 years. It is available in tablets that can be crushed. Metronidazole has a high frequency of gastrointestinal side effects. A pediatric suspension of metronidazole is not commercially available but can be compounded from tablets. Metronidazole is not FDA-approved for the treatment of giardiasis.&lt;br&gt;Supportive Care:&lt;br&gt;• Hydration&lt;br&gt;• Correction of electrolyte abnormalities&lt;br&gt;• Nutritional support&lt;br&gt;Antimotility agents (e.g., loperamide) should be used with caution in young children.</td>
<td>August 22, 2019</td>
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<td>Hepatitis B Virus (HBV)</td>
<td>Treatment of Only HBV Required (Child Does Not Require cART):&lt;br&gt;• IFN-α 3 million units/m² body surface area SQ 3 times a week for 1 week, followed by dose escalation to 6 million units/m² body surface area (max 10 million units/dose), to complete a 24-week course, or&lt;br&gt;• For children aged ≥12 years, adeovir 10 mg by mouth once daily for a minimum of 12 months (uncertain if risk of HIV resistance)</td>
<td>IFN-α 10 million units/m² body surface area SQ 3 times a week for 6 months (sometimes used for retreatment of failed lower-dose interferon therapy)&lt;br&gt;Alternative for 3TC: FTC 6 mg/kg body weight (maximum 200 mg) once daily</td>
<td>Indications for Treatment Include:&lt;br&gt;• Detectable serum HBV DNA, irrespective of HBeAg status, for &gt;6 months; and&lt;br&gt;• Persistent (&gt;6 months) elevation of serum transaminases (≥ twice the upper limit of normal); or&lt;br&gt;• Evidence of chronic hepatitis on liver biopsy&lt;br&gt;IFN-α is contraindicated in children with decompensated liver disease; significant cytopenias, severe renal, neuropsychiatric, or cardiac disorders; and autoimmune disease.&lt;br&gt;Choice of HBV treatment options for HIV/HBV-co-infected children depends upon whether concurrent HIV treatment is warranted.</td>
<td>November 6, 2013</td>
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Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations  (page 9 of 24)

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<tr>
<td><strong>Hepatitis B Virus (HBV)</strong></td>
<td>• For children aged ≥2 years, include TDF as part of cART regimen with 3TC or FTC. For children aged ≥12, TDF dose is 300 mg once daily. For children aged &lt;12 year, and 8 mg/kg body weight per dose once daily (maximum dose 300 mg)</td>
<td>None</td>
<td>3TC and FTC have similar activity (and have cross-resistance) and should not be given together. FTC is not FDA-approved for treatment of HBV. TDF is approved for use in treatment of HIV infection in children aged ≥2 years but it is not approved for treatment of HBV infection in children aged &lt;12 years. It should only be used for HBV in HIV/HBV-infected children as part of a cART regimen. Adefovir is approved for use in children aged ≥12 years. ETV is not approved for use in children younger than age 16 years, but is under study in HIV-uninfected children for treatment of chronic hepatitis B. Can be considered for older HIV-infected children who can receive adult dosage. It should only be used for HBV in HIV/HBV-infected children who also receive an HIV-suppressive cART regimen. IRIS may be manifested by dramatic increase in transaminases as CD4 cell counts rise within the first 6 to 12 weeks of cART. It may be difficult to distinguish between drug-induced hepatotoxicity and other causes of hepatitis and IRIS. In children receiving TDF and 3TC or FTC, clinical and laboratory exacerbations of hepatitis (flare) may occur if the drug is discontinued; thus, once anti-HIV/ HBV therapy has begun, it should be continued unless contraindicated or until the child has been treated for &gt;6 months after HBeAg seroconversion and can be closely monitored on discontinuation. If anti-HBV therapy is discontinued and a flare occurs, reinstitution of therapy is recommended because a flare can be life threatening. Telbivudine has been approved for use in people aged ≥16 years with HBV; there are no data on safety or efficacy in children aged &lt;16 years; a pharmacokinetic study is under way in HIV-uninfected children.</td>
<td>November 6, 2013</td>
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<td><strong>Hepatitis C Virus (HCV)</strong></td>
<td>IFN-α Plus Ribavirin Combination Therapy: • Pegylated IFN-α: Peg-IFN 2a 180 µg/1.73 m² body surface area subcutaneously once per week (maximum dose 180 µg) OR Peg-IFN 2b 60 µg/m² body surface area once per week PLUS • Ribavirin (oral) 7.5 mg/kg body weight twice daily (fixed dose by weight recommended): • 25–36 kg: 200 mg a.m. and p.m.</td>
<td>None</td>
<td>Optimal duration of treatment for HIV/HCV-coinfected children is unknown and based on recommendations for HIV/HCV-coinfected adults. Treatment of HCV in children &lt;3 years generally is not recommended. Indications for treatment are based on recommendations in HIV/HCV-coinfected adults; because HCV therapy is more likely to be effective in younger patients and in those without advanced disease or immunodeficiency, treatment should be considered for all HIV/HCV-coinfected children aged &gt;3 years in whom there are no contraindications to treatment.</td>
<td>November 6, 2013</td>
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Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 10 of 24)

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<tr>
<td><strong>Hepatitis C Virus (HCV), continued</strong></td>
<td>• &gt;36 to 49 kg: 200 mg a.m. and 400 mg p.m.</td>
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<td>For recommendations related to use of telaprevir or boceprevir in adults, including warnings about drug interactions between HCV protease inhibitors and HIV protease inhibitors and other antiretroviral drugs, see Adult OI guidelines. IRIS may be manifested by dramatic increase in transaminases as CD4 cell counts rise within the first 6–12 weeks of cART. It may be difficult to distinguish between IRIS and drug-induced hepatotoxicity or other causes of hepatitis. IFN-α is contraindicated in children with decompensated liver disease, significant cytopenias, renal failure, severe cardiac disorders and non-HCV-related autoimmune disease. Ribavirin is contraindicated in children with unstable cardiopulmonary disease, severe pre-existing anemia or hemoglobinopathy. Didanosine combined with ribavirin may lead to increased mitochondrial toxicities; concomitant use is contraindicated. Ribavirin and zidovudine both are associated with anemia, and when possible, should not be administered together.</td>
<td>November 6, 2013</td>
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| **Herpes Simplex Virus Infections (HSV)**     | **Neonatal CNS or Disseminated Disease:**  |             | **For Neonatal CNS Disease:**  
• Repeat CSF HSV DNA PCR should be performed on days 19 to 21 of therapy. If the repeat CSF HSV DNA PCR is positive, continue IV acyclovir for an additional week, repeating the CSF HSV DNA PCR again near the end of extended treatment. Acyclovir should not be stopped until a repeat CSF HSV DNA PCR is negative. | June 27, 2018 |
|                                                | • Acyclovir 20 mg/kg body weight IV/ dose every 8 hours for ≥21 days |             |                                                                                      |              |
|                                                | **Neonatal Skin, Eye, or Mouth Disease:** |             |                                                                                      |              |
|                                                | • Acyclovir 20 mg/kg body weight IV/ dose every 8 hours for 14 days |             |                                                                                      |              |
| **CNS or Disseminated Disease in Children Outside the Neonatal Period:** | • Acyclovir 10 mg/kg body weight (up to 15 mg/kg body weight/dose in children <12 years) IV every 8 hours for 21 days |             |                                                                                      |              |
Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations  (page 11 of 24)

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<tr>
<td>Herpes Simplex Virus Infections (HSV), continued</td>
<td>Moderate to Severe Symptomatic Gingivostomatitis: • Acyclovir 5–10 mg/kg body weight/dose IV every 8 hours. Patients can be switched to oral therapy after lesions have begun to regress and therapy continued until lesions have completely healed.</td>
<td>• Valacyclovir is approved for immunocompetent adults and adolescents with first-episode mucocutaneous HSV at a dose of 1 g/dose by mouth BID for 7–10 days; also approved for recurrent herpes labialis in children ≥12 years using two, 2 g doses by mouth separated by 12 hours as single-day therapy. • Recurrent genital HSV can be treated with valacyclovir 500 mg BID for 3 days or 1 g by mouth daily for 5 days. • Immunocompetent adults with recurrent herpes labialis can be treated with famciclovir, 1 g/dose by mouth BID for 1 day. • Famciclovir is approved to treat primary genital HSV in immunocompetent adults at a dose of 250 mg/dose by mouth TID for 7–10 days. • Recurrent genital HSV is treated with famciclovir 1 g/dose by mouth BID at a 12-hour interval for 2 doses • Famciclovir is approved for use in HIV-infected adults and adolescents with recurrent mucocutaneous HSV infection at a dose of 500 mg/dose by mouth BID for 7 days.</td>
<td>• There is no pediatric preparation of valacyclovir (although crushed capsules can be used to make a suspension according to specific instructions provided in the U.S. FDA package insert) and data on dosing in children are limited. Valacyclovir can be used by adolescents able to receive adult dosing. • Famciclovir is available in a sprinkle formulation with weight-adjusted dosing. Famciclovir can be used by adolescents able to receive adult dosing.</td>
<td>June 27, 2018</td>
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<td>Mild Symptomatic Gingivostomatitis: • Acyclovir 20 mg/kg body weight (maximum 400 mg/dose) dose by mouth QID for 5 days</td>
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<td>Recurrent Herpes Labialis: • Acyclovir 20 mg/kg body weight (maximum 400 mg/dose) dose by mouth QID for 5 days</td>
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<td>For First-Episode Genital Herpes (Adults and Adolescents): • Acyclovir 20 mg/kg body weight (maximum 400 mg/dose) dose by mouth TID for 7–10 days</td>
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<tr>
<td>Recurrent Genital Herpes (Adults and Adolescents): • Acyclovir 20 mg/kg body weight (maximum 400 mg/dose) dose by mouth TID for 5 days</td>
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<td>Children with HSV Keratoconjunctivitis: • Often treated with topical trifluridine (1%) or graniclovir (0.15%) applied as 1–2 drops 5 times daily. Many experts add oral acyclovir to the topical therapy.</td>
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<td>Children with ARN: • For children old enough to receive adult dose, acyclovir 10–15 mg/kg body weight/dose IV every 8 hours for 10–14 days, followed by oral valacyclovir 1 g/dose TID for 4–6 weeks • As an alternative, oral acyclovir 20 mg/kg body weight/dose QID for 4–6 weeks after IV acyclovir for 10–14 days</td>
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<td>Acyclovir-Resistant HSV Infection: • Foscarnet 40 mg/kg body weight/dose given IV every 8 hours or 60 mg/kg body weight/dose IV every 12 hours should be administered slowly over the course of 2 hours (i.e., no faster than 1 mg/kg/minute).</td>
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Note: Consultation with an ophthalmologist experienced in managing herpes simplex infection involving the eye and its complications in children is strongly recommended when ocular disease is present.
Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 12 of 24)

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<th>Indication</th>
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<td><strong>Histoplasmosis</strong></td>
<td><strong>Acute Primary Pulmonary Histoplasmosis:</strong></td>
<td><strong>Acute Primary Pulmonary Histoplasmosis:</strong></td>
<td>Use same initial itraconazole dosing for capsules as for solution. Itraconazole solution is preferred to the capsule formulation because it is better absorbed; solution can achieve serum concentrations 30% higher than those achieved with the capsules.</td>
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<td>• Itraconazole oral solution loading dose of 2–5 mg/kg body weight (maximum 200 mg) per dose by mouth 3 times daily for first 3 days of therapy, followed by 2–5 mg/kg body weight (max 200 mg) per dose by mouth twice daily for 12 months. Duration of 12 weeks is sufficient for HIV-infected children, with functional cellular immunity (CD4 percentage &gt;20% or if aged ≥6, CD4 cell count &gt;300 cells/mm³), provided monitoring confirms clinical improvement and decreased urine antigen concentrations.</td>
<td>• Fluconazole 3–6 mg/kg body weight (maximum 200 mg) by mouth once daily</td>
<td>Urine antigen concentration should be assessed at diagnosis. If &gt;39 ng/mL, serum concentrations should be followed. When serum levels become undetectable, urine concentrations should be monitored monthly during treatment and followed thereafter to identify relapse. Serum concentrations of itraconazole should be monitored and achieve a level of 1 µg/mL at steady-state. Levels exceeding 10 µg/mL should be followed by dose reduction.</td>
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<td>Mild Disseminated Disease:</td>
<td>Mild Disseminated Disease:</td>
<td>High relapse rate with CNS infection occurs in adults and longer therapy may be required; treatment in children is anecdotal and expert consultation should be considered. Chronic suppressive therapy (secondary prophylaxis) with itraconazole is recommended in adults and children following initial therapy. Amphotericin B deoxycholate is better tolerated in children than in adults. Liposomal amphotericin B is preferred for treatment of parenchymal cerebral lesions.</td>
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<td>• Itraconazole oral solution loading dose of 2–5 mg/kg body weight (maximum 200 mg) per dose by mouth 3 times daily for first 3 days of therapy, followed by 2–5 mg/kg body weight (maximum 200 mg) per dose by mouth twice daily for 12 months</td>
<td>• Fluconazole 5–6 mg/kg body weight IV or by mouth (maximum 300 mg) per dose, twice daily (maximum 600 mg/day) for 12 months</td>
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<td><strong>Moderately Severe to Severe Disseminated Disease:</strong></td>
<td><strong>Moderately Severe to Severe Disseminated Disease:</strong></td>
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<td><strong>Acute Therapy (Minimum 2-Week Induction, Longer if Clinical Improvement is Delayed, Followed by Consolidation Therapy):</strong></td>
<td><strong>Consolidation Therapy (Followed by Chronic Suppressive Therapy):</strong></td>
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<td>• Liposomal amphotericin B 3–5 mg/kg body weight, IV once daily (preferred)</td>
<td>• Itraconazole oral solution initial loading dose of 2–5 mg/kg body weight (maximum 200 mg) per dose by mouth 3 times daily for first 3 days of therapy, followed by 2–5 mg/kg body weight (max 200 mg) per dose by mouth given twice daily for 12 months</td>
<td>If itraconazole not tolerated, amphotericin alone for 4–6 weeks can be used with monitoring that confirms decline in histoplasma urine and serum antigen levels. Liposomal amphotericin B 3–5 mg/kg body weight IV once daily (preferred) for 4–6 weeks Amphotericin B deoxycholate 0.7–1 mg/kg body weight IV once daily (alternative) for 4–6 weeks</td>
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<td>• Amphotericin B deoxycholate 0.7–1 mg/kg body weight IV once daily (alternative)</td>
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Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 13 of 24)

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<tr>
<td>Histoplasmosis, continued</td>
<td>Central Nervous System Infection</td>
<td>Acute Therapy (4–6 Weeks, Followed by Consolidation Therapy):</td>
<td>• Liposomal amphotericin B5 mg/kg body weight IV once daily (AII)</td>
<td>November 6, 2013</td>
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<td>Consolidation Therapy (Followed by Chronic Suppressive Therapy):</td>
<td>• Itraconazole oral solution initial loading dose of 2–5 mg/kg body weight (maximum 200 mg) per dose by mouth 3 times daily for first 3 days of therapy, followed by 2–5 mg/kg body weight (max 200 mg) per dose by mouth given twice daily for ≥12 months and until histoplasma antigen is no longer detected in cerebrospinal fluid</td>
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<td>• Podofilox solution/gel (0.5%) applied topically BID for 3 consecutive days a week up to 4 weeks (patient applied). Withhold treatment for 4 days and repeat the cycle weekly up to 4 times (BIII)</td>
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<td>• Imiquimod cream (5%) applied topically at night and washed off in the morning for 3 non-consecutive nights a week for up to 16 weeks (patient applied) (BII)</td>
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<td>• TCA or BCA (80%–90%) applied topically weekly for up to 3 to 6 weeks (provider applied) (BIII)</td>
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<td>• Podophyllin resin (10%–25% suspension in tincture of benzoin) applied topically and washed off several hours later, repeated weekly for 3 to 6 weeks (provider applied) (CIII)</td>
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<td>• Cryotherapy with liquid nitrogen or cryoprobe applied every 1–2 weeks (BIII)</td>
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<td>• Surgical removal either by tangential excision, tangential shave excision, curettage, or electrosurgery</td>
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<td>• Intraligamental IFN-α is generally not recommended because of high cost, difficult administration, and potential for systemic side effects (CIII)</td>
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<td>• Cidofovir topical gel (1%) is an experimental therapy studied in HIV-infected adults that is commercially available through compounding pharmacies and has very limited use in children; systemic absorption can occur (CIII)</td>
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<td>• 5-FU/epinephrine gel implant should be offered in only severe recalcitrant cases because of inconvenient routes of administration, frequent office visits, and a high frequency of systemic adverse effects.</td>
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<td>Adequate topical anesthetics to the genital area should be given before caustic modalities are applied.</td>
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<td>Sexual contact should be limited while solutions or creams are on the skin.</td>
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<td>Although sinecatechins (15% ointment) applied TID up to 16 weeks is recommended in immunocompetent individuals, data are insufficient on safety and efficacy in HIV-infected individuals.</td>
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<td>cART has not been consistently associated with reduced risk of HPV-related cervical abnormalities in HIV-infected women.</td>
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<td>Laryngeal papillomatosis generally requires referral to a pediatric otolaryngologist. Treatment is directed at maintaining the airway, rather than removing all disease.</td>
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<td>For women who have exophytic cervical warts, a biopsy to exclude HSIL must be performed before treatment.</td>
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<td>Liquid nitrogen or TCA/BCA is recommended for vaginal warts. Use of a cryoprobe in the vagina is not recommended.</td>
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<td></td>
<td>Cryotherapy with liquid nitrogen or podophyllin resin (10%–25%) is recommended for urethral meatal warts.</td>
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<tr>
<td></td>
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<td></td>
<td>Cryotherapy with liquid nitrogen or TCA/BCA or surgical removal is recommended for anal warts.</td>
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<td></td>
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<td></td>
<td>Abnormal Pap smear cytology should be referred to colposcopy for diagnosis and management.</td>
<td></td>
</tr>
</tbody>
</table>
### Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 14 of 24)

<table>
<thead>
<tr>
<th>Indication</th>
<th>First Choice</th>
<th>Alternative</th>
<th>Comments/Special Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Influenza A and B</strong></td>
<td>Oseltamivir:</td>
<td>None</td>
<td><strong>Duration:</strong></td>
</tr>
<tr>
<td>Aged &lt;3 Months:</td>
<td><strong>Aged &lt;3 Months:</strong></td>
<td></td>
<td>• The recommended antiviral treatment duration for either oseltamivir or zanamivir is 5 days. Per CDC recommendations, longer treatment courses can be considered for patients who remain severely ill after 5 days of treatment.²</td>
</tr>
<tr>
<td>• 3 mg/kg/dose twice daily</td>
<td><strong>Aged 3 Months to &lt;1 Year:</strong></td>
<td></td>
<td></td>
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<tr>
<td>• 3 mg/kg/dose twice daily</td>
<td><strong>Aged ≥1 Year to 12 Years:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Weighing ≤15 kg: 30 mg twice daily</td>
<td><strong>Weight-Band Dosing:</strong></td>
<td></td>
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</tr>
<tr>
<td>• Weighing &gt;15 kg to 23 kg: 45 mg twice daily</td>
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<tr>
<td>• Weighing &gt;23 kg to 40 kg: 60 mg twice daily</td>
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<tr>
<td>• Weighing &gt;40 kg: 75 mg twice daily</td>
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<tr>
<td>Aged ≥13 Years:</td>
<td>75 mg twice daily</td>
<td></td>
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<tr>
<td>Zanamivir (Aged ≥7 Years):</td>
<td>10 mg (2 inhalations) twice daily</td>
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<tr>
<td><strong>Oseltamivir Dosing Adjustments</strong></td>
<td></td>
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<tr>
<td>Premature Infants:</td>
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<tr>
<td>• Current weight-based dosing recommendations for oseltamivir are not appropriate for premature infants (i.e., gestational age at delivery &lt;38 weeks).²</td>
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<tr>
<td>Renal Insufficiency:</td>
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<tr>
<td>• Oseltamivir renal dosing is not well established for pediatric patients. For children weighing &gt;40 kg, adult renal dosing can be used.</td>
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<tr>
<td>• CrCl/Dose</td>
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<tr>
<td>• 61–90 mL/minute: 75 mg twice daily</td>
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<tr>
<td>• 31–60 mL/minute: 30 mg twice daily</td>
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<tr>
<td>• 11–30 mL/minute: 30 mg once daily</td>
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<tr>
<td>• ≤10ml/min; ESRD on hemodialysis: 30 mg dose after every hemodialysis cycle</td>
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<tr>
<td>• ≤10ml/min; ESRD continuous ambulatory peritoneal dialysis: single 30 mg dose administered after a dialysis exchange</td>
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<tr>
<td>a Oseltamivir is FDA-approved for treatment of influenza in children aged ≥2 weeks; however, both CDC and AAP recommend use of oral oseltamivir for influenza treatment in infants aged &lt;2 weeks.</td>
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<tr>
<td>b Zanamivir is not recommended for treatment in children aged &lt;7 years or for children with underlying respiratory disease.</td>
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<tr>
<td>c See Fiore 2011 and Influenza Antiviral Medications: Summary for Clinicians for further details.</td>
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<tr>
<td><strong>Isosporiasis</strong></td>
<td>TMP-SMX 5 mg/kg body weight of the TMP component (maximum 160 mg TMP) twice daily by mouth for 10 days</td>
<td></td>
<td>If symptoms worsen or persist, the TMP-SMX dose (5 mg/kg/dose of the TMP component) may be given more frequently (e.g., 3–4 times daily by mouth for 10 days) and/or the duration of treatment may be increased to 3–4 weeks. The optimal duration of treatment with pyrimethamine has not been established. Ciprofloxacin is not a drug of choice in children because of increased incidence of adverse events, including events related to joints and/or surrounding tissues.</td>
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<tr>
<td>(Cystoisosporiasis)</td>
<td>Pyrimethamine 1 mg/kg body weight (maximum 25 mg) plus folic acid 5-15 mg by mouth once daily for 14 days</td>
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<tr>
<td>Second-Line Alternatives:</td>
<td>• Ciprofloxacin 10–20 mg/kg body weight (maximum 500 mg) by mouth twice daily for 7 days</td>
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</tr>
</tbody>
</table>

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**Guidelines for the Prevention and Treatment of Opportunistic Infections In HIV-Exposed and HIV-Infected Children**

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</table>
| **Isosporiasis (Cystoisosporiasis), continued** | | • Nitazoxanide (see doses below) for 3 consecutive days  
*Children Aged 1 Year–3 Years:*  
• Nitazoxanide 100 mg by mouth every 12 hours  
*Children Aged 4 Years–11 years:*  
• Nitazoxanide 200 mg by mouth every 12 hours  
*Adolescents Aged ≥12 Years and Adults:*  
• Nitazoxanide 500 mg by mouth every 12 hours | | | February 8, 2019 |
| **Malaria** | **Uncomplicated *P. Falciparum or Unknown Malaria Species, from Chloroquine-Resistant Areas (All Malaria Areas Except Those Listed as Chloroquine Sensitive) or Unknown Region:**** | • Atovaquone-proguanil (pediatric tablets 62.5 mg/25 mg; adult tablets 250 mg/100 mg), dosed once daily:  
• 5–8 kg; 2 pediatric tablets for 3 days;  
• 9–10 kg; 3 pediatric tablets for 3 days;  
• 11–20 kg; 4 pediatric tablets or 1 adult tablet for 3 days;  
• 21–30 kg; 2 adult tablets for 3 days;  
• 31–40 kg; 3 adult tablets for 3 days;  
• >40 kg; 4 adult tablets for 3 days | • Chloroquine phosphate: 16.6 mg/kg body weight (10 mg/kg body weight chloroquine base) (maximum 1000 mg) by mouth once, then 8.3 mg/kg body weight (maximum 500 mg) by mouth at 6, 24, and 48 hours (total dose = 41.6 mg/kg body weight)  
For quinine-based regimens, doxycycline or tetracycline should be used only in children aged ≥8 years. An alternative for children aged ≥8 years is clindamycin 7 mg/kg body weight per dose by mouth given every 8 hours. Clindamycin should be used for children aged <8 years.  
Before primaquine is given, G6PD status must be verified. Primaquine may be given in combination with chloroquine if the G6PD status is known and negative, otherwise give after chloroquine (when G6PD status is available).  
For most updated prevention and treatment recommendations for specific region, refer to updated CDC treatment table available at [http://www.cdc.gov/malaria/resources/pdf/treatmenttable.pdf](http://www.cdc.gov/malaria/resources/pdf/treatmenttable.pdf)  
For sensitive and resistant malaria map: [http://cdc-malaria.ncsa.uiuc.edu/](http://cdc-malaria.ncsa.uiuc.edu/)  
High treatment failure rates due to chloroquine-resistant *P. vivax* have been documented in Papua New Guinea and Indonesia. | | November 6, 2013 |
### Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 16 of 24)

<table>
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<tbody>
<tr>
<td><strong>Malaria, continued</strong></td>
<td>chloroquine base) (maximum 1000 mg) by mouth once, then 8.3 mg/kg body weight (maximum 500 mg) by mouth at 6, 24, and 48 hours (total dose = 41.6 mg/kg body weight chloroquine phosphate [maximum 2500 mg] = 25 mg/kg body weight chloroquine base)</td>
<td>Malaria: Uncomplicated <em>P. falciparum</em> or Unknown Malaria Species from Chloroquine-Resistant Areas (All Malaria Areas Except Those Listed as Chloroquine Sensitive) or Unknown Region:</td>
<td>Treatment should be selected from one of the three following options:</td>
<td>November 6, 2013</td>
</tr>
<tr>
<td></td>
<td><em>P. vivax, P. ovale, P. malariae, P. knowlesi</em> (All Areas Except Papua New Guinea, Indonesia; See Comments)</td>
<td></td>
<td>• Atovaquone-proguanil plus primaquine phosphate</td>
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<tr>
<td></td>
<td>Initial Therapy (Followed by Anti-Relapse Therapy for <em>P. ovale</em> and <em>P. vivax</em>):</td>
<td></td>
<td>• Quinine sulfate + EITHER doxycycline OR tetracycline PLUS primaquine phosphate.</td>
<td></td>
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<tr>
<td></td>
<td>• Chloroquine phosphate 16.6 mg/kg body weight (10 mg/kg body weight chloroquine base) (maximum 1000 mg) by mouth once, then 8.3 mg/kg body weight (maximum 500 mg) by mouth at 6, 24, and 48 hours (total dose = 41.6 mg/kg body weight chloroquine phosphate [maximum 2500 mg] = 25 mg/kg body weight chloroquine base)</td>
<td></td>
<td>This regimen cannot be used in children aged &lt;8 years.</td>
<td></td>
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<tr>
<td></td>
<td>Anti-Relapse Therapy for <em>P. ovale, P. vivax</em>:</td>
<td></td>
<td>• Mefloquine plus primaquine phosphate</td>
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<tr>
<td></td>
<td>• Primaquine 0.5 mg base/kg body weight (max 30 mg base) by mouth once daily for 14 days</td>
<td></td>
<td>• Artemether-lumefantrine: 1 tablet = 20 mg Artemether and 120 mg lumefantrine, a 3-day treatment schedule for a total of 6 doses. The second dose follows the initial dose 8 hours later, then 1 dose twice daily for the next 2 days.</td>
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<tr>
<td>Indication</td>
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<td>Alternative</td>
<td>Comments/Special Issues</td>
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</tbody>
</table>
| **Malaria**, continued | • 5 to <15 kg; 1 tablet per dose  
• 15 to <25 kg; 2 tablets per dose  
• 25 to <35 kg; 3 tablets per dose  
• >35 kg; 4 tablets per dose | N/A | Quinidine gluconate is a class 1a anti-arrhythmic agent not typically stocked in pediatric hospitals. When regional supplies are unavailable, the CDC Malaria hotline may be of assistance (see below). **Do not** give quinidine gluconate as an IV bolus. Quinidine gluconate IV should be administered in a monitored setting. Cardiac monitoring required. Adverse events including severe hypoglycemia, prolongation of the QT interval, ventricular arrhythmia, and hypotension can result from the use of this drug at treatment doses.  
IND: IV artesunate is available from CDC. Contact the CDC Malaria Hotline at (770) 488-7788 from 8 a.m.–4:30 p.m. EST or (770) 488-7100 after hours, weekends, and holidays. Artesunate followed by one of the following: Atovaquone-proguanil (Malarone™), clindamycin, mefloquine, or (for children aged >8 years) doxycycline.  
Quinidine gluconate: 10 mg = 6.25 mg quinidine base.  
Doxycycline (or tetracycline) should be used in children aged >8 years. For patients unable to take oral medication, may give IV. For children <45 kg, give 2.2 mg/kg IV every 12 hours and then switch to oral doxycycline. For children >45 kg, use the same dosing as per adults. For IV use, avoid rapid administration.  
For patients unable to take oral clindamycin, give 10 mg base/kg loading dose IV, followed by 5 mg base/kg IV every 8 hours. Switch to oral clindamycin (oral dose as above) as soon as a patient can take oral medication. For IV use, avoid rapid administration.  
**Drug Interactions:**  
• Avoid co-administration of quinidine with ritonavir  
• Use quinidine with caution with other protease inhibitors. | November 6, 2013 |
| **Severe Malaria** | • Quinidine gluconate 10 mg/kg body weight  
IV loading dose over 1–2 hours, then 0.02 mg/kg body weight/minute infusion for ≥24 hours (Treatment duration: 7 days in Southeast Asia, Oceania, otherwise 3 days)  
PLUS One of the Following:  
• Doxycycline 100 mg per dose by mouth every 12 hours for 7 days; for children <45 kg, use 2.2 mg/kg body weight per dose  
OR  
• Clindamycin 7 mg/kg body weight per dose by mouth given every 8 hours for 7 days.  
OR  
• Tetracycline 6–12.5 mg/kg body weight per dose every 6 hours (maximum dose 500 mg per dose given 4 times daily) for 7 days  
• Artesunate 2.4 mg/kg body weight IV bolus at 0, 12, 24, and 48 hours  
PLUS One of the Following:  
• Doxycycline (treatment dosing as above), or Atovaquone-proguanil (treatment dosing as above), or  
• Mefloquine 15 mg/kg body weight (maximum 750 mg) by mouth once, then 10 mg/kg body weight (maximum 500 mg) by mouth once given 12 hours later, or  
• Clindamycin (dosing as above) | N/A | November 6, 2013 |
Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 18 of 24)

<table>
<thead>
<tr>
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<th>Alternative</th>
<th>Comments/Special Issues</th>
<th>Last Reviewed</th>
</tr>
</thead>
</table>
| Microsporidiosis         | Effective ART Therapy:                                                        | N/A         | • Supportive care (e.g., hydration, correction of electrolyte abnormalities, nutritional support)  
• Fumagillin for systemic use is unavailable in the United States and data on dosing in children are unavailable. Consultation with an expert is recommended. | December 15, 2016 |
|                          | • Immune reconstitution may lead to microbiologic and clinical response.      |             |                                                                                        |                 |
|                          | For Disseminated (Not Ocular) and Intestinal Infection Attributed to Microsporidia Other Than *E. bieneusi* or *V. corneae*: |             |                                                                                        |                 |
|                          | • Albendazole 7.5 mg/kg body weight (maximum 400 mg/dose) by mouth twice daily (in addition to ART) |             |                                                                                        |                 |
|                          | Treatment Duration:                                                          |             |                                                                                        |                 |
|                          | • Continue until sustained immune reconstitution (longer than 6 months at CDC immunologic category 1 or 2) after initiation of ART and resolution of signs and symptoms |             |                                                                                        |                 |
|                          | For *E. bieneusi* or *V. corneae* Infections:                                |             |                                                                                        |                 |
|                          | • Fumagillin (where available) adult dose 20 mg by mouth 3 times daily, or    |             |                                                                                        |                 |
|                          | • TNP-470 (a synthetic analogue of fumagillin; where available) recommended for treatment of infections caused by *E. bieneusi* in HIV-infected adults (in addition to ART) |             |                                                                                        |                 |
|                          | For Ocular Infection:                                                        |             |                                                                                        |                 |
|                          | • Topical fumagillin bicyclohexylammonium (Fumidil B) 3 mg/mL in saline (fumagillin 70 µg/mL) eye drops: 2 drops every 2 hours for 4 days, then 2 drops QID (investigational use only in United States) **plus**, for microsporidial infection other than *E. bieneusi* and *V. corneae*, albendazole 7.5 mg/kg body weight (maximum 400 mg/dose) by mouth twice daily for management of systemic infection in systemic infection (in addition to ART) |             |                                                                                        |                 |
|                          | Treatment Duration:                                                          |             |                                                                                        |                 |
|                          | • Continue until sustained immune reconstitution (longer than 6 months at CDC immunologic category 1 or 2) after initiation of ART and resolution of signs and symptoms. |             |                                                                                        |                 |
Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 19 of 24)

<table>
<thead>
<tr>
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<th>Comments/Special Issues</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Mycobacterium avium Complex (MAC)</strong></td>
<td>Initial Treatment (≥2 Drugs):</td>
<td>If Intolerant to Clarithromycin:</td>
<td>Combination therapy with a minimum of 2 drugs is recommended for ≥12 months.</td>
<td>January 8, 2019</td>
</tr>
<tr>
<td></td>
<td>• Clarithromycin 7.5–15 mg/kg body weight (maximum 500 mg/dose) orally twice daily plus ethambutol 15–25 mg/kg body weight (maximum 2.5 g/day) orally once daily followed by chronic suppressive therapy</td>
<td>• Azithromycin 10–12 mg/kg body weight (maximum 500 mg/day) orally once daily</td>
<td>Clofazimine is associated with increased mortality in adults with HIV infection and should not be used.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>For Severe Disease, Add:</td>
<td>If Rifabutin Cannot Be Administered and a Third Drug is Needed in Addition to a Macrolide and Ethambutol, or if a Fourth Drug is Needed in Addition to Rifabutin for Patients with More Severe Symptoms or Disseminated Disease:</td>
<td>Children receiving ethambutol who are old enough to undergo routine eye testing should have monthly monitoring of visual acuity and color discrimination.</td>
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<tr>
<td></td>
<td>• Rifabutin 10–20 mg/kg body weight (maximum 300 mg/day) orally once daily</td>
<td>• Ciprofloxacin 10–15 mg/kg orally twice daily (maximum 1.5 g/day), or • Levofloxacin 500 mg orally once daily, or • Amikacin 15–30 mg/kg body weight IV in 1 or 2 divided doses (maximum 1.5 g/day)</td>
<td>Fluoquinolones (e.g., ciprofloxacin and levofloxacin) are not labeled for use in children aged &lt;18 years because of concerns regarding potential effects on cartilage; use in children aged &lt;18 years requires an assessment of potential risks and benefits.</td>
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<td></td>
<td>Intrathoracic Disease</td>
<td>Chronic suppressive therapy (secondary prophylaxis) is recommended in children and adults following initial therapy.</td>
<td></td>
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<tr>
<td><strong>Mycobacterium Tuberculosis</strong></td>
<td><strong>Drug-Susceptible TB</strong></td>
<td>Alternative for Rifampin:</td>
<td></td>
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<tr>
<td></td>
<td><strong>Intensive Phase (2 Months):</strong></td>
<td>Rifabutin 10–20 mg/kg body weight (maximum 300 mg/day) by mouth once daily, plus</td>
<td>Only DOT.</td>
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<tr>
<td></td>
<td>• Isoniazid, 10–15 mg/kg body weight (maximum 300 mg/day) by mouth once daily, plus</td>
<td>Rifampin 10–20 mg/kg body weight (maximum 600 mg/day) by mouth once daily, plus</td>
<td>If cART-naive, start TB therapy immediately and initiate cART within 2–8 weeks.</td>
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<tr>
<td></td>
<td>• Rifampin 10–20 mg/kg body weight (maximum 600 mg/day) by mouth once daily, plus</td>
<td>• Pyrazinamide 30–40 mg/kg body weight (maximum 2 g/day) by mouth once daily, plus</td>
<td>Already on cART; review to minimize potential toxicities and drug-drug interactions; start TB treatment immediately.</td>
<td></td>
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<tr>
<td></td>
<td>• Ethambutol 15–25 mg/kg body weight (maximum 2.5 g/day) by mouth once daily</td>
<td>• Discuss with an expert.</td>
<td>Potential drug toxicity and interactions should be reviewed at every visit.</td>
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<td></td>
<td><strong>Continuation Phase (7 Months):</strong></td>
<td>Alternative Continuation Phase If Good Adherence and Treatment Response:</td>
<td>Adjunctive Treatment:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Isoniazid 10–15 mg/kg body weight (maximum 300 mg/day) by mouth once daily, plus</td>
<td>• Isoniazid 20–30 mg/kg body weight (maximum 900 mg/day) by mouth, plus</td>
<td>• Co-trimoxazole prophylaxis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Rifampin 10–20 mg/kg body weight (maximum 600 mg/day) by mouth once daily</td>
<td>• Rifampin 10–20 mg/kg body weight (maximum 600 mg/day) three times a week.</td>
<td>• Pyridoxine 1–2 mg/kg body weight/day (maximum 25–50 mg/day) with isoniazid or cycloserine/terizidone or, if malnourished; pyridoxine supplementation is recommended for exclusively breastfed infants and for children and adolescents on meat- and milk-deficient diets; children with nutritional deficiencies, including all symptomatic HIV-infected children; and pregnant adolescents and women.</td>
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<td></td>
<td><strong>Extrathoracic Disease:</strong></td>
<td>In children with minimal disease with fully drug-susceptible TB in the absence of significant immune compromise, a 3-drug intensive phase regimen (excluding ethambutol) and a continuation phase of 4 months can be considered (total duration of therapy of 6 months).</td>
<td>• Corticosteroids (2 mg/kg body weight per day of prednisone [maximum, 60 mg/day] or its equivalent for 4–6 weeks followed by tapering) with CNS disease or pericardial effusion; may be considered with pleural effusions, severe airway compression, or severe IRIS.</td>
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<td>Note: Depends on disease entity</td>
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<tr>
<td></td>
<td>• Lymph node TB—treat as minimal intrathoracic disease</td>
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</tbody>
</table>

Guidelines for the Prevention and Treatment of Opportunistic Infections In HIV-Exposed and HIV-Infected Children

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<tbody>
<tr>
<td><strong>Mycobacterium Tuberculosis, continued</strong></td>
<td>• Bone or joint disease—consider extending continuation phase to 10 months (for total duration of therapy of 12 months).</td>
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<td></td>
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<tr>
<td><strong>TB Meningitis:</strong></td>
<td>• As alternative to ethambutol or streptomycin, 20–40 mg/kg body weight (maximum 1 g/day) IM once daily—during intensive phase, consider ethionamide, 15–20 mg/kg body weight by mouth (maximum 1 g/day), initially divided into 2 doses until well tolerated)</td>
<td>• Consider extending continuation phase to 10 months (for total duration of therapy of 12 months).</td>
<td>Second-Line Drug Doses: • Amikacin 15–30 mg/kg body weight (maximum 1 g/day) IM or IV once daily • Kanamycin 15–30 mg/kg body weight (maximum 1 g/day) IM or IV once daily • Capreomycin 15–30 mg/kg body weight (maximum 1 g/day) IM once daily • Ofloxacin 15–20 mg/kg body weight (maximum 800 mg/day), or levofoxacin 7.5–10 mg/kg body weight (maximum 750 mg/day) by mouth once daily. Because some fluoroquinolones are approved by the FDA for use only in people aged 18 years and older, their use in younger patients necessitates careful assessment of the potential risks and benefits. • Cycloserine/Terizidone 10–20 mg/kg body weight (maximum 1 g/day) by mouth once daily • Ethionamide/prothionamide, 15–20 mg/kg body weight (maximum 1 g/day) by mouth in 2–3 divided doses • Para-aminosalicylic acid 200–300 mg/kg body weight by mouth divided into 3–4 doses per day (maximum 10 g/day). • Thiacetazone can cause severe reactions in HIV-infected children including rash and aplastic anemia, and should not be used.</td>
<td>November 6, 2013</td>
</tr>
<tr>
<td><strong>Drug-Resistant TB</strong></td>
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<tr>
<td><strong>MDR-TB:</strong></td>
<td>• Therapy should be based on resistance pattern of child (or of source case where child’s isolate is not available); consult an expert.</td>
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<tr>
<td><strong>Treatment Duration:</strong></td>
<td>• 18–24 months after non-bacteriological diagnosis or after culture conversion; ≥12 months if minimal disease</td>
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<td></td>
<td>• Discuss with an expert.</td>
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<tr>
<td>Indication</td>
<td>First Choice</td>
<td>Alternative</td>
<td>Comments/Special Issues</td>
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<tr>
<td>Pneumocystis</td>
<td>TMP-SMX 3.75–5 mg/kg body weight/dose TMP (based on TMP component) every 6 hours IV or orally given for 21 days (followed by secondary prophylaxis dosing)</td>
<td>If TMP-SMX-Intolerant or Clinical Treatment Failure After 5–7 Days of TMP-SMX Therapy&lt;br&gt;&lt;br&gt;&lt;strong&gt;Pentamidine:&lt;/strong&gt;&lt;br&gt;• 4 mg/kg body weight/dose IV/IM &lt;br&gt;once daily is the first choice alternative regimen. Note: Pentamidine can be changed to atovaquone after 7–10 days IV therapy.&lt;br&gt;&lt;br&gt;&lt;strong&gt;Atovaquone&lt;/strong&gt;&lt;br&gt;&lt;br&gt;&lt;strong&gt;Daily Dosing:&lt;/strong&gt;&lt;br&gt;• Children aged 1–3 months and &gt;24 months–12 years: 30-40 mg/kg body weight/dose by mouth once daily with food&lt;br&gt;• Children aged 4–24 months: 45 mg/kg body weight/dose by mouth once daily with food&lt;br&gt;&lt;br&gt;&lt;strong&gt;Twice-Daily Dosing*:&lt;/strong&gt;&lt;br&gt;• Children aged ≥13 years: 750 mg/dose by mouth twice daily&lt;br&gt;* Some experts use twice-daily dosing of atovaquone as alternative treatment for PCP in children aged &lt;12 years:&lt;br&gt;• Children aged 1–3 months and &gt;24 months to 12 years: 15–20 mg/kg body weight/dose by mouth twice daily with food&lt;br&gt;• Children aged 4–24 months: 22.5 mg/kg body weight/dose by mouth twice daily with food</td>
<td>After acute pneumonitis resolved in mild-moderate disease, IV TMP-SMX can be changed to oral. For oral administration, total daily dose of TMP-SMX can also be administered in 3 divided doses (every 8 hours).&lt;br&gt;&lt;br&gt;Dapsone 2 mg/kg body weight by mouth once daily (maximum 100 mg/day) plus trimethoprim 5 mg/kg body weight by mouth every 8 hours has been used in adults but data in children are limited.&lt;br&gt;&lt;br&gt;Primaquine base 0.3 mg/kg body weight by mouth once daily (maximum 30 mg/day) plus clindamycin 10 mg/kg body weight/dose IV or by mouth (maximum 600 mg given IV and 300–450 mg given orally) every 6 hours has been used in adults, but data in children are not available.</td>
<td>November 6, 2013</td>
</tr>
</tbody>
</table>

Indications for Corticosteroids:<br>• PaO₂ <70 mm Hg at room air or alveolar-arterial oxygen gradient >35 mm Hg<br><br><strong>Prednisone Dose:</strong><br>• 1 mg/kg body weight/dose by mouth twice daily for 5 days, then<br>• 0.5–1 mg/kg body weight/dose by mouth twice daily for 5 days, then<br>• 0.5 mg/kg body weight by mouth once daily for days 11 to 21.<br><br>Alternative Corticosteroid Regimens Include:<br>• Adult dosage of prednisone: 40 mg/dose twice daily on days 1–5, 40 mg/dose once daily on days 6–10, 20 mg/dose once daily on days 11–21, and<br>• Methylprednisolone IV 1 mg/kg/dose every 6 hours on days 1–7, 1 mg/kg/dose twice daily on days 8–9, 0.5 mg/kg/dose twice daily on days 10 and 11, and 1 mg/kg/dose once daily on days 12–16.<br><br>Chronic suppressive therapy (secondary prophylaxis) with TMP/SMX is recommended in children and adults following initial therapy (see Secondary Prophylaxis).
### Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 22 of 24)

<table>
<thead>
<tr>
<th>Indication</th>
<th>First Choice</th>
<th>Alternative</th>
<th>Comments/Special Issues</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Syphilis</strong></td>
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<tr>
<td>Proven or Highly Probable Disease:</td>
<td>• Aqueous crystalline penicillin G 100,000–150,000 units/kg body weight per day, administered as 50,000 units/kg body weight per dose IV every 12 hours for the first 7 days of life, and then every 8 hours for 10 days</td>
<td>• Procaine penicillin G 50,000 units/kg body weight IM once daily for 10 days</td>
<td>For treatment of congenital syphilis, repeat the entire course of treatment if &gt;1 day of treatment is missed. Examinations and serologic testing for children with congenital syphilis should occur every 2–3 months until the test becomes non-reactive or there is a fourfold decrease in titer. Children with increasing titers or persistently positive titers (even if low levels) at ages 6–12 months should be evaluated and considered for re-treatment. In the setting of maternal and possible infant HIV infection, the more conservative choices among scenario-specific treatment options may be preferable. Children and adolescents with acquired syphilis should have clinical and serologic response monitored at 3, 6, 9, 12, and 24 months after therapy.</td>
<td>November 6, 2013</td>
</tr>
<tr>
<td>Possible Disease:</td>
<td>• Treatment options are influenced by several factors, including maternal treatment, titer, and response to therapy; and infant physical exam, titer, and test results. Scenarios that include variations of these factors are described and treatment recommendations are provided in detail on pages 36–37 of the Centers for Disease Control STD Treatment Guidelines, 2010.</td>
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<tr>
<td>Acquired:</td>
<td>Early Stage (Primary, Secondary, Early Latent):</td>
<td>• Benzathine penicillin 50,000 units/kg body weight (maximum 2.4 million units) IM for 1 dose</td>
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<td></td>
<td>Late Latent:</td>
<td>• Benzathine penicillin 50,000 units/kg body weight (maximum 2.4 million units) IM once weekly for 3 doses</td>
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<td></td>
<td>Neurosyphilis (Including Ocular):</td>
<td>• Aqueous penicillin G 200,000–300,000 units/kg body weight per day administered as 50,000 units/kg body weight per dose IV every 4–6 hours (maximum 18–24 million units per day) for 10–14 days</td>
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</tbody>
</table>
### Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 23 of 24)

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</thead>
<tbody>
<tr>
<td>Toxoplasmosis</td>
<td><strong>Congenital Toxoplasmosis:</strong></td>
<td>For Sulfonamide-Intolerant Patients:</td>
<td><strong>Congenital Toxoplasmosis:</strong> For infants born to mothers with symptomatic <em>Toxoplasma</em> infection during pregnancy, empiric therapy of the newborn should be strongly considered irrespective of the mother’s treatment during pregnancy.</td>
<td>November 6, 2013</td>
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<td></td>
<td>• Pyrimethamine loading dose—2 mg/kg body weight by mouth once daily for 2 days, then 1 mg/kg body weight by mouth once daily for 2–6 months, then 1 mg/kg body weight by mouth 3 times weekly, <strong>plus</strong> • Leucovorin (folinic acid) 10 mg by mouth or IM with each dose of pyrimethamine, <strong>plus</strong> • Sulfadiazine 50 mg/kg body weight by mouth twice daily</td>
<td>• Clindamycin 5–7.5 mg/kg body weight (maximum 600 mg/dose) by mouth or IV per dose given 4 times a day can be substituted for sulfadiazine combined with pyrimethamine and leucovorin</td>
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<td><strong>Treatment Duration:</strong></td>
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<tr>
<td></td>
<td>• 12 months</td>
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<tr>
<td>Acquired Toxoplasmosis</td>
<td><strong>Acute Induction Therapy (Followed by Chronic Suppressive Therapy):</strong></td>
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<tr>
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<td>• Pyrimethamine: loading dose—2 mg/kg body weight (maximum 50 mg) by mouth once daily for 3 days, then 1 mg/kg body weight (maximum 25 mg) by mouth once daily, <strong>plus</strong> • Sulfadiazine 25–50 mg/kg body weight (maximum 1–1.5 g/dose) by mouth per dose 4 times daily, <strong>plus</strong> • Leucovorin 10–25 mg by mouth once daily, followed by chronic suppressive therapy</td>
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<tr>
<td></td>
<td><strong>Treatment Duration (Followed by Chronic Suppressive Therapy):</strong></td>
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<td>• ≥6 weeks (longer duration if clinical or radiologic disease is extensive or response in incomplete at 6 weeks)</td>
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<tr>
<td>For Sulfonamide-Intolerant Patients:</td>
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Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 24 of 24)

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</tr>
</thead>
<tbody>
<tr>
<td>Varicella-Zoster Virus (VZV)</td>
<td>Children with No or Moderate Immune Suppression (CDC Immunologic Categories 1 and 2) and Mild Varicella Disease:</td>
<td>Patients Unresponsive to Acyclovir:</td>
<td>In children ≥1 year of age, some experts base IV acyclovir dosing on body surface area (500 mg/m² body surface area/dose IV every 8 hours) instead of body weight. Valacyclovir is approved for use in adults and adolescents with zoster at 1 g/dose by mouth TID for 7 days; the same dose has been used for varicella infections. Data on dosing in children are limited and there is no pediatric preparation, although 500 mg capsules can be extemporaneously compounded to make a suspension to administer 20 mg/kg body weight/dose (maximum dose 1 g) given TID (see prescribing information). Famciclovir is approved for use in adults and adolescents with zoster at 500 mg/dose by mouth TID for 7 days; the same dose has been used for varicella infections. There is no pediatric preparation and data on dosing in children are limited; can be used by adolescents able to receive adult dosing. Involvement of an ophthalmologist with experience in managing herpes zoster ophthalmicus and its complications in children is strongly recommended when ocular involvement is evident. Optimal management of PORN has not been defined.</td>
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<td></td>
<td>Acyclovir 20 mg/kg body weight/dose by mouth (max 800 mg/dose) QID for 7–10 days and until no new lesions for 48 hours</td>
<td>• Foscarnet (40–60 mg/kg body weight/dose IV every 8 hours) for 7–10 days or until no new lesions have appeared for 48 hours</td>
<td>November 6, 2013</td>
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<td>Children with Severe Immune Suppression (CDC Immunologic Category 3):</td>
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<tr>
<td></td>
<td>Acyclovir 10 mg/kg body weight 500 mg/m²/dose IV every 8 hours for 7–10 days and until no new lesions for 48 hours</td>
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<tr>
<td>Zoster</td>
<td>Children with Uncomplicated Zoster:</td>
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<td></td>
<td>Acyclovir 20 mg/kg body weight/dose (max 800 mg/dose) by mouth QID for 7–10 days.</td>
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<td></td>
<td>Children with Severe Immunosuppression (CDC Immunologic Category 3), Trigeminal or Sacral Nerve Involvement, Extensive Multidermatomal, or Disseminated Zoster:</td>
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<td></td>
<td>Acyclovir 10 mg/kg body weight/dose IV every 8 hours until cutaneous lesions and visceral disease are clearly resolving, then can switch to acyclovir by mouth to complete a 10 to 14-day course</td>
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<td>Children with Progressive Outer Retinal Necrosis:</td>
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<tr>
<td></td>
<td>• Ganciclovir 5 mg/kg body weight/dose IV every 12 hours, plus</td>
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<td></td>
<td>• Foscarnet 90 mg/kg body weight/dose IV every 12 hours, plus</td>
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<td></td>
<td>• Ganciclovir 2 mg/0.05mL intravitreal twice weekly and/or Foscarnet 1.2 mg/0.05 mL intravitreal twice weekly</td>
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<td>Children with ARN:</td>
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<td></td>
<td>Acyclovir 10–15 mg/kg body weight/dose IV every 8 hours daily for 10–14 days, followed by</td>
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<td></td>
<td>Oral valacyclovir 1 g/dose TID for 4–6 weeks (for children old enough to receive adult dose). Alternative oral acyclovir dose: 20 mg/kg body weight/dose QID for 4–6 weeks</td>
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Key to Acronyms: LIP = lymphocytic interstitial pneumonia; PCP = pneumocystis jirovecii pneumonia; IV = intravenous; PK = pharmacokinetic; CSF = cerebrospinal fluid; CNS = central nervous system; ICP = intracranial pressure; cART = combination antiretroviral therapy; ART = antiretroviral therapy; BSA = body surface area; CrCl = (estimated) creatinine clearance; HBV = hepatitis B virus; SQ = subcutaneous; HCV = hepatitis C virus; IFN-α = interferon-α; BID = twice daily; TID = three times daily; QID = four times daily; CNS = central nervous system; CSF = cerebrospinal fluid; HSV = herpes simplex virus; PCR = polymerase chain reaction; BCA = bichloroacetic acid; IFN = interferon; TCA = trichloroacetic acid; TMP-SMX = trimethoprim-sulfamethoxazole; DOT = directly observed therapy; IGRA = interferon-gamma release assay; IM = intramuscular; TB = tuberculosis; IRIS = immune reconstitution inflammatory syndrome; TE = toxoplasmic encephalitis

Guidelines for the Prevention and Treatment of Opportunistic Infections In HIV-Exposed and HIV-Infected Children

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### Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities  
(Last updated November 6, 2013; last reviewed November 6, 2013) (page 1 of 22)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Preparations</th>
<th>Major Toxicities&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Special Instructions</th>
</tr>
</thead>
</table>
|              |                           | Indicating Need for Medical Attention | Indicating Need for Medical Attention if Persistent or Bothersome | Requires dose adjustment in patients with renal impairment.  
Avoid other nephrotoxic drugs.  
Administer IV preparation by slow IV infusion over at least 1 hour at a final concentration not to exceed 7 mg/mL. This is to avoid renal tubular damage related to crystalluria; must be accompanied by adequate hydration. |
| Acyclovir    | Oral                      |                              |                                                                                      |
| (Zovirax)    | Suspension: 40 mg/mL       |                              |                                                                                      |
|              | Capsules: 200 mg           |                              |                                                                                      |
|              | Tablets: 400 mg            |                              |                                                                                      |
|              | Tablets: 800 mg            |                              |                                                                                      |
|              | IV                        |                              |                                                                                      |
|              |                           | More Frequent:                |                                                                                      |
|              |                           | Phlebitis (at injection site when given IV) |                                                                                      |
|              |                           | Less Frequent:                |                                                                                      |
|              |                           | Acute renal failure (parenteral use, more common with rapid infusion) |                                                                                      |
|              |                           | Rare                          |                                                                                      |
|              |                           | Parenteral Form Only:         |                                                                                      |
|              |                           | Encephalopathy                |                                                                                      |
|              |                           | Hematologic toxicity          |                                                                                      |
|              |                           | (leukopenia, neutropenia, thrombocytopenia, anemia, hemolysis) |                                                                                      |
|              |                           | Crystalluria, hematuria       |                                                                                      |
|              |                           | Disseminated intravascular coagulation |                                                                                      |
|              |                           | Hypotension                   |                                                                                      |
|              |                           | Neuropsychiatric toxicity     |                                                                                      |
|              |                           | (with high doses)             |                                                                                      |
|              |                           | Parenteral and Oral Forms:    |                                                                                      |
|              |                           | Rash (urticarial, exfoliative skin disorders including SJS) |                                                                                      |
|              |                           | Anaphylaxis                   |                                                                                      |
|              |                           | Seizures                      |                                                                                      |
|              |                           | Elevated transaminase enzymes |                                                                                      |
|              |                           | Fever, hallucinations         |                                                                                      |
|              |                           | Leukopenia                    |                                                                                      |
|              |                           | Lymphadenopathy               |                                                                                      |
|              |                           | Peripheral edema              |                                                                                      |
|              |                           | Visual abnormalities          |                                                                                      |
|              |                           | More Frequent:                |                                                                                      |
|              |                           | GI disturbances (anorexia, diarrhea, nausea, vomiting) |                                                                                      |
|              |                           | Headache, lightheadedness     |                                                                                      |
|              |                           | Malaise                       |                                                                                      |
|              |                           | Less Frequent (More Marked in Older Adults): |                                                                                      |
|              |                           | Agitation                     |                                                                                      |
|              |                           | Alopecia                      |                                                                                      |
|              |                           | Dizziness                     |                                                                                      |
|              |                           | Myalgia, paresthesia          |                                                                                      |
|              |                           | Somnolence                    |                                                                                      |
| Albendazole  | Tablets: 200 mg            |                              |                                                                                      |
| (Albenza)    |                           | More Frequent:                |                                                                                      |
|              |                           | Abnormal liver function tests |                                                                                      |
|              |                           | (LFTs)                        |                                                                                      |
|              |                           | Less Frequent:                |                                                                                      |
|              |                           | Hypersensitivity (rash, pruritus) |                                                                                      |
|              |                           | Neutropenia (with high doses) |                                                                                      |
|              |                           | Rare:                         |                                                                                      |
|              |                           | Pancytopenia                  |                                                                                      |
|              |                           | Less frequent:                |                                                                                      |
|              |                           | CNS effects (dizziness, headache) |                                                                                      |
|              |                           | GI disturbances (abdominal pain, diarrhea, nausea, vomiting) |                                                                                      |
|              |                           | Rare:                         |                                                                                      |
|              |                           | Alopecia                      |                                                                                      |
|              |                           | Should be given with food.    |                                                                                      |
|              |                           | May crush or chew tablets and give with water.  
Monitor CBC and LFTs prior to each cycle. |                                                                                      |
Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities  (page 2 of 22)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Preparations</th>
<th>Indicating Need for Medical Attention</th>
<th>Indicating Need for Medical Attention if Persistent or Bothersome</th>
<th>Special Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>IV</td>
<td>More Frequent:</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Nephrotoxicity</td>
<td></td>
<td>Must be infused over 30 to 60 minutes to avoid neuromuscular blockade.</td>
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<tr>
<td></td>
<td></td>
<td>• Neurotoxicity (including muscle twitching, seizures)</td>
<td></td>
<td>Requires dose adjustment in patients with impaired renal function.</td>
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<tr>
<td></td>
<td></td>
<td>• Ototoxicity, both auditory and vestibular</td>
<td></td>
<td>Should monitor renal function and hearing periodically (e.g., monthly) in children on prolonged therapy.</td>
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<tr>
<td></td>
<td></td>
<td>Less Frequent:</td>
<td></td>
<td>Therapeutic drug monitoring (TDM). indicated</td>
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<tr>
<td></td>
<td></td>
<td>• Hypersensitivity (skin rash, redness, or swelling)</td>
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<td></td>
<td>Rare:</td>
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<tr>
<td></td>
<td></td>
<td>• Neuromuscular blockade</td>
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<tr>
<td>Amphotericin B Deoxycholate (Fungizone)</td>
<td>IV</td>
<td>More Frequent:</td>
<td>• GI disturbance (nausea, vomiting, diarrhea, abdominal pain)</td>
<td>Monitor BUN, Cr, CBC, electrolytes, LFTs.</td>
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<tr>
<td></td>
<td></td>
<td>• Infusion-related reactions (fever/chills; nausea/vomiting; hypotension; anaphylaxis)</td>
<td>• Headache</td>
<td>Infuse over 1 to 2 hours; in patients with azotemia, hyperkalemia, or getting doses &gt;1 mg/kg, infuse over 3 to 6 hours.</td>
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<tr>
<td></td>
<td></td>
<td>• Anemia</td>
<td></td>
<td>Requires dose reduction in patients with impaired renal function.</td>
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<tr>
<td></td>
<td></td>
<td>• Hypokalemia</td>
<td></td>
<td>Avoid other nephrotoxic drugs, when possible, because nephrotoxicity is exacerbated with concomitant use of other nephrotoxic drugs; permanent nephrotoxicity is related to cumulative dose.</td>
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<tr>
<td></td>
<td></td>
<td>• Renal function impairment</td>
<td></td>
<td>Nephrotoxicity may be ameliorated by hydration with 0.9% saline IV over 30 minutes prior to the amphotericin B infusion.</td>
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<tr>
<td></td>
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<td>• Thrombophlebitis (at injection site)</td>
<td></td>
<td>Infusion-related reactions less frequent in children than adults; the onset is usually 1 to 3 hours after infusion, duration &lt;1 hour; frequency decreases over time.</td>
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<tr>
<td></td>
<td></td>
<td>Less Frequent or Rare:</td>
<td></td>
<td>Pre-treatment with acetaminophen and/or diphenhydramine may alleviate febrile reactions.</td>
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<td></td>
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<td>• Blurred or double vision</td>
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<td></td>
<td></td>
<td>• Cardiac arrhythmias, usually with rapid infusions</td>
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<tr>
<td></td>
<td></td>
<td>• Hypersensitivity (rash)</td>
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<td></td>
<td></td>
<td>• Leukopenia</td>
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<td></td>
<td>• Polyneuropathy</td>
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<td></td>
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<td>• Seizures</td>
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<tr>
<td></td>
<td></td>
<td>• Thrombocytopenia</td>
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<tbody>
<tr>
<td><strong>Amphotericin B Lipid Complex</strong> (Abelcet)</td>
<td>IV</td>
<td><strong>Indicating Need for Medical Attention</strong>&lt;br&gt;More Frequent:  • Infusion-related reactions (fever/chills, nausea/vomiting; headache, nausea and vomiting)&lt;br&gt;<strong>Less Frequent:</strong>&lt;br&gt;  • Anemia  • Leukopenia  • Respiratory distress  • Thrombocytopenia  • Renal function impairment</td>
<td><strong>Indicating Need for Medical Attention if Persistent or Bothersome</strong>&lt;br&gt;• GI disturbance (loss of appetite, nausea, vomiting, diarrhea, abdominal pain)&lt;br&gt;Monitor BUN, Cr, CBC, electrolytes, and LFTs.&lt;br&gt;Infuse diluted solution at rate of 2.5 mg/kg/hour.&lt;br&gt;In-line filters should not be used.&lt;br&gt;Use with caution with other drugs that are bone marrow suppressants or that are nephrotoxic; renal toxicity is dose-dependent, but less renal toxicity than seen with conventional amphotericin B. Consider dose reduction in patients with impaired renal function.</td>
</tr>
<tr>
<td><strong>Amphotericin B Liposome</strong> (AmBisome)</td>
<td>IV</td>
<td><strong>Indicating Need for Medical Attention</strong>&lt;br&gt;More Frequent:  • Fever, chills  • Hypokalemia&lt;br&gt;<strong>Less Frequent:</strong>&lt;br&gt;  • Back pain  • Chest pain  • Dark urine  • Dyspnea  • Infusion-related reaction (fever/chills, headache)&lt;br&gt;  • Jaundice  • Renal function impairment&lt;br&gt;<strong>Rare:</strong>&lt;br&gt;  • Anaphylactic reaction</td>
<td><strong>Indicating Need for Medical Attention if Persistent or Bothersome</strong>&lt;br&gt;• GI disturbance (nausea, vomiting, diarrhea, abdominal pain)&lt;br&gt;• Headache&lt;br&gt;• Skin rash&lt;br&gt;Monitor BUN, Cr, CBC, electrolytes, and LFTs.&lt;br&gt;Infuse over 2 hours.&lt;br&gt;Consider dose reduction in patients with impaired renal function.</td>
</tr>
<tr>
<td><strong>Artesunate</strong></td>
<td>IV:&lt;br&gt;• Only available from CDC Malaria Hotline; telephone: (770) 488-7788</td>
<td><strong>Indicating Need for Medical Attention</strong>&lt;br&gt;Rare:  • Anaphylactic reaction  • Neutropenia  • Bradycardia</td>
<td><strong>Indicating Need for Medical Attention if Persistent or Bothersome</strong>&lt;br&gt;• GI disturbance (nausea, vomiting)&lt;br&gt;• Headache&lt;br&gt;• Skin rash&lt;br&gt;Monitor CBC, LFTs, and electrolytes.&lt;br&gt;~40% less mortality than with quinidine use in severe malaria&lt;br&gt;50% lower incidence of hypoglycemia than quinidine</td>
</tr>
<tr>
<td><strong>Atovaquone</strong> (Mepron)</td>
<td>Oral Suspension:&lt;br&gt;• 150 mg/mL</td>
<td><strong>Indicating Need for Medical Attention</strong>&lt;br&gt;Frequent:  • Fever  • Skin rash</td>
<td><strong>Indicating Need for Medical Attention if Persistent or Bothersome</strong>&lt;br&gt;• GI disturbances (nausea, vomiting, diarrhea)&lt;br&gt;• Headache&lt;br&gt;• Cough&lt;br&gt;• Insomnia&lt;br&gt;Should be administered with a meal to enhance absorption; bioavailability increases 3-fold when administered with high-fat meal.</td>
</tr>
</tbody>
</table>
Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 4 of 22)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Preparations</th>
<th>Major Toxicitiesa</th>
<th>Indicating Need for Medical Attention if Persistent or Bothersome</th>
<th>Special Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atovaquone/ Proguanil (Malarone)</td>
<td>Tablets:  • Pediatric tablets; 62.5 mg/25 mg  • Adult tablets; 250 mg/100 mg</td>
<td>Less frequent:  • Vomiting  • Pruritus</td>
<td>N/A</td>
<td>Pediatric tablets are available to make dosing easier.  Side effects requiring discontinuation in ~1%–2% of patients. Not recommended for prophylaxis in patients with CrCl &lt;30 mL/min.</td>
</tr>
<tr>
<td>Azithromycin (Zithromax)</td>
<td>Oral Suspension:  • 20 mg/mL  • 40 mg/mL  Tablets:  • 250 mg  • 500 mg  • 600 mg IV</td>
<td>More Frequent:  • Thrombophlebitis (IV form)  Rare:  • Acute interstitial nephritis  • Allergic reactions/anaphylaxis (dyspnea, hives, rash)  • Pseudomembranous colitis</td>
<td>• GI disturbances (abdominal discomfort or pain, diarrhea, nausea, vomiting)  • Dizziness, headache</td>
<td>Administer 1 hour before or 2 hours after a meal; do not administer with aluminum- and magnesium-containing antacids. IV should be infused at concentration of 1 mg/mL over a 3-hour period, or 2 mg/mL over a 1-hour period; should not be administered as a bolus. Use with caution in patients with hepatic function impairment; biliary excretion is the main route of elimination. Potential drug interactions.</td>
</tr>
<tr>
<td>Capreomycin (Capastat)</td>
<td>IM</td>
<td>Less Frequent:  • Hypersensitivity (rash, fever)  • Hypokalemia  • Neuromuscular blockade  • Ototoxicity, both auditory and vestibular  • Injection site pain, sterile abscess</td>
<td>N/A</td>
<td>Requires dose adjustment in patients with impaired renal function. Administer only by deep IM injection into large muscle mass (superficial injections may result in sterile abscess). Should monitor renal function and hearing periodically (e.g., monthly) in children on prolonged therapy. Monitor LFTs and electrolytes.</td>
</tr>
<tr>
<td>Caspofungin (Cancidas)</td>
<td>IV</td>
<td>More Frequent:  • Histamine-mediated symptoms (fever, facial swelling, pruritus, bronchospasm)  Rare:  • Hypokalemia  • Anaphylactic reaction</td>
<td>•GI disturbances (nausea, vomiting, diarrhea)  • Headache  • Skin rash, facial flushing  • Elevated liver transaminases  • Thrombophlebitis</td>
<td>Requires dose adjustment in moderate-to-severe hepatic insufficiency. IV infusion over 1 hour in normal saline (do not use diluents containing dextrose)</td>
</tr>
</tbody>
</table>
### Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities

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<thead>
<tr>
<th>Drug</th>
<th>Preparations</th>
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<th>Major Toxicities</th>
<th>Indicating Need for Medical Attention if Persistent or Bothersome</th>
<th>Special Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroquine Phosphate</td>
<td>Tablets:</td>
<td>More Frequent:</td>
<td>Major Toxicities</td>
<td>Psoriasis exacerbations</td>
<td>Store in child-proof containers and protect from light.</td>
</tr>
<tr>
<td>(Aralen)</td>
<td>• 500 mg</td>
<td>• Pruritus: Common in individuals of black race (25%–33%)</td>
<td></td>
<td>GI disturbances (nausea, vomiting, diarrhea)</td>
<td>Can be toxic in overdose.</td>
</tr>
<tr>
<td></td>
<td>• 250 mg</td>
<td>Less Frequent, but More Severe:</td>
<td></td>
<td>Visual disturbances including photosensitivity</td>
<td>Bitter tasting, so consider administering with foods that can mask the taste.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Auditory toxicity</td>
<td></td>
<td>Tinnitus</td>
<td>Solution available worldwide, but not in United States.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ocular toxicity</td>
<td></td>
<td>Muscle weakness</td>
<td>Caution in patients with G6PD deficiency or seizure disorder.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Neuropsychiatric disorders</td>
<td></td>
<td></td>
<td>Monitor CBC, periodic neurologic and ophthalmologic exams in patients on prolonged therapy.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• QT prolongation</td>
<td></td>
<td></td>
<td>Infuse over 1 hour.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hepatitis</td>
<td></td>
<td></td>
<td>Should not be used in patients with severe renal impairment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Bone marrow suppression</td>
<td></td>
<td></td>
<td>Nephrotoxicity risk is decreased with pre-hydration with IV normal saline and probenecid with each infusion. Probenecid is administered prior to each dose and repeated for two additional doses after infusion. Additional hydration after infusion is recommended if tolerated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Peripheral neuropathy</td>
<td></td>
<td></td>
<td>Concurrent use of other nephrotoxic drugs should be avoided.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Indicating Need for Medical Attention</td>
<td></td>
<td></td>
<td>Monitor renal function, urinalysis, electrolytes, and CBC and perform ophthalmologic exams.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Indicating Need for Medical Attention if Persistent or Bothersome</td>
<td></td>
<td></td>
<td>Administer oral formulations at least 2 hours before, or 6 hours after, sucralfate or antacids or other products containing calcium, zinc, or iron (including daily products or calcium-fortified juices). Take with full glass of water to avoid crystalluria. Possible phototoxicity reactions with sun exposure.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Indicating Need for Medical Attention if Persistent or Bothersome</td>
<td></td>
<td></td>
<td>IV infusions should be over 1 hour.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Indicating Need for Medical Attention if Persistent or Bothersome</td>
<td></td>
<td></td>
<td>Do not split, crush, or chew extended-release tablets.</td>
</tr>
</tbody>
</table>

Guidelines for the Prevention and Treatment of Opportunistic Infections In HIV-Exposed and HIV-Infected Children

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Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 6 of 22)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Preparations</th>
<th>Major Toxicities&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Special Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Indicating Need for Medical Attention</td>
<td>Indicating Need for Medical Attention if Persistent or Bothersome</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>Oral Suspension: 25 mg/mL, 50 mg/mL Tablets: 250 mg, 500 mg</td>
<td>Rare: Hepatotoxicity, Hypersensitivity reaction (rash, pruritus, dyspnea), Pseudomembranous colitis, Thrombocytopenia, QT interval prolongation</td>
<td>More Frequent: GI disturbances (abdominal discomfort or pain, diarrhea, nausea, vomiting), Less Frequent: Abnormal taste sensation, Headache, Rash</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Clindamycin</td>
<td>Oral Solution: 15 mg/mL Capsules: 75 mg, 150 mg, 300 mg IV</td>
<td>More Frequent: Pseudomembranous colitis Less Frequent: Hypersensitivity (skin rash, redness, pruritus), Neutropenia, Thrombocytopenia</td>
<td>More Frequent: GI disturbances (abdominal pain, nausea, vomiting, diarrhea), Less Frequent: Fungal overgrowth, rectal and genital areas</td>
</tr>
<tr>
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</tr>
<tr>
<td>Cycloserine</td>
<td>Capsules: 250 mg</td>
<td>More Frequent: CNS toxicity (including confusion, anxiety) Less Frequent: Hypersensitivity (skin rash), Peripheral neuropathy, Seizures, Psychosis Rare: Cardiac arrhythmias</td>
<td>Headache, dizziness, drowsiness, confusion, Rare: Photosensitivity</td>
</tr>
</tbody>
</table>
Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities  (page 7 of 22)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Preparations</th>
<th>Major Toxicities</th>
<th>Special Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dapsone</strong></td>
<td><strong>Syrup (available under Compassionate Use IND):</strong></td>
<td><strong>Indicating Need for Medical Attention</strong></td>
<td>Protect from light; dispense syrup in amber glass bottles.</td>
</tr>
<tr>
<td></td>
<td>• 2 mg/mL</td>
<td><strong>More Frequent:</strong></td>
<td>Monitor CBC and LFTs.</td>
</tr>
<tr>
<td></td>
<td><strong>Tablets:</strong></td>
<td>• Hemolytic anemia (especially if G6PD deficiency)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 25 mg</td>
<td>• Methemoglobinemia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 100 mg</td>
<td>• Skin rash</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Rare:</strong></td>
<td>• Blood dyscrasias</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Exfoliative skin disorders (including SJS)</td>
<td>• Hepatic toxicity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Mood or other mental changes</td>
<td>• Photosensitivity reactions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Peripheral neuritis</td>
<td><strong>Indicating Need for Medical Attention if Persistent or Bothersome</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Hypersensitivity reaction (fever, rash, jaundice, anemia)</td>
<td>• CNS toxicity (headache, insomnia, nervousness)</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Special Instructions</strong></td>
<td>• GI disturbances (anorexia, nausea, vomiting)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Protect from light; dispense syrup in amber glass bottles.</td>
<td>• Photosensitivity reactions</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Monitor CBC and LFTs.</strong></td>
<td><strong>Swallow with adequate amounts of fluids</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Avoid antacids, milk, dairy products, and iron for 1 hour before or 2 hours</strong></td>
<td><strong>Use with caution in hepatic and renal disease.</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Patient should avoid prolonged exposure to direct sunlight (skin sensitivity).</strong></td>
<td><strong>IV doses should be infused over 1 to 4 hours.</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Generally not recommended for use in children aged &lt;8 years because of risk</strong></td>
<td><strong>Patient should avoid prolonged exposure to direct sunlight (skin sensitivity).</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>of tooth enamel hypoplasia and discoloration, unless benefit outweighs risk.</strong></td>
<td><strong>Monitor renal function, CBC, and LFTs if prolonged therapy.</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Tablets and Capsules:</strong></td>
<td><strong>Staining of teeth a concern for individuals aged &lt;8 years</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 20 mg</td>
<td>• Photo-onycholysis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 50 mg</td>
<td>• GI disturbances (nausea, vomiting, abdominal cramps)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 75 mg</td>
<td><strong>Special Instructions</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 100 mg</td>
<td><strong>Avoid antacids, milk, dairy products, and iron for 1 hour before or 2 hours</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Oral Suspension and Syrup:</strong></td>
<td><strong>Use with caution in hepatic and renal disease.</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 5 mg/mL oral suspension</td>
<td><strong>IV doses should be infused over 1 to 4 hours.</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 10 mg/mL oral syrup IV</td>
<td><strong>Patient should avoid prolonged exposure to direct sunlight (skin sensitivity).</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Tablets and Capsules:</strong></td>
<td><strong>Generally not recommended for use in children aged &lt;8 years because of risk</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 20 mg</td>
<td><strong>of tooth enamel hypoplasia and discoloration, unless benefit outweighs risk.</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 50 mg</td>
<td><strong>Monitor renal function, CBC, and LFTs if prolonged therapy.</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 75 mg</td>
<td><strong>Swallow with adequate amounts of fluids</strong></td>
<td></td>
</tr>
<tr>
<td>Doxycycline (Vibramycin)</td>
<td><strong>Tablets and Capsules:</strong></td>
<td><strong>Avoid antacids, milk, dairy products, and iron for 1 hour before or 2 hours</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 20 mg</td>
<td><strong>Use with caution in hepatic and renal disease.</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 50 mg</td>
<td><strong>IV doses should be infused over 1 to 4 hours.</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 75 mg</td>
<td><strong>Patient should avoid prolonged exposure to direct sunlight (skin sensitivity).</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 100 mg</td>
<td><strong>Generally not recommended for use in children aged &lt;8 years because of risk</strong></td>
<td></td>
</tr>
</tbody>
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<th>Indicating Need for Medical Attention if Persistent or Bothersome</th>
<th>Special Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythromycin</td>
<td>Erythromycin-Base Tablet:</td>
<td>Less Frequent:</td>
<td>GI disturbances (nausea, vomiting, abdominal cramps)</td>
<td>Use with caution in liver disease.</td>
</tr>
<tr>
<td></td>
<td>• 250 mg</td>
<td>• Estolate may cause cholestatic jaundice, although hepatotoxicity is uncommon (2% of reported cases).</td>
<td>• Rash, urticaria</td>
<td>Oral therapy should replace IV therapy as soon as possible.</td>
</tr>
<tr>
<td></td>
<td>• 333 mg</td>
<td></td>
<td>• Increased LFTs</td>
<td>Give oral doses after meals.</td>
</tr>
<tr>
<td></td>
<td>• 500 mg</td>
<td></td>
<td></td>
<td>Parenteral administration should consist of a continuous drip or slow infusion over 1 hour or longer.</td>
</tr>
<tr>
<td></td>
<td>Delayed-Release Tablet:</td>
<td>Rare:</td>
<td></td>
<td>Adjust dose in renal failure.</td>
</tr>
<tr>
<td></td>
<td>• 250 mg</td>
<td>• QT prolongation</td>
<td></td>
<td>Erythromycin should be used with caution in neonates; hypertrophic pyloric stenosis and life-threatening episodes of ventricular tachycardia associated with prolonged QTc interval have been reported.</td>
</tr>
<tr>
<td></td>
<td>• 333 mg</td>
<td>• Hypersensitivity reactions (rash, exfoliative skin disorders including SJS)</td>
<td></td>
<td>High potential for interaction with many ARVs and other drugs.</td>
</tr>
<tr>
<td></td>
<td>• 500 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Delayed-Release Capsule:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 250 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Erythromycin Ethyl Succinate Suspension:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 200 mg</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>• 400 mg/5 mL</td>
<td></td>
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<tr>
<td></td>
<td>Oral Drops:</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>• 100 mg/2.5 mL</td>
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<tr>
<td>Erythromycin</td>
<td>Chewable Tablet:</td>
<td></td>
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<tr>
<td></td>
<td>• 200 mg</td>
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<tr>
<td></td>
<td>Tablet:</td>
<td></td>
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<tr>
<td></td>
<td>• 400 mg</td>
<td></td>
<td></td>
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<tr>
<td>Erythromycin</td>
<td>Erythromycin Estolate Suspension:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 125 mg</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>• 250 mg/5 mL</td>
<td></td>
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<tr>
<td>Erythromycin</td>
<td>Erythromycin Stearate Tablet:</td>
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<tr>
<td></td>
<td>• 250 mg</td>
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<tr>
<td></td>
<td>• 500 mg</td>
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<tr>
<td>Erythromycin</td>
<td>Erythromycin Gluceptate:</td>
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<td></td>
<td>• IV</td>
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<tr>
<td>Erythromycin</td>
<td>Erythromycin Lactobionate:</td>
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<tr>
<td></td>
<td>• IV</td>
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<tr>
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<th>Preparations</th>
<th>Major Toxicities&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Indicating Need for Medical Attention if Persistent or Bothersome</th>
<th>Special Instructions</th>
</tr>
</thead>
</table>
| Ethambutol (Myambutol) | Tablets:  
  • 100 mg  
  • 400 mg | Less Frequent:  
  • Acute gouty arthritis (secondary to hyperuricemia)  
  Rare:  
  • Hypersensitivity (rash, fever, joint pain)  
  • Peripheral neuropathy  
  • Retrobulbar optic neuritis, decreased visual acuity, loss of red-green color discrimination  
  • Bone marrow suppression  
  • Abnormal LFTs, hepatotoxicity | • GI disturbances (abdominal pain, anorexia, nausea, vomiting)  
  • Confusion  
  • Disorientation  
  • Headache | Requires dose adjustment in patients with impaired renal function.  
  Take with food to minimize gastric irritation.  
  Monitor visual acuity and red-green color discrimination regularly.  
  Monitor renal function, LFTs, and CBC.  
  Avoid concomitant use of drugs with neurotoxicity. |
| Ethionamide (Trecator-SC) | Tablets:  
  • 250 mg | Less Frequent:  
  • Hepatitis, jaundice  
  • Peripheral neuritis  
  • Psychiatric disturbances  
  Rare:  
  • Goiter or hypothyroidism  
  • Hypoglycemia  
  • Optic neuritis  
  • Skin rash | More Frequent:  
  • GI disturbances (anorexia, metallic taste, nausea, vomiting, stomatitis)  
  • Orthostatic hypotension  
  Rare:  
  • Gynecomastia | Avoid use of other neurotoxic drugs that could increase potential for peripheral neuropathy and optic neuritis.  
  Administration of pyridoxine may alleviate peripheral neuritis.  
  Take with food to minimize gastric irritation.  
  Monitor LFTs, glucose, and thyroid function. Perform periodic ophthalmologic exams. |
| Fluconazole (Diflucan) | Oral Suspension:  
  • 10 mg/mL  
  • 40 mg/mL  
  Tablets:  
  • 50 mg  
  • 100 mg  
  • 150 mg  
  • 200 mg  
  • IV | Less Frequent:  
  • Hypersensitivity (fever, chills, skin rash)  
  Rare:  
  • Agranulocytosis, eosinophilia, leukopenia, thrombocytopenia  
  • Exfoliative skin disorders (including SJS)  
  • Hepatotoxicity  
  • QT prolongation  
  • Thrombocytopenia | More Frequent:  
  • GI disturbances (abdominal pain, constipation, diarrhea, anorexia, nausea, vomiting)  
  Less Frequent:  
  • CNS effects (dizziness, drowsiness, headache)  
  • Alopecia | Can be given orally without regard to meals.  
  Shake suspension well before dosing.  
  Requires dose adjustment in patients with impaired renal function.  
  IV administration should be administered over 1–2 hours at a rate ≤200 mg/hour.  
  Daily dose is the same for oral and IV administration.  
  Multiple potential drug interactions  
  Monitor periodic LFTs, renal function, and CBC. |
Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities  (page 10 of 22)

<table>
<thead>
<tr>
<th>Drug</th>
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</tr>
</thead>
</table>
| Flucytosine  | Capsules: 250 mg, 500 mg; Oral Liquid: Extemporaneous preparation | Indicating Need for Medical Attention:  
  - More Frequent:  
    - Bone marrow suppression (especially leukopenia and thrombocytopenia)  
    - Less Frequent:  
      - Hepatotoxicity  
      - Renal toxicity (including crystalluria)  
  - Rare:  
    - Cardiac toxicity (ventricular dysfunction, myocardial toxicity, cardiac arrest)  
    - CNS symptoms (hallucinations, seizures, peripheral neuropathy)  
    - Anaphylaxis  
    - Hearing loss  
  - GI disturbances (abdominal pain, constipation, diarrhea, anorexia, nausea, vomiting)  
  - Elevated liver transaminases  
  - Skin rash  
  - CNS symptoms (headache, drowsiness, confusion, vertigo)  
  - Crystalluria  
| Monitor serum concentrations and adjust dose to maintain therapeutic levels and minimize risk of bone marrow suppression.  
Requires dose adjustment in patients with impaired renal function; use with extreme caution.  
Fatal aplastic anemia and agranulocytosis have been rarely reported.  
Oral preparations should be administered with food over a 15-minute period to minimize GI side effects  
Monitor CBC, LFTs, renal function, and electrolytes. |
| Foscarnet     | IV                                                | Indicating Need for Medical Attention if Persistent or Bothersome:  
  - Frequent:  
    - GI disturbances (abdominal pain, anorexia, nausea, vomiting)  
    - Anxiety, confusion, dizziness, headache  
    - Fever  
| Requires dose adjustment in patients with impaired renal function.  
Use adequate hydration to decrease nephrotoxicity. Avoid concomitant use of other drugs with nephrotoxicity.  
Monitor serum electrolytes, renal function, and CBC.  
Consider monitoring serum concentrations (TDM).  
IV solution of 24 mg/mL can be administered via central line but must be diluted to a final concentration not to exceed 12 mg/mL if given via peripheral line.  
Must be administered at a constant rate by infusion pump over ≥2 hours (or no faster than 1 mg/kg/minute). |
# Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 11 of 22)

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<th>Major Toxicities&lt;sup&gt;a&lt;/sup&gt;</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Ganciclovir (Cytovene)</td>
<td>Capsules: • 250 mg • 500 mg IV</td>
<td><strong>More Frequent:</strong> • Granulocytopenia • Thrombocytopenia <strong>Less Frequent:</strong> • Anemia • CNS effects (confusion, headache) • Hypersensitivity (fever, rash) • Elevated transaminase enzymes • Increase in creatinine, BUN • Phlebitis (at injection sites) <strong>Rare:</strong> • Retinal detachment • Seizures • Psychosis • Cardiac (hypertension, chest pain)</td>
<td><strong>Indicating Need for Medical Attention if Persistent or Bothersome</strong> • GI disturbances (abdominal pain, anorexia, nausea, vomiting) • Rash Requires dose adjustment in patients with renal impairment. Avoid other nephrotoxic drugs. IV infusion over at least 1 hour. In-line filter required. Maintain good hydration. Undiluted IV solution is alkaline (pH 11); use caution in handling and preparing solutions and avoid contact with skin and mucus membranes. Administer oral doses with food to increase absorption. Do not open or crush capsules. Monitor CBC, LFTs, renal function; conduct ophthalmologic examinations.</td>
</tr>
<tr>
<td>Interferon-alfa-2B (IFN-α-2B; Intron)</td>
<td>Parenteral (SQ or IV use)</td>
<td><strong>More Frequent:</strong> • Hematologic toxicity (leukopenia, thrombocytopenia) • Neurotoxicity (confusion, depression, insomnia, anxiety) • Injection erythema <strong>Less Frequent:</strong> • Cardiovascular effects (chest pain, hypertension, arrhythmias, hypotension) • Hypoesthesia/paresthesia <strong>Rare:</strong> • Abnormality or loss of vision • Allergic reaction (rash, hives) • Hypothyroidism • Development of antinuclear antibodies</td>
<td><strong>More Frequent:</strong> • Flu-like syndrome (myalgia, arthralgia, fever, chills, headache, back pain, malaise, fatigue) • GI disturbances (abdominal pain, anorexia, nausea, vomiting, diarrhea, dyspepsia) • Pharyngitis, dry mouth <strong>Less Frequent:</strong> • Alopecia • Epistaxis • Elevated serum transaminases, serum creatinine and BUN, glucose, triglycerides</td>
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### Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 12 of 22)

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</thead>
<tbody>
<tr>
<td><strong>Interferon-alfa-2B</strong> (IFN-α-2B; Intron), continued</td>
<td></td>
<td></td>
<td>(ascites, coagulopathy, jaundice). IFN-α-2B should be discontinued. Reconstituted solution stable for 24 hours when refrigerated. Monitor CBC, renal function, LFTs, thyroid function, and glucose.</td>
</tr>
<tr>
<td><strong>Isoniazid</strong> (Nydrazid)</td>
<td>Oral Syrup: • 10 mg/mL Tablets: • 100 mg • 300 mg IM</td>
<td><strong>More Frequent:</strong> • Hepatitis prodromal syndrome (anorexia, weakness, vomiting) • Hepatitis • Peripheral neuritis  <strong>Rare:</strong> • Blood dyscrasias • Hypersensitivity (fever, rash, joint pain) • Neurotoxicity (includes seizure) • Optic neuritis  <strong>More Frequent:</strong> • GI disturbances (abdominal pain, nausea, vomiting, diarrhea) • Elevated liver transaminases • Pyridoxine deficiency</td>
<td>Take with food to minimize gastric irritation. Take ≥1 hour before aluminum-containing antacids. Hepatitis less common in children. Use with caution in patients with hepatic function impairment, severe renal failure, or history of seizures. Pyridoxine supplementation should be provided for all HIV-infected children. Monitor LFTs and periodic ophthalmologic examinations.</td>
</tr>
<tr>
<td><strong>Itraconazole</strong> (Sporanox)</td>
<td>Oral Solution: • 10 mg/mL Capsules: • 100 mg IV</td>
<td><strong>Less frequent:</strong> • Hypersensitivity (fever, chills, skin rash) • Hypokalemia (can be associated with cardiac arrhythmias)  <strong>Rare:</strong> • Hepatotoxicity • Hematologic abnormalities (thrombocytopenia, leukopenia)  <strong>More Frequent:</strong> • GI disturbances (abdominal pain, constipation, diarrhea, anorexia, nausea, vomiting)  <strong>Less Frequent:</strong> • CNS effects (dizziness, drowsiness, headache) • Rash</td>
<td>Oral Solution: • Give on an empty stomach because gastric acid increases absorption. Capsules: • Administer after a full meal to increase absorption. Itraconazole oral solution has 60% greater bioavailability compared with capsules, and the oral solution and capsules should not be used interchangeably. IV infusion over 1 hour. Multiple potential drug interactions Monitor LFTs and potassium levels. Monitor serum concentrations (TDM) in severe infections.</td>
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</table>
### Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities

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<th>Special Instructions</th>
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<tbody>
<tr>
<td><strong>Kanamycin</strong></td>
<td>IV IM</td>
<td>More Frequent:</td>
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<tr>
<td></td>
<td></td>
<td>• Nephrotoxicity</td>
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<td></td>
<td></td>
<td>• Neurotoxicity (including</td>
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<td></td>
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<td>muscle twitching, seizures)</td>
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<td></td>
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<td>• Ototoxicity, both auditory</td>
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<td></td>
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<td>and vestibular</td>
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<td>Less Frequent:</td>
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<tr>
<td></td>
<td></td>
<td>• Hypersensitivity (skin rash,</td>
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<td>redness or swelling)</td>
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<td>Rare:</td>
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<td></td>
<td></td>
<td>• Neuromuscular blockade</td>
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<tr>
<th>Drug</th>
<th>Preparations</th>
<th>Major Toxicities&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Special Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketocanazole (Nizoral)</td>
<td>Tablets: 200 mg</td>
<td>Less Frequent:</td>
<td>Adverse GI effects occur less often when administered with food.</td>
</tr>
<tr>
<td></td>
<td>Topical:</td>
<td>• Hypersensitivity (fever,</td>
<td>Drugs that decrease gastric acidity or sucralfate should be administered ≥2 hours after ketocanazole.</td>
</tr>
<tr>
<td></td>
<td>Shampoo</td>
<td>chill, skin rash)</td>
<td>Disulfiram-like reactions have occurred in patients ingesting alcohol.</td>
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<td></td>
<td>Cream</td>
<td>• Hepatotoxicity (including</td>
<td>Hepatotoxicity is an idiosyncratic reaction, usually reversible when stopping the drug, but rare fatalities can occur any time during therapy; more common in females and adults &gt;40 years, but cases reported in children.</td>
</tr>
<tr>
<td></td>
<td>Gel</td>
<td>hepatic failure)</td>
<td>High-dose ketocanazole suppresses corticosteroid secretion, lowers serum testosterone concentration (reversible).</td>
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<td></td>
<td>Foam</td>
<td>Rare:</td>
<td>Multiple potential drug interactions.</td>
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<td></td>
<td>Suspension:</td>
<td>• Gynecomastia</td>
<td>Monitor LFTs.</td>
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<td></td>
<td>Extemporaneous preparation</td>
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<tr>
<td></td>
<td></td>
<td>• Impotence</td>
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<td></td>
<td></td>
<td>• Menstrual irregularities</td>
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<td>• Photophobia</td>
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<tr>
<td><strong>Mefloquine (Lariam)</strong></td>
<td>Tablets: 250 mg</td>
<td>More Frequent: CNS (psychosis, depression, hallucinations, paranoia, seizures)</td>
<td>Side effects less prominent in children.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rare: Blood dyscrasias</td>
<td>Administer with food and plenty of water.</td>
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<td></td>
<td></td>
<td>Cholestasis, elevated bilirubin</td>
<td>Tablets can be crushed and added to food; bitter tasting so administer with foods that can mask the taste</td>
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<tr>
<td></td>
<td></td>
<td>Indicating Need for Medical Attention</td>
<td>Monitor LFTs.</td>
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<td></td>
<td></td>
<td>Indicating Need for Medical Attention if Persistent or Bothersome</td>
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<tr>
<td></td>
<td></td>
<td>Rash</td>
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<tr>
<td></td>
<td></td>
<td>GI disturbances (abdominal pain, constipation, diarrhea, anorexia, nausea, vomiting)</td>
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<tr>
<td></td>
<td></td>
<td>CNS (dizziness, vivid dreams, insomnia)</td>
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<td></td>
<td></td>
<td>Tinnitus, blurred vision</td>
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<tr>
<td><strong>Nitazoxanide (Alinia)</strong></td>
<td>Oral Suspension 20 mg/mL Tablets: 500 mg</td>
<td>More Frequent: GI disturbances (abdominal pain, nausea, vomiting)</td>
<td>Should be given with food.</td>
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<tr>
<td></td>
<td></td>
<td>Headache</td>
<td>Shake suspension well prior to dosing.</td>
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<td></td>
<td></td>
<td>Rare: Scleral icterus</td>
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<tr>
<td></td>
<td></td>
<td>Rash</td>
<td></td>
</tr>
<tr>
<td><strong>P-Aminosalicylic Acid (Paser)</strong></td>
<td>Delayed Release Granules 4 g per packet</td>
<td>Rare: Hypersensitivity (fever, skin rash, exfoliative dermatitis, mono-like or lymphoma-like syndrome, jaundice, hepatitis, pericarditis, vasculitis, hematologic abnormalities including hemolytic anemia, hypoglycemia, optic neuritis, encephalopathy, reduction in prothrombin) Crystalluria Hemolytic anemia</td>
<td>Should not be administered to patients with severe renal disease.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Indicating Need for Medical Attention</td>
<td>Drug should be discontinued at first sign of hypersensitivity reaction (rash, fever, and GI symptoms typically precede jaundice).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Indicating Need for Medical Attention if Persistent or Bothersome</td>
<td>Vitamin B12 therapy should be considered in patients receiving for &gt;1 month.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>GI disturbances (abdominal pain, nausea, vomiting, diarrhea)</td>
<td>Administer granules by sprinkling on acidic foods such as applesauce or yogurt or a fruit drink like tomato or orange juice.</td>
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<td>Maintain urine at neutral or alkaline pH to avoid crystalluria.</td>
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<td>The granule soft “skeleton” may be seen in the stool.</td>
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<td></td>
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<td></td>
<td>Monitor CBC and LFTs.</td>
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</tbody>
</table>
### Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities

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</table>
| Pegylated Interferon Alfa-2A (Pegasys)    | Injection: Vials and prefilled syringes | More Frequent:  
- Hematologic toxicity (leukopenia, thrombocytopenia)  
- Neurotoxicity (confusion, depression, insomnia, anxiety)  
- Injection erythema  
- Less Frequent:  
- Cardiovascular effects (chest pain, hypertension, arrhythmias, hypotension)  
- Hypoesthesia/paresthesia  
- Rare:  
- Vision abnormalities or loss of vision  
- Allergic reaction (rash, hives)  
- Hypothyroidism  
- Development of antinuclear antibodies | More Frequent:  
- Flu-like syndrome (myalgia, arthralgia, fever, chills, headache, back pain, malaise, fatigue)  
- GI disturbances (abdominal pain, anorexia, nausea, vomiting, diarrhea, dyspepsia)  
- Pharyngitis, dry mouth  
- Less Frequent:  
- Alopecia  
- Epistaxis  
- Elevated serum transaminases, serum creatinine and BUN, glucose, triglycerides | Toxicity dose-related. Dose modifications based on type and degree of toxicity.  
For non-life threatening reactions, reduce dose or temporarily discontinue drug and restart at low doses with stepwise increases.  
If patients have visual complaints, an ophthalmologic exam should be performed to detect possible retinal hemorrhage or retinal artery or vein obstruction.  
Should not be used in children with decompensated hepatic disease, significant cytopenia, autoimmune disease, or significant pre-existing renal or cardiac disease.  
If symptoms of hepatic decompensation occur (ascites, coagulopathy, jaundice), Peg-IFN-α-2A should be discontinued.  
Monitor CBC, renal function, LFTs, thyroid function, and glucose.  
Store vials and syringes in refrigerator. Protect from light.  
Administer SQ in abdomen or thigh. Rotate injection sites. |
| Pegylated Interferon Alfa-2B (Peginteron) | Injection: Vials and prefilled syringes | More Frequent:  
- Hematologic toxicity (leukopenia, thrombocytopenia)  
- Neurotoxicity (confusion, depression, insomnia, anxiety)  
- Injection erythema  
- Less Frequent:  
- Cardiovascular effects (chest pain, hypertension, arrhythmias, hypotension)  
- Hypoesthesia/paresthesia | More Frequent:  
- Flu-like syndrome (myalgia, arthralgia, fever, chills, headache, back pain, malaise, fatigue)  
- GI disturbances (abdominal pain, anorexia, nausea, vomiting, diarrhea, dyspepsia)  
- Pharyngitis, dry mouth  
- Less Frequent:  
- Alopecia  
- Epistaxis  
- Elevated serum | Toxicity dose-related. Dose modifications based on type and degree of toxicity.  
For non-life threatening reactions, reduce dose or temporarily discontinue drug and restart at low doses with stepwise increases.  
If patients have visual complaints, an ophthalmologic exam should be performed to detect possible retinal hemorrhage or retinal artery or vein obstruction. |
Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities  (page 16 of 22)

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<td></td>
<td>Indicating Need for Medical Attention</td>
<td>Indicating Need for Medical Attention if Persistent or Bothersome</td>
</tr>
<tr>
<td>Pegylated Interferon Alfa-2B (Peginterferon)</td>
<td>IV, Aerosol</td>
<td>Rare:</td>
<td>transaminases, serum creatinine and BUN, glucose, triglycerides</td>
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<tr>
<td></td>
<td></td>
<td>Abnormality or loss of vision</td>
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<td>Allergic reaction (rash, hives)</td>
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<td>Hypothyroidism</td>
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<td></td>
<td>Development of antinuclear antibodies</td>
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<td>Should not be used in children with decompensated hepatic disease, significant cytopenia, autoimmune disease, or significant pre-existing renal or cardiac disease. If symptoms of hepatic decompensation occur (ascites, coagulopathy, jaundice), Peg-IFN-α-2A should be discontinued. Monitor CBC, renal function, LFTs, thyroid function, and glucose. Store vials and syringes in refrigerator. Protect from light. Administer SQ in abdomen or thigh. Rotate injection sites.</td>
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<tr>
<td>Pentamidine (Pentam)</td>
<td>IV, Aerosol</td>
<td>IV More Frequent:</td>
<td>Rapid infusion may result in precipitous hypotension; IV infusion should be administered over ≥1 hour (preferably 2 hours). Cytolytic effect on pancreatic beta islet cells, leading to insulin release, can result in prolonged severe hypoglycemia (usually occurs after 5–7 days of therapy, but can also occur after the drug is discontinued); risk increased with higher dose, longer duration of therapy, and re-treatment within 3 months of prior treatment. Hyperglycemia and diabetes mellitus can occur up to several months after drug discontinued. Monitor LFTs, renal function, glucose, electrolytes, BP. Inhalation: A special nebulizer is required for aerosol administration. Medical personnel should be trained in the proper administration of aerosolized pentamidine.</td>
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<td>Nephrotoxicity</td>
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<td>Hypoglycemia</td>
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<td>Hyperglycemia or diabetes mellitus</td>
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<td>Elevated liver transaminases</td>
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<td>Hypotension</td>
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<td>Leukopenia or neutropenia</td>
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<td>Thrombocytopenia</td>
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<td>Less Frequent:</td>
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<td></td>
<td></td>
<td>Anemia</td>
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<td></td>
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<td>Cardiac arrhythmias</td>
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<td>Hypersensitivity (skin rash, fever)</td>
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<td>Pancreatitis</td>
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<td>Phlebitis</td>
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<td>Sterile abscess (at site injection)</td>
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<td>Aresol More Frequent:</td>
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<td></td>
<td></td>
<td>Sneezing</td>
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<td></td>
<td>Cough</td>
<td></td>
</tr>
</tbody>
</table>
### Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities

<table>
<thead>
<tr>
<th>Drug</th>
<th>Preparations</th>
<th>Major Toxicities&lt;sup&gt;a&lt;/sup&gt; Indicating Need for Medical Attention</th>
<th>Special Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Posaconazole</strong></td>
<td>Oral Solution:</td>
<td>Less frequent:</td>
<td>Must be given with meals. Adequate absorption is dependent on food for efficacy.</td>
</tr>
<tr>
<td>(Noxafil)</td>
<td>• 40 mg/mL</td>
<td>• Hypersensitivity (fever, chills, skin rash)</td>
<td>Monitor LFTs, renal function and electrolytes.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Anaphylactoid reaction with IV infusion</td>
<td>Monitor serum drug concentrations (TDM).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Rare:</td>
<td>Shake suspension prior to dosing.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hepatotoxicity (including hepatic failure)</td>
<td></td>
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<td></td>
<td></td>
<td>• Exfoliative skin disorders (including SJS)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Renal dysfunction</td>
<td></td>
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<td></td>
<td></td>
<td>• Cardiac arrhythmias (QT interval prolongation, torsades de pointes, hypertension)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Hemolytic uremic syndrome</td>
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<td></td>
<td></td>
<td>• Pulmonary embolism</td>
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<td></td>
<td></td>
<td>• Neutropenia</td>
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<td></td>
<td></td>
<td><strong>Indicating Need for Medical Attention if Persistent or Bothersome</strong></td>
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<tr>
<td></td>
<td></td>
<td>• Bone marrow suppression</td>
<td></td>
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<td></td>
<td></td>
<td>• Muscular pain</td>
<td></td>
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<td></td>
<td></td>
<td>• CNS: headache, dizziness, fatigue</td>
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<td></td>
<td></td>
<td>• Elevated serum transaminases</td>
<td></td>
</tr>
<tr>
<td><strong>Primaquine</strong></td>
<td>Tablets:</td>
<td>More Frequent:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 15 mg (base) = 26.3 mg primaquine phosphate</td>
<td>• Hemolytic anemia (with G6PD deficiency)</td>
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<tr>
<td></td>
<td></td>
<td><strong>Less Frequent:</strong></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Methemoglobinemia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Rare:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Leukopenia</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Indicating Need for Medical Attention if Persistent or Bothersome</strong></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• GI disturbances (nausea, vomiting)</td>
<td></td>
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<td></td>
<td></td>
<td><strong>Special Instructions</strong></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Take with meals or antacids to minimize gastric irritation.</td>
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<td></td>
<td>• Store in a light-resistant container.</td>
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<td></td>
<td></td>
<td>• Bitter taste.</td>
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<tr>
<td></td>
<td></td>
<td>• Monitor CBC.</td>
<td></td>
</tr>
<tr>
<td><strong>Pyrazinamide</strong></td>
<td>Tablets:</td>
<td>More Frequent:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 500 mg</td>
<td>• Arthralgia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oral Suspension:</td>
<td><strong>Less Frequent:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Extemporaneous preparation</td>
<td>• Hepatotoxicity (dose-related)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Rare:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Acute gouty arthritis secondary to hyperuricemia</td>
<td></td>
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<td></td>
<td></td>
<td>• Thrombocytopenia, anemia</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Interstitial nephritis</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Porphyria</td>
<td></td>
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<td></td>
<td><strong>Indicating Need for Medical Attention if Persistent or Bothersome</strong></td>
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<tr>
<td></td>
<td></td>
<td>• Skin rash, pruritus</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Photosensitivity</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Malaise</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• GI disturbances (nausea, vomiting)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Arthralgia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hyperuricemia</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Special Instructions</strong></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Avoid in patients with severe hepatic impairment.</td>
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<td></td>
<td></td>
<td>• Reduce dose in patients with renal or hepatic impairment.</td>
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<tr>
<td></td>
<td></td>
<td>• Monitor LFTs and uric acid.</td>
<td></td>
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<tr>
<td><strong>Pyrimethamine</strong></td>
<td>Tablet:</td>
<td>Less Frequent:</td>
<td></td>
</tr>
<tr>
<td>(Daraprim)</td>
<td>• 25 mg</td>
<td>• Neutopenia</td>
<td></td>
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<tr>
<td></td>
<td>Oral Suspension:</td>
<td>• Thrombocytopenia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Extemporaneous preparation</td>
<td>• Megaloblastic anemia</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Rare:</strong></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• SJS</td>
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<tr>
<td></td>
<td></td>
<td>• Seizure</td>
<td></td>
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<td></td>
<td></td>
<td><strong>Indicating Need for Medical Attention if Persistent or Bothersome</strong></td>
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<tr>
<td></td>
<td></td>
<td>• Skin rash</td>
<td></td>
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<td></td>
<td></td>
<td>• Photosensitivity</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Dry mouth</td>
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<td></td>
<td></td>
<td>• GI disturbances (nausea, vomiting)</td>
<td></td>
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<td></td>
<td></td>
<td>• CNS (depression, insomnia)</td>
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<td></td>
<td></td>
<td><strong>Special Instructions</strong></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• To prevent hematologic toxicity, administer with leucovorin.</td>
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<td></td>
<td></td>
<td>• Monitor CBC.</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Indicating Need for Medical Attention:
- Less frequent:
- More frequent:
- Rare:

**Special Instructions**:
- Must be given with meals. Adequate absorption is dependent on food for efficacy.
- Monitor LFTs, renal function and electrolytes.
- Monitor serum drug concentrations (TDM).
- Shake suspension prior to dosing.
- Take with meals or antacids to minimize gastric irritation.
- Store in a light-resistant container.
- Bitter taste.
- Monitor CBC.
- Avoid in patients with severe hepatic impairment.
- Reduce dose in patients with renal or hepatic impairment.
- Monitor LFTs and uric acid.
- To prevent hematologic toxicity, administer with leucovorin.
- Monitor CBC.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Preparations</th>
<th>Major Toxicities&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Special Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Indicating Need for Medical Attention</td>
<td>Indicating Need for Medical Attention if Persistent or Bothersome</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Very Frequent:</td>
<td></td>
</tr>
<tr>
<td>Quinidine</td>
<td>IV</td>
<td>Serious:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cardiac arrhythmias</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• QT interval prolongation</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hypoglycemia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hemolytic anemia (with G6PD deficiency)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hepatotoxicity</td>
<td></td>
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<td></td>
<td></td>
<td>EKG monitoring is standard of care.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Do not give by bolus infusion.</td>
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<tr>
<td></td>
<td></td>
<td>If EKG changes observed, slow infusion rate.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monitor CBC and LFTs.</td>
<td></td>
</tr>
<tr>
<td>Ribavirin</td>
<td>Virazole Powder for solution for nebulization</td>
<td>Very Frequent:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rebetol Oral capsules and oral solution</td>
<td>• Cinchonism—syndrome of tinnitus, reversible high-frequency hearing loss, deafness, vertigo,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Copegus, Ribosphere, Ribapak Oral tablets and capsules</td>
<td>• blurred vision, diplopia, photophobia, headache, confusion, and delirium; dose dependent</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Powder for Solution for Nebulization:</td>
<td>• Hemolytic anemia (with associated potential for increase in unconjugated bilirubin and uric</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Reconstituted product contains 20 mg/mL</td>
<td>acid)</td>
<td></td>
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<tr>
<td></td>
<td>Oral Solution:</td>
<td>Less Frequent:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 40 mg/mL</td>
<td>• Neutropenia, thrombocytopenia, anemia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Capsules:</td>
<td>• Pancreatitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 200 mg</td>
<td>• CNS effects (fatigue, headache, insomnia, depression)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tablets:</td>
<td>• GI disturbances (abdominal pain, nausea, vomiting)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 200 mg</td>
<td>• Skin rash</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 400 mg</td>
<td>• Myalgia, arthralgia, weakness</td>
<td></td>
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<tr>
<td></td>
<td>• 600 mg</td>
<td>• Enhances phosphorylation of didanosine; use with caution because of increased risk of</td>
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<td></td>
<td></td>
<td>Pancreatitis/mitochondrial toxicity.</td>
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<td></td>
<td></td>
<td>Oral solution contains propylene glycol.</td>
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<td></td>
<td></td>
<td>Teratogenic/embryocidal.</td>
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<tr>
<td></td>
<td></td>
<td>Contraindicated in pregnant women and their male partners. Avoid pregnancy for additional</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>6 months after treatment.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monitor CBC, renal function, LFTs, and thyroid function. Perform pregnancy tests regularly</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>while on therapy.</td>
<td></td>
</tr>
</tbody>
</table>
### Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities

<table>
<thead>
<tr>
<th>Drug</th>
<th>Preparations</th>
<th>Major Toxicities&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Special Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rifabutin</strong></td>
<td>Capsules: 150 mg</td>
<td>More Frequent:</td>
<td>Preferably take on empty stomach, but may be administered with food in patients with GI intolerance.</td>
</tr>
<tr>
<td>(Mycobutin)</td>
<td>Oral Suspension: Extemporaneous preparation</td>
<td>• Allergic reaction (rash, pruritus)</td>
<td>The contents of capsules may be mixed with applesauce if patient is unable to swallow capsule.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Neutropenia</td>
<td>May cause reddish to brown-orange color urine, feces, saliva, sweat, skin, or tears (can discolor soft contact lenses).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less Frequent:</td>
<td>Ulveitis seen with high-dose rifabutin (i.e., adults &gt;300 mg/day), especially when combined with clarithromycin.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Asthenia</td>
<td>Multiple potential drug interactions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rare:</td>
<td>Use with caution in patients with renal or hepatic impairment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Arthralgia, myalgia</td>
<td>Monitor CBC, LFTs; conduct ophthalmologic examinations.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Change in taste</td>
<td>Reduce dose in patients with renal impairment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pseudojaundice</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Thrombocytopenia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Uveitis</td>
<td></td>
</tr>
<tr>
<td><strong>Rifampin</strong></td>
<td>Oral Suspension: Extemporaneous preparation</td>
<td>Less Frequent:</td>
<td>Preferably take on empty stomach, but can be administered with food in patients with GI intolerance; take with full glass of water.</td>
</tr>
<tr>
<td>(Rifadin)</td>
<td>Capsules: 150 mg</td>
<td>• Flu-like syndrome</td>
<td>Suspension formulation stable for 30 days. Shake well prior to dosing.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rare:</td>
<td>May cause reddish to brown-orange color urine, feces, saliva, sweat, skin, or tears (can discolor soft contact lenses).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Blood dyscrasias</td>
<td>Multiple potential drug interactions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hepatitis prodromal syndrome (anorexia, nausea, vomiting, weakness)</td>
<td>Use with caution in patients with hepatic impairment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hepatitis</td>
<td>Administer IV by slow infusion. Extravasation may cause local irritation and inflammation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Interstitial nephritis</td>
<td>Monitor CBC and LFTs.</td>
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<td></td>
<td></td>
<td>• Exfoliative skin disorders (including SJS)</td>
<td></td>
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<td></td>
<td>• GI disturbances (abdominal pain, diarrhea)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• CNS effects (fatigue, headache, insomnia, depression)</td>
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<tr>
<td></td>
<td></td>
<td>• Rash</td>
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<td></td>
<td>• Discoloration of body fluids</td>
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<td></td>
<td></td>
<td>• Elevated serum transaminases</td>
<td></td>
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<td></td>
<td></td>
<td>• Visual changes</td>
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</tbody>
</table>
Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 20 of 22)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Preparations</th>
<th>Major Toxicities&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Special Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Indicating Need for</td>
<td>Indicating Need for Medical Attention if Medical Attention if Persistent or Bothersome</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Medical Attention</td>
<td>Persistent or Bothersome</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>IM</td>
<td>More Frequent:</td>
<td>• CNS effects (headache, ataxia, dizziness)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Nephrotoxicity</td>
<td>Usual route of administration is deep IM injection into large muscle mass.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Neurotoxicity (including</td>
<td>For patients who cannot tolerate IM injections, dilute to 12–15 mg in 100 mL of 0.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>muscle twitching, seizures)</td>
<td>sodium chloride; must be infused over 30 to 60 minutes to avoid neuromuscular blockade.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Peripheral neuritis</td>
<td>Requires dose adjustment in patients with impaired renal function.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ototoxicity, both auditory</td>
<td>Monitor renal function and hearing periodically (e.g., monthly) in children on prolonged therapy.</td>
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<tr>
<td></td>
<td></td>
<td>and vestibular</td>
<td>Monitor serum concentrations (TDM).</td>
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<tr>
<td></td>
<td></td>
<td>Less Frequent:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hypersensitivity (skin rash,</td>
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<td></td>
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<td>redness, or swelling)</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>• Optic neuritis</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Bone marrow suppression</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rare:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Neuromuscular blockade</td>
<td></td>
</tr>
<tr>
<td>Sulfadiazine</td>
<td>Tablets:</td>
<td>Rare:</td>
<td>• GI disturbances (abdominal pain, diarrhea, nausea)</td>
</tr>
<tr>
<td></td>
<td>• 500 mg</td>
<td>• Crystalluria, renal failure</td>
<td>Ensure adequate fluid intake to avoid crystalluria.</td>
</tr>
<tr>
<td></td>
<td>Oral Suspension:</td>
<td>• Bone marrow suppression/</td>
<td>Monitor CBC, renal function, and urinalysis.</td>
</tr>
<tr>
<td></td>
<td>• Extemporaneous</td>
<td>blood dyscrasias</td>
<td>Monitor serum concentrations (TDM) if serious infection.</td>
</tr>
<tr>
<td></td>
<td>preparation</td>
<td>• Severe hypersensitivity</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>syndrome</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Hemolytic anemia (with</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>G6PD deficiency)</td>
<td></td>
</tr>
<tr>
<td>Trimethoprim-Sulfamethoxazole (TMP-SMX) (Bactrim, Septra)</td>
<td>Oral Suspension:</td>
<td>More Frequent:</td>
<td>• GI disturbances (anorexia, nausea, vomiting, diarrhea)</td>
</tr>
<tr>
<td></td>
<td>• TMP 8 mg/mL and SMX 40 mg/mL</td>
<td>• Skin rash</td>
<td>Requires dose adjustment in patients with impaired renal function.</td>
</tr>
<tr>
<td></td>
<td>Tablets</td>
<td>Less Frequent:</td>
<td>Maintain adequate fluid intake to prevent crystalluria and stone formation (take with full glass of water).</td>
</tr>
<tr>
<td></td>
<td>Single Strength:</td>
<td>• Hypersensitivity reactions</td>
<td>Potential for photosensitivity skin reaction with sun exposure.</td>
</tr>
<tr>
<td></td>
<td>• TMP 80 mg and SMX 400 mg</td>
<td>(skin rash, fever)</td>
<td>IV infusion over 60 to 90 minutes</td>
</tr>
<tr>
<td></td>
<td>Double Strength:</td>
<td>• Hematologic toxicity</td>
<td>Monitor CBC, renal function.</td>
</tr>
<tr>
<td></td>
<td>• TMP 160 mg and SMX 800 mg</td>
<td>(leukopenia, neutropenia,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>thrombocytopenia, anemia)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rare:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Exfoliative skin disorders</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(including SJS)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hemolytic anemia (with G6PD deficiency)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Methemoglobinemia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Renal toxicity (crystalluria, nephritis, tubular necrosis)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• CNS toxicity (aseptic meningitis)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pseudomembranous colitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cholestatic hepatitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Thyroid function</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>disturbance</td>
<td></td>
</tr>
</tbody>
</table>
### Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities

<table>
<thead>
<tr>
<th>Drug</th>
<th>Preparations</th>
<th>Major Toxicities&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Special Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Indicating Need for Medical Attention</td>
<td>Indicating Need for Medical Attention if Persistent or Bothersome</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Thrombotic thrombocytopenia purpura/hemolytic uremic syndrome has been reported in HIV-infected adults with advanced disease receiving high (i.e., 8 g/day) but not low doses. Monitor CBC and renal function.</td>
</tr>
</tbody>
</table>
| Valacyclovir (Valtrex)      | Tablets:  
• 500 mg  
• 1 g  
**Note:** An oral suspension formulation 50 mg/mL can be prepared in Ora-Sweet or Syrpsa syrups | Rare:  
• Renal failure  
• Bone marrow suppression  
• Thrombotic microangiopathy/hemolytic uremic syndrome  
• CNS (psychosis, seizures, delirium) | More Frequent:  
• Headache, nausea  
**Less Frequent:**  
• Arthralgia  
• Dizziness, fatigue  
• GI disturbances (diarrhea or constipation, anorexia, abdominal pain, vomiting)  
• Dysmenorrhea |
| Valganciclovir (Valcyte)   | Tablets:  
• 450 mg  
**Oral Solution:**  
• 50 mg/mL | More Frequent:  
• Granulocytopenia  
• Thrombocytopenia  
**Less Frequent:**  
• Anemia  
• CNS effects (seizures, psychosis, hallucinations  
• Hypersensitivity (fever, rash)  
• Elevated transaminase enzymes  
• Increase in creatinine, BUN  
• Retinal detachment | More Frequent:  
• GI disturbances (abdominal pain, anorexia, nausea, vomiting)  
• CNS effects (headache, insomnia)  
Requires dose adjustment in patients with renal impairment.  
Avoid other nephrotoxic drugs.  
Tablets should not be broken or crushed.  
Monitor CBC and renal function.  
Potentially teratogenic and carcinogenic. |
Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities  (page 22 of 22)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Preparations</th>
<th>Major Toxicitiesa</th>
<th>Special Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voriconazole</td>
<td>Tablet:</td>
<td></td>
<td>Oral tablets should be taken 1 hour before or after a meal.</td>
</tr>
<tr>
<td></td>
<td>• 50 mg</td>
<td></td>
<td>Shake oral suspension well prior to dosing.</td>
</tr>
<tr>
<td></td>
<td>• 200 mg</td>
<td></td>
<td>Maximum IV infusion rate 3 mg/kg/hour over 1 to 2 hours.</td>
</tr>
<tr>
<td></td>
<td>Oral Suspension:</td>
<td></td>
<td>Oral administration to patients with impaired renal function if possible (accumulation of IV vehicle occurs in patients with renal insufficiency)</td>
</tr>
<tr>
<td></td>
<td>• 40 mg/mL</td>
<td></td>
<td>Dose adjustment needed if hepatic insufficiency.</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td></td>
<td>Visual disturbances common (&gt;30%) but transient and reversible when drug is discontinued.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Multiple potential drug interactions</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Monitor renal function, electrolytes, and LFTs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Consider monitoring serum concentrations (TDM).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less Frequent:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hypersensitivity (fever, chills, skin rash)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Anaphylactoid reaction with IV infusion</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rare:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hepatotoxicity (including hepatic failure)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Exfoliative skin disorders (including SJS)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Renal dysfunction</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cardiac arrhythmias</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pancreatitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• QT prolongation</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Electrolyte abnormalities</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Optic neuritis, papilledema</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>More Frequent:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Visual changes, dose-related (photophobia, blurry vision)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• CNS effects (dizziness, drowsiness, headache)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• GI disturbances (abdominal pain, constipation, diarrhea, anorexia, nausea, vomiting)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Photosensitivity</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rare:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Gynecomastia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Elevated serum transaminases</td>
<td></td>
</tr>
</tbody>
</table>

*a The toxicities listed in the table have been selected based on their potential clinical significance and are not inclusive of all side effects reported for a particular drug.

Key to Acronyms: ARV = antiretroviral; BP = blood pressure; BUN = blood urea nitrogen; CBC = complete blood count; CDC = Centers for Disease Control and Prevention; CNS = central nervous system; Cr = creatinine; CrCl = creatinine clearance; EKG = electrocardiogram; G6PD = glucose-6-phosphate dehydrogenase; GI = gastrointestinal; IFN-α = interferon alfa; IM = intramuscular; IND = investigational new drug; IV = intravenous; LFT = liver function test; SJS = Stevens-Johnson Syndrome; SMX = sulfamethoxazole; SQ = subcutaneous; TDM = therapeutic drug monitoring; TMP = trimethoprim
There is the potential for significant drug interactions and overlapping toxicities in patients receiving medications for treatment or prevention of opportunistic infections (OIs). These patients often are receiving other medications, including antiretrovirals that interfere with metabolism or elimination of OI medications. In particular, protease inhibitors and non-nucleoside reverse transcriptase inhibitors affect the CYP450 or other transporter systems and may be associated with clinically significant drug interactions. The integrase inhibitor raltegravir is metabolized by UGT1A1 and may be a suitable option when trying to minimize interactions with other drug classes.

Table 5 provides clinicians with information regarding known or suspected drug interactions between drugs commonly used for treatment or prevention of HIV-associated OIs and treatment of HIV infection. Drug interaction information is generally obtained from studies involving healthy adult volunteers. Some pharmacokinetic (PK) data are available from studies involving HIV-infected adults, whereas data in children are extremely limited. New information continues to become available and it is important to carefully review a patient’s current medications, including prescription and over-the-counter medications. It is difficult to predict the interaction potential when three or more drugs with similar metabolic pathways are co-administered and there is substantial inter-patient variability in the magnitude of these interactions. When possible, alternative agents with less drug interaction potential or use of therapeutic drug monitoring should be considered.

Table 5 contains only a partial listing of drug interactions for drugs used to treat or prevent OIs. The links below are excellent resources for investigating the potential for drug interactions. These tools include more comprehensive information and provide up-to-date information as new PK data become available.

http://www.hiv-druginteractions.org/
http://tdm.pharm.buffalo.edu/home/di_search/
http://www.drugs.com/drug_interactions.html
http://hivinsite.ucsf.edu/InSite?page=ar-00-02
http://www.nynjaetc.org/clinical_support.html
http://epocrates.com
Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Overlapping Toxicities</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir (Zovirax)</td>
<td>Overlapping Toxicities:</td>
<td>Monitor for toxicities of these drugs.</td>
</tr>
<tr>
<td></td>
<td>• Nephrotoxic drugs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>* The drug interactions included in this table were selected on the basis of their potential clinical significance and are not</td>
<td></td>
</tr>
<tr>
<td></td>
<td>inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information</td>
<td></td>
</tr>
<tr>
<td></td>
<td>on drug interactions).</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Increased Concentrations (Both Drugs) and Overlapping Toxicities:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Antivirals: valacyclovir, valganciclovir, ganciclovir, cidovir, cidovir</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ARVs: tenofovir</td>
<td></td>
</tr>
<tr>
<td>Albendazole</td>
<td>Increases Albendazole Concentrations:</td>
<td>Caution advised.</td>
</tr>
<tr>
<td></td>
<td>• Anthelmintic drugs: praziquantel</td>
<td></td>
</tr>
<tr>
<td>Amikacin</td>
<td>Overlapping Toxicities:</td>
<td>Caution advised. Avoid combination of amikacin and cidovir.</td>
</tr>
<tr>
<td></td>
<td>• Anti-tuberculosis drugs (injectable): streptomycin, kanamycin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Nephrotoxic or ototoxic drugs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Antimycobacterial drugs: capreomycin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Antivirals: cidovir</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Bone marrow suppressant drugs: corticosteroids</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Nephrotoxic drugs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Neuromuscular blocking drugs</td>
<td></td>
</tr>
<tr>
<td>Atovaquone</td>
<td>Decreases Atovaquone Concentrations:</td>
<td>Co-administration of atovaquone and rifampin should be avoided.</td>
</tr>
<tr>
<td></td>
<td>• Antimycobacterial drugs: rifampin, rifabutin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ARVs: lopinavir/ritonavir, atazanavir/ritonavir</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Antibiotics: doxycycline</td>
<td></td>
</tr>
<tr>
<td>Azithromycin</td>
<td>Overlapping Toxicities:</td>
<td>Caution advised. Increased risk of QT prolongation.</td>
</tr>
<tr>
<td></td>
<td>• Artemether/lumefantrine, chloroquine, quinine</td>
<td></td>
</tr>
<tr>
<td>Boceprevir</td>
<td>Please see Adult OI guidelines for information about drug interactions, including warnings about interactions between boceprevir and HIV protease inhibitors.</td>
<td></td>
</tr>
<tr>
<td>Capreomycin</td>
<td>Overlapping Toxicities:</td>
<td>Caution advised.</td>
</tr>
<tr>
<td></td>
<td>• Nephrotoxic or ototoxic drugs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Neuromuscular blocking drugs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Antibacterial drugs: aminoglycosides (parenteral)</td>
<td></td>
</tr>
<tr>
<td>Caspofungin</td>
<td>Decreases Caspofungin Concentrations:</td>
<td>Increase in dose of caspofungin is recommended when co-administered with CYP450 inducers.</td>
</tr>
<tr>
<td></td>
<td>• Anticonvulsant drugs: phenytoin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Antimycobacterial drugs: rifampin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ARV drugs: efavirenz, nevirapine</td>
<td></td>
</tr>
</tbody>
</table>
Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 2 of 9)

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Overlapping Toxicities</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cidofovir</td>
<td>Overlapping Toxicities:</td>
<td>Monitor for toxicities of these drugs.</td>
</tr>
<tr>
<td></td>
<td>• Antibacterial drugs: aminoglycosides</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Antiviral drugs: foscarnet</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Nephrotoxic drugs</td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Decreases Ciprofloxacin Absorption:</td>
<td>Give oral ciprofloxacin 2 hours before or 6 hours after drugs that may interfere with absorption.</td>
</tr>
<tr>
<td></td>
<td>• ARV drugs: didanosine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Minerals: ferrous sulfate, zinc</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Gastrointestinal drugs: antacids, sucralfate, magnesium-containing laxatives</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Overlapping Toxicities:</td>
<td>Caution advised.</td>
</tr>
<tr>
<td></td>
<td>• Artemether/lumefantrine, clarithromycin, quinine</td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>Increases Clarithromycin Concentrations:</td>
<td>Caution advised. Concern for QTc prolongation. Decrease clarithromycin dose or consider switching to azithromycin, which has less potential for drug interactions.</td>
</tr>
<tr>
<td></td>
<td>• ARV drugs: atazanavir/ritonavir, lopinavir/ritonavir</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Antifungals: itraconazole (itraconazole concentrations also increased)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Increases Concentration of Other Medications:</td>
<td>Consider alternative agent.</td>
</tr>
<tr>
<td></td>
<td>• ARV drugs: etravirine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Decreases Clarithromycin Concentrations:</td>
<td>Consider switching to azithromycin, which has less potential for drug interaction. For concomitant use of rifabutin and clarithromycin, consider decreasing dose of rifabutin or switching to azithromycin.</td>
</tr>
<tr>
<td></td>
<td>• ARV drugs: efavirenz, etravirine, nevirapine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Antimycobacterial drugs: rifampin, rifabutin (rifabutin concentrations also increased)</td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>Decreases Clindamycin Antibacterial Efficacy:</td>
<td>Avoid concomitant use.</td>
</tr>
<tr>
<td></td>
<td>• Antibacterial drugs: chloramphenicol, erythromycins</td>
<td></td>
</tr>
<tr>
<td>Cycloserine</td>
<td>Overlapping Toxicities:</td>
<td>Caution advised.</td>
</tr>
<tr>
<td></td>
<td>• Antimycobacterial drugs: ethionamide, isoniazid</td>
<td></td>
</tr>
<tr>
<td>Dapsone</td>
<td>Decreases Dapsone Concentrations:</td>
<td>Co-administration should be avoided if possible. Consider alternatives for dapsone or use rifabutin.</td>
</tr>
<tr>
<td></td>
<td>• Antimycobacterial drugs: rifampin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Decreases Dapsone Absorption:</td>
<td>For co-administration with antacids or didanosine suspension, give dapsone 1 hour before or 4 hours after the other medication.</td>
</tr>
<tr>
<td></td>
<td>• ARV drugs: didanosine suspension</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Gastrointestinal drugs: antacids</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Overlapping Toxicities:</td>
<td>Caution advised.</td>
</tr>
<tr>
<td></td>
<td>• Bone marrow suppressant drugs or drugs associated with hemolysis</td>
<td></td>
</tr>
<tr>
<td>Doxycycline</td>
<td>Decreases Doxycycline Concentrations:</td>
<td>Potential for decreased doxycycline efficacy. Monitor for therapeutic failure.</td>
</tr>
<tr>
<td></td>
<td>• Anticonvulsant drugs: phenytoin, carbamazepine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Antimycobacterial drugs: rifampin</td>
<td></td>
</tr>
</tbody>
</table>
Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Overlapping Toxicities</th>
<th>Recommendation</th>
</tr>
</thead>
</table>
| Erythromycin | Increases Concentrations of Erythromycin and Co-Administered Medication:  
• Antifungals: itraconazole | Monitor for toxicities of both drugs, potential for QT prolongation. |
| Ethambutol | Overlapping Toxicities:  
• Neurotoxic drugs | Caution advised. |
| Ethionamide | Potential for Increased Toxicity Due to Overlapping Toxicity:  
• Neurotoxic drugs  
• Antimycobacterial drugs: cycloserine, isoniazid | Caution advised. |
| Fluconazole | Decreases Fluconazole Levels:  
• Anticonvulsant drugs: phenytoin  
• Antimycobacterial drugs: rifampin  
• ARV drugs: rilpivirine | Monitor for efficacy. May need to increase fluconazole dose. |
|  | Increases Concomitant Drug Concentrations:  
• ARV drugs: saquinavir, tipranavir, nevirapine, and etravirine | May need to decrease dose of saquinavir. Avoid tipranavir with high doses of fluconazole (maximum fluconazole dose in adults: 200 mg). Caution advised with etravirine. |
|  | • Antimycobacterial drugs: rifabutin | May need to decrease dose of rifabutin. |
|  | • Statins: simvastatin, lovastatin, atorvastatin | Do not co-administer with simvastatin or lovastatin. Avoid use of atorvastatin if possible. Alternative statins such as fluvastatin, rosuvastatin, pravastatin are preferred or discontinue statin during antifungal therapy. |
| Flucytosine | Increases Flucytosine Concentrations:  
• Nephrotoxic drugs | Caution advised. |
| Foscarnet | Overlapping Toxicities:  
• Antiviral drugs: cidofovir  
• Anti-pneumocystis drugs: pentamidine  
• Nephrotoxic drugs | Monitor for toxicities of these drugs. |
| Ganciclovir | Increases Ganciclovir Concentrations :  
• ARV drugs: tenofovir (concentrations also increased) | Monitor for toxicities of these drugs. |
|  | Increases Concomitant Drug Concentrations:  
• ARV drugs: didanosine, tenofovir | Caution advised. |
|  | Overlapping Toxicities:  
• Antibacterial drugs: imipenem-cilastatin  
• ARV drugs: zidovudine  
• Bone marrow suppressant drugs  
• Nephrotoxic drugs | Caution advised. Increased risk of seizures with imipenem-cilastatin. |
Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 4 of 9)

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Overlapping Toxicities</th>
<th>Recommendation</th>
</tr>
</thead>
</table>
| **Interferon-Alpha** | Overlapping Toxicities:  
  - ARV drugs: zidovudine, lamivudine  
  - Bone marrow suppressant drugs | Co-administration of zidovudine and lamivudine should be avoided if possible. Caution advised with other bone marrow suppressant drugs. |
| **Isoniazid** | Decreases Isoniazid Concentrations:  
  - Corticosteroids: glucocorticoids (e.g., prednisolone)  
  - Gastrointestinal drugs: antacids | Use with caution. |
| | Decreases Isoniazid Absorption:  
  - Corticosteroids: antacids | Caution advised. |
| | Increases Concomitant Drug Concentrations:  
  - Diazepam | Caution advised. |
| | Decreases Concomitant Drug Concentrations:  
  - Anti-infective drugs: ketoconazole, itraconazole | Co-administration should be avoided, if possible. |
| | Overlapping Toxicities:  
  - Anti-microbial drugs: rifampin, cycloserine, ethionamide  
  - Hepatotoxic drugs  
  - Neurotoxic drugs | Caution advised. |
| **Itraconazole** | Increases Itraconazole Concentration:  
  - Antibacterial: clarithromycin, erythromycin, ciprofloxacin  
  - ARVs: protease inhibitors | Monitor for toxicities. Monitor itraconazole concentration. Consider azithromycin instead of other macrolides. High doses of itraconazole are not recommended with PIs. |
| | Increases Concomitant Drug Concentrations:  
  - ARV drugs: etravirine, maraviroc, protease inhibitors | Caution advised. Monitor for toxicities. Decrease adult maraviroc dose to 150 mg twice daily. |
| | Statins: lovastatin, simvastatin, atorvastatin | Do not co-administer with simvastatin or lovastatin. Avoid use of atorvastatin if possible. Alternative statins such as fluvastatin, rosuvastatin, pravastatin are preferred or discontinue statin during antifungal therapy. |
| | Antibacterial: clarithromycin, erythromycin | Consider switching to azithromycin, which has less potential for drug interaction. |
| | Sedatives/hypnotics: midazolam, alprazolam, diazepam | Co-administration of midazolam and alprazolam should be avoided. Co-administration of diazepam should be avoided, if possible. |
| | Cardiac: quinidine | Co-administration of quinidine should be avoided. QT prolongation. |
| | Decreases Itraconazole Concentrations:  
  - ARV drugs: efavirenz, etravirine, nevirapine, rilpivirine  
  - Anticonvulsant drugs: carbamazepine, (fos)phenytoin | Monitor itraconazole concentration. Co-administration of efavirenz should be avoided if possible. |

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Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections

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<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Itraconazole, continued</strong></td>
<td>• Antimycobacterial drugs: rifampin, rifabutin, rifapentine, isoniazid</td>
<td>Co-administration with rifampin should be avoided. Co-administration with rifabutin should be avoided, if possible. Monitor for toxicities. Monitor itraconazole concentration.</td>
</tr>
<tr>
<td></td>
<td>Decreases Itraconazole Absorption: • ARV drugs: didanosine • Gastrointestinal drugs: antacids, anticholinergics/antispasmodics, histamine H2-receptor antagonists, omeprazole, sucralfate</td>
<td>Monitor itraconazole concentration.</td>
</tr>
<tr>
<td><strong>Lumefantrine</strong></td>
<td>Increases Concomitant Drug Levels: • ARV drugs: nevirapine</td>
<td>Monitor for nevirapine toxicity.</td>
</tr>
<tr>
<td></td>
<td>Overlapping Toxicities: • ARV drugs: protease inhibitors • Antibacterial drugs: macrolides, fluoroquinolones • Antifungal drugs: fluconazole, voriconazole • Antimalarial drugs: quinine, quinidine • Psychotropic drugs: quetiapine, tricyclic antidepressants</td>
<td>Co-administration with fluconazole or voriconazole should be avoided. For all other drugs, co-administration should be avoided, if possible; monitor for toxicities (QT prolongation).</td>
</tr>
<tr>
<td><strong>Mefloquine</strong></td>
<td>Decreases Mefloquine Concentrations: • Antimalarial drugs: quinine • Antimycobacterial: rifampin</td>
<td>Monitor for decreased mefloquine efficacy. Co-administration of rifampin should be avoided, if possible; use rifabutin instead.</td>
</tr>
<tr>
<td></td>
<td>Decreases Concomitant Drug Concentrations: • ARV drugs: ritonavir, possibly other protease inhibitors</td>
<td>Monitor for virologic failure of protease inhibitor-containing ART regimen.</td>
</tr>
<tr>
<td></td>
<td>Overlapping Toxicities: • Anti-malarial drugs: quinine • Other drugs that can cause prolonged QT</td>
<td>Avoid co-administration, if possible. Monitor for toxicities (EKG changes, cardiac arrest; also seizures with quinine). If co-administered with quinine, give mefloquine at least 12 hours after last dose of quinine.</td>
</tr>
<tr>
<td><strong>Nitazoxanide</strong></td>
<td>Increases Concomitant Drug Concentrations: • Phenytoin</td>
<td>Potential for interaction with other medications that are highly protein bound. Use with caution as interaction will increase concentrations of concomitant medication.</td>
</tr>
<tr>
<td><strong>Paromomycin</strong></td>
<td>Overlapping Toxicities: • Neuromuscular blocking drugs</td>
<td>Use with caution.</td>
</tr>
</tbody>
</table>
Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections
(page 6 of 9)

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<thead>
<tr>
<th>Drug Name</th>
<th>Overlapping Toxicities</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pentamidine</strong></td>
<td>- Overlapping Toxicities: - Antiviral drugs: foscarnet</td>
<td>Co-administration should be avoided, if possible. Monitor for toxicities (hypocalcaemia, QT prolongation).</td>
</tr>
<tr>
<td></td>
<td>- ARV drugs: protease inhibitors, didanosine</td>
<td>Co-administration should be avoided, if possible. Monitor for toxicities (QT prolongation with protease inhibitors; pancreatitis for didanosine).</td>
</tr>
<tr>
<td></td>
<td>- Bone marrow suppressant drugs</td>
<td>Monitor for toxicities.</td>
</tr>
<tr>
<td></td>
<td>- Nephrotoxic drugs</td>
<td>Monitor for toxicities.</td>
</tr>
<tr>
<td></td>
<td>- Other drugs that can cause prolonged QT</td>
<td>Monitor for toxicities. Avoid co-administration, if possible.</td>
</tr>
<tr>
<td><strong>Posaconazole</strong></td>
<td>Decreases Posaconazole Drug Concentrations: - ARV drugs: efavirenz, fosamprenavir, ripivirine</td>
<td>Co-administration of fosamprenavir should be avoided. Co-administration of efavirenz should be avoided, if possible. If co-administered, monitor posaconazole concentrations and adjust dose accordingly.</td>
</tr>
<tr>
<td></td>
<td>- Anticonvulsant drugs: phenytoin</td>
<td>Co-administration should be avoided, if possible. If co-administered, monitor posaconazole concentrations and adjust dose accordingly.</td>
</tr>
<tr>
<td></td>
<td>- Antimycobacterial drugs: rifabutin, rifampin</td>
<td>Co-administration should be avoided, if possible. If co-administered, monitor posaconazole concentrations and adjust dose accordingly.</td>
</tr>
<tr>
<td></td>
<td>Increases Concomitant Drug Concentrations: - ARV drugs: atazanavir, saquinavir, lopinavir, etravirine, and ritonavir</td>
<td>Co-administration should be avoided, if possible. Monitor for toxicities. Consider monitoring concentrations and adjust dose as necessary.</td>
</tr>
<tr>
<td></td>
<td>- Antibacterial drugs: erythromycin, clarithromycin</td>
<td>Co-administration should be avoided.</td>
</tr>
<tr>
<td></td>
<td>- Anticonvulsant drugs: phenytoin</td>
<td>Co-administration should be avoided.</td>
</tr>
<tr>
<td></td>
<td>- Sedatives/hypnotics: midazolam, alprazolam, diazepam</td>
<td>Co-administration should be avoided, if possible. Monitor for toxicities.</td>
</tr>
<tr>
<td></td>
<td>- Antimycobacterial drugs: rifabutin</td>
<td>Co-administration should be avoided.</td>
</tr>
<tr>
<td></td>
<td>- Statins: simvastatin, lovastatin, atorvastatin</td>
<td>Do not co-administer with simvastatin or lovastatin. Avoid use of atorvastatin if possible. Alternative statins such as fluvastatin, rosuvastatin, pravastatin are preferred or discontinue statin during antifungal therapy.</td>
</tr>
<tr>
<td></td>
<td>- Antimalarials: Quinidine, quinine, mefloquine, lumefantrine, halofantrine</td>
<td>Co-administration should be avoided.</td>
</tr>
<tr>
<td></td>
<td>Decreases Concomitant Drug Concentrations: - ARV drugs: fosamprenavir</td>
<td>Co-administration should be avoided.</td>
</tr>
<tr>
<td></td>
<td>- Other drugs that can cause prolonged QT</td>
<td>Use with caution. Monitor for toxicities.</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Overlapping Toxicities</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Proguanil</strong></td>
<td>Decreases Proguanil Concentrations: • Atazanavir/ritonavir, lopinavir/ritonavir, efavirenz</td>
<td>Use with caution.</td>
</tr>
<tr>
<td><strong>Pyrazinamide</strong></td>
<td>Overlapping Toxicities: • Antimycobacterial drugs: rifampin, ethionamide • Hepatotoxic drugs</td>
<td>Use with caution. Monitor for hepatotoxicity.</td>
</tr>
<tr>
<td><strong>Quinidine</strong></td>
<td>Increases Quinidine Concentrations: • Protease inhibitors • Itraconazole, posaconazole, voriconazole</td>
<td>Co-administration of PIs should be avoided. Increased risk of arrhythmia. Co-administration may be necessary in presence of life-threatening, severe malaria and in the absence of other therapy, while artesunate is obtained from the CDC.</td>
</tr>
<tr>
<td></td>
<td>Decreases Quinidine Concentrations: • Etravirine</td>
<td>Use with caution. Monitor quinidine levels.</td>
</tr>
<tr>
<td></td>
<td>Increases Concomitant Drug Concentrations: • Tricyclic antidepressants</td>
<td>Co-administration should be avoided, if possible. Monitor for toxicities.</td>
</tr>
<tr>
<td></td>
<td>Overlapping Toxicities: • Other drugs that can prolong QT interval</td>
<td>Co-administration should be avoided, if possible. Monitor for toxicities (QT prolongation).</td>
</tr>
<tr>
<td><strong>Ribavirin</strong></td>
<td>Increases Concentrations Of Concomitant Drug: • ARV drugs: didanosine</td>
<td>Co-administration should be avoided. Potential for increased risk of pancreatitis and mitochondrial toxicity.</td>
</tr>
<tr>
<td></td>
<td>Decreases Concentrations of Concomitant Drug: • Zidovudine, stavudine</td>
<td>Co-administration should be avoided, if possible.</td>
</tr>
<tr>
<td></td>
<td>Overlapping Toxicities: • Zidovudine, all NRTIs</td>
<td>Co-administration should be avoided, if possible. Monitor for toxicities (anemia for zidovudine; lactic acidosis for all NRTIs).</td>
</tr>
<tr>
<td><strong>Rifabutin</strong></td>
<td>Increases Rifabutin Concentrations: • HIV protease inhibitors • Fluconazole • Voriconazole, itraconazole, posaconazole • Clarithromycin</td>
<td>Use with caution. Monitor for rifabutin toxicity. Reduce rifabutin dose if co-administered with PIs.</td>
</tr>
<tr>
<td></td>
<td>Increases Concomitant Drug Concentrations: • Didanosine</td>
<td>Use with caution. Monitor for didanosine toxicity.</td>
</tr>
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<tr>
<td>Rifabutin, continued</td>
<td>Decreases Rifabutin Concentrations:</td>
<td>Use with caution. Higher rifabutin dose required when efavirenz co-administered. Consider TDM.</td>
</tr>
<tr>
<td></td>
<td>• Efavirenz, etravirine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Decreases Concomitant Drug Concentrations:</td>
<td>Co-administration should be avoided.</td>
</tr>
<tr>
<td></td>
<td>• ARV drugs: rilpivirine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ARV drugs: saquinavir, etravirine, maraviroc</td>
<td>Co-administration should be avoided, if possible.</td>
</tr>
<tr>
<td></td>
<td>• Antibacterial drugs: dapsone, atovaquone</td>
<td>Use with caution. Monitor for dapsone treatment failure.</td>
</tr>
<tr>
<td></td>
<td>• Antifungal drugs: azoles (except for fluconazole)</td>
<td>Co-administration should be avoided, if possible. If co-administered, consider TDM and monitor for rifabutin toxicities (andazole clinical efficacy).</td>
</tr>
<tr>
<td></td>
<td>• Contraceptives: oral</td>
<td>Oral contraceptives less effective. Additional non-hormonal contraceptive or alternative recommended.</td>
</tr>
<tr>
<td>Rifampin</td>
<td>Decreases Concomitant Drug Concentrations:</td>
<td>Oral contraceptives less effective. Additional non-hormonal contraceptive or alternative recommended.</td>
</tr>
<tr>
<td></td>
<td>• Contraceptives: oral</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ARV drugs: PIs ± ritonavir, nevirapine, raltegravir, rilpivirine</td>
<td>Significantly decreases PI exposure; co-administration should be avoided. Nevirapine: use only if other options not available and close virologic and immunologic monitoring can be done; consider efavirenz instead. Raltegravir dose increase may be required. Rilpivirine co-administration should be avoided.</td>
</tr>
<tr>
<td></td>
<td>• Antimicrobial: atovaquone, dapsone, clarithromycin, doxycycline</td>
<td>Co-administration of atovaquone and rifampin should be avoided. Consider switching clarithromycin to azithromycin, which has less potential for drug interaction. Dapsone and Doxycycline efficacy may be reduced.</td>
</tr>
<tr>
<td></td>
<td>• Antifungal drugs: azoles, caspofungin</td>
<td>Increase in dose of caspofungin is recommended when co-administered with CYP450 inducers.</td>
</tr>
<tr>
<td></td>
<td>• Other: corticosteroids, methadone</td>
<td>Caution advised with corticosteroids (decreased efficacy).</td>
</tr>
<tr>
<td></td>
<td>Overlapping Toxicities:</td>
<td>Methadone: Monitor for efficacy and/or opiate withdrawal symptoms with methadone.</td>
</tr>
<tr>
<td></td>
<td>• Bone marrow suppressant drugs</td>
<td>Monitor for toxicities of these drugs.</td>
</tr>
<tr>
<td></td>
<td>• Hepatotoxic drugs</td>
<td></td>
</tr>
<tr>
<td>Streptomycin</td>
<td>Potential for Increased Toxicity Due to Overlapping Toxicity:</td>
<td>Monitor for toxicities of these drugs.</td>
</tr>
<tr>
<td></td>
<td>• Nephrotoxic drugs</td>
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<td></td>
<td>• Neuromuscular blocking drugs</td>
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</table>
| Telaprevir | **Overlapping Toxicities:**
• Folate antagonists  
• Bone marrow suppressant drugs | Monitor for toxicities of these drugs. |
| Trimethoprim-Sulfamethoxazole | **Potential For Increased Concentrations (of Both Drugs) and Overlapping Toxicity:**
• Antivirals: acyclovir, valganciclovir, ganciclovir, cidofovir  
• ARVs: tenofovir | Monitor for toxicities of these drugs. |
| Valacyclovir | **Potential For Increased Concentrations (of Both Drugs) and Overlapping Toxicity:**
• Antivirals: valacyclovir, acyclovir, ganciclovir, cidofovir  
• ARVs: tenofovir | Monitor for toxicities of these drugs. |
| Valganciclovir | **Decreases Voriconazole Concentrations:**
• Anticonvulsant drugs: carbamazepine, long-acting barbiturates  
• Antimycobacterial drugs: rifabutin, rifampin  
• ARV drugs: efavirenz, nevirapine, PIs boosted with ritonavir | Caution advised. |
| Voriconazole | **Increases Voriconazole Concentrations:**
• ARV drugs: etravirine | Monitor voriconazole concentrations to reduce toxicity. |
| | **Increases Concomitant Drug Concentrations:**
• Antimycobacterial drugs: rifabutin  
• ARV drugs: protease inhibitors boosted with ritonavir, efavirenz, etravirine  
• Statins: simvastatin, lovastatin, atorvastatin  
• Sedatives/hypnotics: midazolam, alprazolam, triazolam | Caution advised. |
| | Rifabutin and Rifampin co-administration should be avoided. |
| | Standard doses of efavirenz and voriconazole should not be used; voriconazole dose may need to be increased and efavirenz dose decreased, or use alternative antifungal agent. |
| | Potential for increased PI concentrations and decreased voriconazole concentrations; consider monitoring voriconazole concentrations and adjust dose accordingly; monitor for PI-associated toxicities or consider using an alternative antifungal agent. |
| | Statins: Do not co-administer with simvastatin or lovastatin. Avoid use of atorvastatin if possible. Alternative statins such as fluvastatin, rosuvastatin, pravastatin are preferred or discontinue statin during antifungal therapy. |
| | Co-administration should be avoided if possible. Monitor for toxicities. |

**Key to Acronyms:** ART = antiretroviral therapy; ARV = antiretroviral; CDC = Centers for Disease Control and Prevention; EKG = electrocardiogram; NNRTI = non-nucleoside reverse transcriptase inhibitors; NRTI = nucleoside reverse transcriptase inhibitors; OI = opportunistic infection; PI = protease inhibitors; PK = pharmacokinetic; TDM = therapeutic drug monitoring

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