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

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Table 2: Secondary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations  (Last updated December 15, 2016; last reviewed December 15, 2016) (page 1 of 6)

<table>
<thead>
<tr>
<th>Indication</th>
<th>First Choice</th>
<th>Alternative</th>
<th>Comments/Special Issues</th>
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<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: • &gt;2 serious bacterial infections in a 1-year period in children who are unable to take cART</td>
<td>November 6, 2013</td>
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<td>Criteria for Discontinuing Secondary Prophylaxis: • 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: • &gt;2 serious bacterial infections in a 1-year period despite cART</td>
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<td><strong>Candidiasis</strong></td>
<td>Not routinely recommended, but can be considered for frequent severe recurrences. • Fluconazole, 3–6 mg/kg body weight daily (maximum 200 mg), or itraconazole oral solution, 2.5 mg/kg body weight/ dose twice daily</td>
<td>N/A</td>
<td>Secondary Prophylaxis Indicated: • Frequent or severe recurrences</td>
<td>November 6, 2013</td>
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<td>Criteria for Discontinuing Secondary Prophylaxis: • When CD4 count or percentage has risen to CDC immunologic Category 2 or 1</td>
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<td></td>
<td>Criteria for Restarting Secondary Prophylaxis: • Frequent severe recurrences</td>
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<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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<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: • Documented disease</td>
<td>November 6, 2013</td>
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<td>Criteria For Discontinuing Secondary Prophylaxis If All of the Following Criteria are Fulfilled: • Age ≥6 years • Asymptomatic on ≥12 months of secondary prophylaxis • CD4 count ≥100 cells/mm³ with undetectable HIV viral load on cART for &gt;3 months</td>
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<td></td>
<td>Criteria for Restarting Secondary Prophylaxis: • CD4 count &lt;100/mm³</td>
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<td>a Secondary prophylaxis is also referred to as maintenance therapy or suppressive therapy</td>
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<td><strong>Cryptosporidiosis</strong></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>November 6, 2013</td>
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</tbody>
</table>
### Table 2: Secondary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 2 of 6)

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| **Cytomegalovirus (CMV)** | • Ganciclovir 5 mg/kg body weight IV once daily, or  
• For older children who can receive adult dose (based on their BSA), valganciclovir tablets 900 mg orally once daily with food, or  
• 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  
• Foscarnet 90–120 mg/kg body weight IV once daily | • Cidofovir 5 mg/kg body weight per dose IV every other week. Must be given with probenecid and IV hydration. | **Secondary Prophylaxis Indicated For:**  
• Prior disseminated disease, retinitis, neurologic disease, or GI disease with relapse  
**Criteria for Discontinuing Secondary Prophylaxis If All of the Following Criteria Are Fulfilled:**  
• Completed ≥6 months of cART  
• Consultation with ophthalmologist (if retinitis)  
• Age <6 years with CD4 percentage ≥15% for >6 consecutive months  
• Age ≥6 years with CD4 cell count >100 cells/mm³ for >6 consecutive months  
• For retinitis, routine (i.e., every 3–6 months) ophthalmological follow-up is recommended for early detection of relapse or immune restoration uveitis.  
**Criteria for Restarting Secondary Prophylaxis:**  
• Age <6 years with CD4 percentage <15%  
• Age ≥6 years with CD4 cell count <100 cells/mm³ | November 6, 2013 |
| **Giardiasis**   | N/A                                                      | N/A                                   | N/A                                                                                     | November 6, 2013 |
| **Hepatitis B Virus (HBV)** | Hepatitis A Vaccine                                      | N/A                                   | **Secondary Prophylaxis Indicated for:**  
• Chronically HBV-infected individuals to prevent further liver injury  
**Criteria for Discontinuing Secondary Prophylaxis:**  
• N/A  
**Criteria for Restarting Secondary Prophylaxis:**  
• N/A | November 6, 2013 |
| **Hepatitis C Virus (HCV)** | None                                                     | N/A                                   | N/A                                                                                     | November 6, 2013 |
Table 2: Secondary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 3 of 6)

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<tr>
<td>Herpes Simplex Virus (HSV) Infections</td>
<td><strong>Mucocutaneous Disease:</strong>&lt;br&gt;• Acyclovir 20 mg/kg body weight/dose (maximum 800 mg/dose) by mouth BID&lt;br&gt;&lt;br&gt;<strong>Suppressive Therapy After Neonatal Skin, Eye, Mouth, or CNS Disease:</strong>&lt;br&gt;• Acyclovir 300 mg/m² body surface area/dose by mouth TID for 6 months</td>
<td><strong>Mucocutaneous Disease, For Adolescents Old Enough to Receive Adult Dosing:</strong>&lt;br&gt;• Valacyclovir 500 mg by mouth BID, or&lt;br&gt;• Famciclovir 500 mg by mouth BID</td>
<td><strong>Secondary Prophylaxis Indicated:</strong>&lt;br&gt;• Suppressive secondary prophylaxis can be considered for children with severe and recurrent mucocutaneous (oral or genital) disease&lt;br&gt;&lt;br&gt;<strong>Criteria for Discontinuing Secondary Prophylaxis:</strong>&lt;br&gt;• 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.</td>
<td>November 6, 2013</td>
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<td>Histoplasmosis (Suppressive Therapy)</td>
<td>Itraconazole oral solution 5–10 mg/kg body weight (maximum 200 mg) per dose by mouth daily</td>
<td>Fluconazole 3–6 mg/kg body weight (maximum 200 mg) by mouth once daily</td>
<td><strong>Secondary Prophylaxis Indicated:</strong>&lt;br&gt;• Documented histoplasmosis in a patient with impaired immune function&lt;br&gt;&lt;br&gt;<strong>Criteria For Discontinuing Secondary Prophylaxis:</strong>&lt;br&gt;**<em>If All of the Following Criteria Are Fulfilled:</em>&lt;br&gt;• CD4 percentage &gt;15% at any age; or CD4 cell count &gt;150 cells/mm³ aged ≥6 years.&lt;br&gt;• Received ≥1 year itraconazole maintenance therapy&lt;br&gt;• Established (e.g., ≥6 months) adherence to effective cART&lt;br&gt;• Negative Histoplasma blood cultures&lt;br&gt;• Serum Histoplasma antigen &lt;2 ng/mL&lt;br&gt;&lt;br&gt;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>
<td>November 6, 2013</td>
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<tr>
<td>Human Papillomavirus (HPV)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>November 6, 2013</td>
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<td>Influenza</td>
<td>N/A</td>
<td>N/A</td>
<td>No role for secondary chemoprophylaxis</td>
<td>November 6, 2013</td>
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Table 2: Secondary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 4 of 6)

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| Isosporiasis (Cystoisosporiasis)    | If Severe Immunosuppression:  
  • Administer TMP-SMX 2.5 mg/kg body weight of TMP component twice daily by mouth 3 times per week                                                                                                       | Pyrimethamine 1 mg/kg body weight (maximum 25 mg) plus folinic acid, 10–25 mg by mouth once daily.  
  **Second-Line Alternative:**  
  • Ciprofloxacin, 10–20 mg/kg body weight given twice daily by mouth 3 times per week                                                                                                                   | Consider discontinuing secondary prophylaxis in a patient receiving cART after sustained improvement from severe immunosuppression (from CDC immunologic category 3 to CD4 values that fall within category 1 or 2) for longer than 6 months.  
  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 similar data exist for children. Thus, the recommended dosing for secondary prophylaxis in children is 1 mg/kg per dose (maximum 25 mg) once daily.  
  Ciprofloxacin is generally not a drug of first choice in children due to increased incidence of adverse events, including events related to joints and/or surrounding tissues.                                                                 | November 6, 2013 |
| Malaria                             | For *P. vivax* or *P. ovale*:  
  • 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                                                                                                   | N/A                                  | 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.  
| Microsporidiosis                    | Disseminated, Non-Ocular Infection or GI Infection Caused by Microsporidia Other Than *E. Bieneusi* or *V. Corneae*:  
  • Albendazole 7.5 mg/kg body weight (maximum 400 mg/dose) by mouth twice daily                                                                                                                             | N/A                                  | 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)                                                                                                                                                                                                                                                                                                                                 | December 15, 2016 |
|                                     | Ocular Infection:  
  • Topical fumagillin bicyclohexylimmonium (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 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 for management of systemic infection |                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |               |
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<tr>
<td><strong>Mycobacterium avium Complex (MAC)</strong>&lt;br&gt;(Chronic Suppressive Therapy)</td>
<td>• Clarithromycin 7.5 mg/kg body weight (maximum 500 mg) orally twice daily, <strong>plus</strong>&lt;br&gt;• Ethambutol 15–25 mg/kg body weight (maximum 2.5 g) orally once daily, <strong>with or without</strong> food&lt;br&gt;• Children aged &gt;5 years who received rifabutin as part of initial treatment: Rifabutin 5 mg/kg body weight (maximum 300 mg) orally once daily with food</td>
<td>• Azithromycin 5 mg/kg body weight (maximum 250 mg) orally once daily, <strong>plus</strong>&lt;br&gt;• Ethambutol 15–25 mg/kg body weight (max 2.5 g) orally once daily, <strong>with or without</strong> food&lt;br&gt;• Children aged &gt;5 years who received rifabutin as part of initial treatment: Rifabutin 5 mg/kg body weight (maximum 300 mg) orally once daily with food.</td>
<td>Secondary Prophylaxis Indicated:  &lt;br&gt;• Prior disease  &lt;br&gt;Criteria for Discontinuing Secondary Prophylaxis  &lt;br&gt;Fulfillment of All of the Following Criteria:  &lt;br&gt;• Completed ≥6 months of cART  &lt;br&gt;• Completed ≥12 months MAC therapy  &lt;br&gt;• Asymptomatic for signs and symptoms of MAC  &lt;br&gt;• Aged 2 to &lt;6 years with CD4 count &gt;200 cells/mm³ for ≥6 consecutive months  &lt;br&gt;• Aged ≥6 years with CD4 count &gt;100 cells/mm³ for ≥6 consecutive months  &lt;br&gt;Criteria for Restarting Secondary Prophylaxis:  &lt;br&gt;• Aged 2 to &lt;6 years with CD4 count &lt;200 cells/mm³  &lt;br&gt;• Aged ≥6 years with CD4 count &lt;100 cells/mm³</td>
<td>November 6, 2013</td>
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<td><strong>Mycobacterium Tuberculosis</strong></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>November 6, 2013</td>
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</table>
| **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) | TMP-SMX  
*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 |
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<tr>
<td>Syphilis</td>
<td>N/A</td>
<td>N/A</td>
<td>Secondary Prophylaxis Indicated:</td>
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<td>• N/A</td>
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<td>Criteria For Discontinuing Secondary Prophylaxis:</td>
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<td>Criteria For Restarting Secondary Prophylaxis:</td>
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<td><strong>Note:</strong> Alternate regimens with very limited data in children. TMP-SMX only to be used if patient intolerant to other regimens</td>
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<td><strong>Secondary Prophylaxis Indicated:</strong></td>
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<td></td>
<td>• Prior toxoplasmic encephalitis</td>
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<tr>
<td>Toxoplasmosis (Suppressive Therapy)</td>
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<td><strong>Secondary Prophylaxis Indicated:</strong></td>
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<td><strong>Criteria For Discontinuing Secondary Prophylaxis:</strong></td>
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<td><strong>If All of the Following Criteria are Fulfilled:</strong></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>• Aged 1 to &lt;6 years; CD4 percentage ≥15% for &gt;6 consecutive months</td>
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<td>• Aged ≥6 years; CD4 cell count &gt;200 cells/mm³ for &gt;6 consecutive months</td>
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<td><strong>Criteria For Restarting Secondary Prophylaxis:</strong></td>
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<td>• Aged 1 to &lt;6 years with CD4 percentage &lt;15%</td>
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<td></td>
<td>• Aged ≥6 years with CD4 cell count &lt;200 cells/mm³</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>
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</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