Table 2. Secondary Prophylaxis of Opportunistic Infections in Children With and Exposed to HIV—Summary of Recommendations

Updated: April 23, 2026
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Indication	First Choice	Alternative	Comments/Special Issues
Bacterial Infections (*S. pneumoniae* and other invasive bacteria)	TMP-SMX 75/375 mg/m^2 BSA per dose by mouth twice daily	IVIG 400 mg/kg body weight every 2–4 weeks	Secondary Prophylaxis Indicated • More than two serious bacterial infections in a 1-year period in children who are unable to take ART Criteria for Discontinuing Secondary Prophylaxis • Sustained (≥3 months) immune reconstitution (CD4 percentage ≥25% if ≤6 years old; CD4 percentage ≥20% or CD4 count >350 cells/mm^3 if >6 years old) Criteria for Restarting Secondary Prophylaxis • More than two serious bacterial infections in a 1-year period despite ART
Candida Infections	Not routinely recommended but can be considered for frequent severe recurrences despite ART. • Fluconazole 6 mg/kg body weight (maximum 200 mg/dose) PO three times weekly	• Fluconazole 3–6 mg/kg body weight PO daily (maximum 200 mg/day) • Itraconazole oral solution, 2.5 mg/kg body weight/dose PO twice daily	Secondary Prophylaxis Indicated (Limited Data in Children) • Frequent or severe recurrences despite ART • In patients with initial fluconazole-refractory OPC or esophageal candidiasis that subsequently responded to voriconazole, posaconazole, or an echinocandin: may consider continuation of the effective drug until immune reconstitution Criteria for Discontinuing Secondary Prophylaxis • When CD4 count or percentage has risen to HIV stage 1 or 2 (see HIV Infection Stage Table) Criteria for Restarting Secondary Prophylaxis

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			• Frequent severe recurrences
Coccidioidomycosis	• Fluconazole 6 mg/kg body weight (maximum 400 mg) per dose IV or PO once daily, *or* • For Coccidioidal Meningitis: o Continue initial treatment with fluconazole (12 mg/kg body weight per dose IV or PO once daily)	Itraconazole 2–5 mg/kg body weight (maximum dose 200 mg) PO per dose twice daily	Secondary Prophylaxis Indicated • Prior meningitis or disseminated disease • Milder disease if CD4 count <250 cells/mm^3 or CD4 percentage <15%. Criteria for Discontinuing Secondary Prophylaxis • Lifelong therapy for meningitis or disseminated disease • Consider lifelong therapy for milder disease, regardless of ART or immune reconstitution
COVID-19	N/A	N/A	N/A
Cryptococcosis[a]	Fluconazole 6 mg/kg body weight (maximum 200 mg) by mouth once daily	Itraconazole oral solution 5 mg/kg body weight (maximum 200 mg) by mouth once daily	Secondary Prophylaxis Indicated • Documented disease 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/mm^3 with undetectable HIV viral load on ART for >3 months Criteria for Restarting Secondary Prophylaxis • CD4 count <100/mm^3 [a] Secondary prophylaxis is also referred to as maintenance therapy or suppressive therapy.

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Cryptosporidiosis	N/A	N/A	N/A
Cytomegalovirus Infection (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 aged 4 months to 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 m^2) 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 (All of the Following Criteria Must Be Fulfilled) • Completed ≥6 months of ART • Age <6 years with CD4 percentage ≥15% for >6 consecutive months • Age ≥6 years with CD4 count >100 cells/mm^3 for >6 consecutive months • Consultation with ophthalmologist (if retinitis) o 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 count <100 cells/mm^3
Giardiasis	N/A	N/A	N/A
Hepatitis B Virus Infection (HBV)	HepA vaccine	N/A	Secondary Prophylaxis Indicated for— • Individuals with chronic HBV infection to prevent further liver injury. Criteria for Discontinuing Secondary Prophylaxis • N/A

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			Criteria for Restarting Secondary Prophylaxis • N/A
Hepatitis C Virus Infection (HCV)	N/A	N/A	N/A
Herpes Simplex Virus (HSV) Infection	Mucocutaneous Disease • Acyclovir 20 mg/kg body weight/dose (maximum 800 mg/dose) by mouth twice daily Suppressive Therapy After Neonatal HSV Disease (Skin, Eye, Mouth, CNS, or Disseminated Disease) • Acyclovir 300 mg/m^2 BSA/dose by mouth three times daily for 6 months	Mucocutaneous Disease, for Adolescents Old Enough to Receive Adult Dosing • Valacyclovir 500 mg by mouth twice daily, *or* • Famciclovir 500 mg by mouth twice daily	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	Secondary Prophylaxis Indicated • Documented histoplasmosis in a patient with impaired immune function Criteria for Discontinuing Secondary Prophylaxis *If All of the Following Criteria Are Fulfilled* • CD4 percentage >15% at any age; or CD4 cell count >150 cells/mm^3 aged ≥6 years • Received ≥1 year itraconazole maintenance therapy • Established (e.g., ≥6 months) adherence to effective ART • Negative *Histoplasma* blood cultures

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			• Serum Histoplasma antigen <2 ng/mL 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.
Human Papillomavirus Disease (HPV)	N/A	N/A	N/A
Isosporiasis (Cystoisosporiasis)	If Severe Immunosuppression— • TMP-SMX 2.5 mg/kg body weight of the TMP component (maximum 80 mg TMP) twice daily by mouth three times per week	Pyrimethamine 1 mg/kg body weight (maximum 25 mg) ***plus*** folinic acid, 5–15 mg by mouth once daily. Second-Line Alternative • Ciprofloxacin, 10–20 mg/kg body weight (maximum 500 mg) by mouth three times per week	Consider discontinuing secondary prophylaxis in patients without evidence of active *Isospora* infection who have sustained improvement in immunologic status (from CDC immunologic category 3 to CD4 values that fall within category 1 or 2) for >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.
Malaria	For *P. vivax* or *P. ovale* • Primaquine 0.5 mg/kg base (0.8mg/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. http://wwwnc.cdc.gov/travel/yellowbook/2012/chapter-3-infectious-diseases-related-to-travel/malaria.htm#1939

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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 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 four times a day (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	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)
Mycobacterium avium Complex (MAC) (Chronic Suppressive Therapy)	• Clarithromycin[a] 7.5 mg/kg body weight (maximum 500 mg/dose) PO twice daily, *plus* • Ethambutol 15–25 mg/kg body weight (maximum 2.5 g/day) PO once daily, with or without food • *For Children Aged ≥6 Years Who Received Rifabutin as Part of Initial Treatment:* rifabutin[a] 5 mg/kg	• 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 • *For Children Aged ≥6 Years Who Received Rifabutin as Part of Initial Treatment:* rifabutin[a] 5 mg/kg	Secondary Prophylaxis Indicated • Prior disease Criteria for Discontinuing Secondary Prophylaxis • Children with a history of disseminated MAC and continued immunosuppression should receive lifelong prophylaxis to prevent recurrence. • There are limited data to recommend discontinuation of secondary prophylaxis in children aged <2 years. However, if continuation of secondary prophylaxis for

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	(maximum 300 mg) PO once daily with food	(maximum 300 mg) PO once daily with food	MAC is complicating ART compliance, discontinuation of MAC prophylaxis may be appropriate. *Fulfillment of All of the Following Criteria* • Completed ≥6 months of stable ART, *and* • Completed ≥12 months of MAC therapy, *and* • Asymptomatic for signs and symptoms of MAC, *and either* • *Aged 2 to <6 Years:* CD4 count >200 cells/mm^3 for ≥6 consecutive months, *or* • *Aged ≥6 Years:* CD4 count >100 cells/mm^3 for ≥6 consecutive months Criteria for Restarting Secondary Prophylaxis • *Aged 2 to <6 Years:* CD4 count ≤200 cells/mm^3 • *Aged ≥6 Years:* CD4 count ≤100 cells/mm^3
Mycobacterium tuberculosis	N/A	N/A	N/A
Pneumocystis Pneumonia	• TMP-SMX: 5–10 mg/kg/DAY (TMP component) • Maximum individual dose: 160 mg/DOSE (TMP component). • Several dosing regimens have been used successfully: o 3 days per week on consecutive or alternate days in divided doses every 12 hours o Daily as a single dose o Administration 2 days per week on consecutive or alternate days	Dapsone and atovaquone are both first-line alternatives (see text for relative risks and benefits), followed by aerosolized pentamidine as second line and IV pentamidine as third line. Dapsone • *Children Aged ≥1 Month:* 2 mg/kg/dose (maximum: 100 mg/dose) PO once daily or 4 mg/kg/dose (maximum 200 mg/dose) PO once weekly	Secondary Prophylaxis Indicated for: • Children with prior episode of PCP Criteria for Discontinuing Secondary Prophylaxis • *Children Aged <1 Year:* Continue primary prophylaxis in children with HIV throughout the first year of life • *Children Aged 1 Year and Older on ART for ≥6 Months With CD4 Count Above Age-Specific Stage 3 Cutoff for >3 Consecutive Months:* o *Children Aged 1 Year to <6 Years:* ≥500 cells/mm^3 *or* ≥22%

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	in doses divided every 12 hours has been used successfully in pediatric oncology patients.	Atovaquone • *Children Aged 1–3 Months or >24 Months to 12 Years:* 30–40 mg/kg/dose PO once daily with food (maximum: 1,500 mg/dose) • *Children Aged 4–24 Months:* 45 mg/kg/dose PO once daily with food (maximum: 1,500 mg/dose) • *Children Aged ≥13 Years:* 1,500 mg PO once daily Aerosolized Pentamidine Via Respirgard II Nebulizer *For Children Able to Comply With Its Use* • *Children Aged <5 Years:* Limited data regarding dosing. 9 mg/kg/dose or 150 mg/dose every month have been suggested. • *Children Aged ≥5 Years:* 300 mg every month IV Pentamidine • 4 mg/kg/dose every 3 to 4 weeks; maximum dose: 300 mg/dose • Limited data regarding dosing frequency; based on use in oncology patients	o *Children Aged ≥6 Years:* ≥200 cells/mm^3 or ≥14% • Discontinuation can be considered in children ≥6 Years if on ART for ≥6 months with undetectable viral load and CD4 count 101–200 cells/mm^3 if intolerant of prophylaxis medications Criteria for Restarting Secondary Prophylaxis • CD4 count below age-specific stage 3 cutoff (see above)

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Syphilis	N/A	N/A	Secondary Prophylaxis Indicated • N/A Criteria for Discontinuing Secondary Prophylaxis • N/A Criteria for Restarting Secondary Prophylaxis • N/A
Toxoplasmosis (Suppressive Therapy)	• Sulfadiazine 85–120 mg/kg body weight per day in 2–4 divided doses (maximum 2–4 g per day) PO, *plus* • Pyrimethamine 1 mg/kg body weight or 15 mg/m^2 BSA (maximum 25 mg) PO once daily, *plus* • Leucovorin 5 mg PO once every 3 days	• Clindamycin 7–10 mg/kg body weight per dose (max 600 mg/dose) PO three times daily, *plus* • Pyrimethamine 1 mg/kg body weight or 15 mg/m^2 BSA (maximum 25 mg) PO once daily, *plus* • Leucovorin 5 mg PO once every 3 days Children Aged 1–3 Months and >24 Months • Atovaquone 30 mg/kg body weight PO (maximum 1,500 mg) once daily with food, *plus* • TMP-SMX, 150/750 mg/m^2 BSA PO once daily Children Aged 4–24 Months *Option 1* • Atovaquone 45 mg/kg body weight PO once daily with food, *with or without*	Secondary Prophylaxis Indicated • Prior TE Note: Limited data in children is available for alternative regimens. TMP-SMX only to be used if individual is intolerant to other regimens. Criteria for Discontinuing Secondary Prophylaxis *If All of the Following Criteria Are Fulfilled*: • Completed initial therapy for TE, *and* • Asymptomatic for TE, *and* • Aged ≥6 years old with CD4 >200 cells/mm^3 in those or CD4% >22% (CD4 count >500 cells/mm^3) in those aged 1–5 years for 3 consecutive months Criteria for Restarting Secondary Prophylaxis: • CD4 count ≤200 cells/mm^3 and CD4% ≤22% (CD4 count ≤500 cells/mm^3) in those aged 1–5 years Note: Sulfadiazine may be given as 2–4 equal doses per day as long as the total daily dose is 85–120 mg/kg body weight.

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		• Pyrimethamine 1 mg/kg body weight or 15 mg/m^2 BSA (maximum 25 mg) PO once daily, *plus* leucovorin (when using pyrimethamine), 5 mg PO every 3 days *Option 2* • Atovaquone 45 mg/kg body weight (maximum 1,500 mg) PO once daily with food, *plus* • TMP-SMX, 150/750 mg/m^2 BSA PO once daily	
Varicella-Zoster Virus Disease (VZV)	N/A	N/A	There is no indication for secondary prophylaxis.

[a] Careful monitoring of drug–drug interactions is critical when using rifabutin or clarithromycin in children on ARVs.

Key: ART = antiretroviral therapy; BSA = body surface area; CD4 = CD4 T lymphocyte; CDC = Centers of Disease Control and Prevention; CNS = central nervous system; CrCl = (estimated) creatinine clearance; GI = gastrointestinal; HBV = hepatitis B virus; HepA = hepatitis A [vaccine]; HSV = herpes simplex virus; IV = intravenous; IVIG = intravenous immunoglobulin; MAC = *Mycobacterium avium* complex; PO = orally; PCP = *Pneumocystis* pneumonia; TE = *Toxoplasma* encephalitis; TMP = trimethoprim; TMP-SMX = trimethoprim-sulfamethoxazole