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

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Table 1: Primary 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 9)

Indication:	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Bacterial Infections *S. pneumoniae* and other invasive bacteria	• Pneumococcal, meningococcal, and Hib vaccines • Intravenous immune globulin (400 mg/kg body weight every 2 to 4 weeks)	• TMP-SMX 75/375 mg/m^2 body surface area per dose by mouth twice daily	See Figures 1 and 2 for detailed vaccines recommendations. Vaccines Routinely Recommended for Primary Prophylaxis. Additional Primary Prophylaxis Indicated For: • Hypogammaglobulinemia (that is, IgG < 400mg/dL) Criteria for discontinuing primary prophylaxis: • Resolution of hypogammaglobulinemia Criteria for restarting primary prophylaxis: • Relapse of hypogammaglobulinemia	November 6, 2013
Candidiasis	• Not routinely recommended	N/A	N/A	November 6, 2013
Coccidioidomycosis	N/A	N/A	Primary prophylaxis not routinely indicated in children.	November 6, 2013
Cryptococcosis	Not recommended	Not recommended	N/A	November 6, 2013
Cryptosporidiosis	ARV therapy to avoid advanced immune deficiency	N/A	N/A	November 6, 2013
Cytomegalovirus (CMV)	• For older children who can receive adult dose (based on their BSA), valganciclovir tablets 900 mg orally once daily with food • 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 m^2) orally once daily with food (maximum dose 900 mg/day)	N/A	Primary Prophylaxis Can Be Considered for: • CMV antibody positivity and severe immunosuppression (i.e., CD4 cell count <50 cells/mm^3 in children ≥6 years; CD4 percentage <5% in children <6 years) Criteria for Discontinuing Primary Prophylaxis: • CD4 cell count >100 cells/mm^3 for children ≥6 years; CD4 percentage >10% in children <6 years Criteria for Considering Restarting Primary Prophylaxis: • CD4 cell count <50 cells/mm^3 in children ≥6 years; CD4 percentage <5% in children <6 years	November 6, 2013
Giardiasis	cART to avoid advanced immunodeficiency	N/A	N/A	November 6, 2013
Hepatitis B Virus (HBV)	• Hepatitis B vaccine • Combination of hepatitis B immunoglobulin and hepatitis B vaccine for infants born to mothers with hepatitis B infection	Hepatitis B immunoglobulin following exposure	See Figures 1 and 2 for detailed vaccine recommendations. Primary Prophylaxis Indicated for: • All individuals who are not HBV infected Criteria for Discontinuing Primary Prophylaxis: • N/A Criteria for Restarting Primary Prophylaxis • N/A	November 6, 2013
Hepatitis C Virus (HCV)	None	N/A	N/A	November 6, 2013

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Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Herpes Simplex Virus Infections (HSV)	None	None	Primary prophylaxis is not indicated.	November 6, 2013
Histoplasmosis	N/A	N/A	Primary Prophylaxis indicated for selected HIV-infected adults but not children. Criteria for Discontinuing Primary Prophylaxis: • N/A Criteria for Restarting Primary Prophylaxis: • N/A	November 6, 2013
Human Papillomavirus (HPV)	HPV vaccine	N/A	See Figure 2 for detailed vaccine recommendations.	November 6, 2013
Influenza **Primary Chemoprophylaxis** Influenza A and B	Oseltamivir for 10 days[a] • Aged <3 months; not recommended[b] • Aged 3 months to <1 year; 3 mg/kg body weight/dose once daily[b] • Aged ≥1 to 12 years; weight-band dosing[b] • ≤15 kg: 30 mg once-daily • >15 kg to 23 kg: 45 mg once daily • >23 kg to 40 kg: 60 mg once daily • >40 kg: 75 mg once daily • Aged ≥13 years; 75 mg once daily Zanamivir (aged ≥5 yr) for 10 days: • 10 mg (2 inhalations) once daily[c]	None	Primary chemoprophylaxis is indicated for unvaccinated HIV-infected children with moderate-to-severe immunosuppression (as assessed by immunologic and/or clinical diagnostic categories) who are household contacts or close contacts of individuals with confirmed or suspected influenza. Chemoprophylaxis of vaccinated HIV-infected children with severe immunosuppression also may be indicated based on health-care provider assessment of the exposure situation. Post-exposure antiviral chemoprophylaxis should be initiated as soon as possible after exposure. [a] **Oseltamivir chemoprophylaxis duration:** Recommended duration is 10 days when administered after a household exposure and 7 days after the most recent known exposure in other situations. For control of outbreaks in long-term care facilities and hospitals, CDC recommends antiviral chemoprophylaxis for a minimum of 2 weeks and up to 1 week after the most recent known case was identified (see www.cdc.gov/mmwr/preview/mmwrhtml/rr6001a1.htm). [b] Oseltamivir is approved by the FDA for treatment of influenza in children aged ≥2 weeks. It is not approved for prophylaxis in children aged <1 year. However, the CDC recommends that health-care providers who treat children ages ≥3 months to <1 year administer a chemoprophylaxis dose of 3 mg/kg body weight/dose once daily. Chemoprophylaxis for infants aged <3 months is not recommended unless the exposure situation is judged to be critical. **Premature infants:** Current weight-based dosing recommendations for oseltamivir are not appropriate for premature infants (i.e., gestational age at delivery <38 weeks). See *J Infect Dis* 202 [4]:563-566, 2010 for dosing recommendations in premature infants. **Renal insufficiency:** A reduction in dose of oseltamivir is recommended for patients with creatinine clearance <30 mL/min. [c] **Zanamivir:** Zanamivir is not recommended for chemoprophylaxis in children aged <5 years old.	November 6, 2013

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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)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Influenza **Primary Chemoprophylaxis** Influenza A (ONLY) *Oseltamivir-resistant, adamantane-sensitive strains* Based on CDC influenza surveillance;http://www.cdc.gov/flu/weekly	Amantadine or rimantadine for 10 daysd: Aged 1–9 years; 2.5 mg/kg body weight/dose twice daily (maximum dose of 150 mg/day) Aged ≥10 years <40 kg; 2.5 mg/kg body weight/dose twice daily ≥40 kg; 100 mg per dose twice daily (maximum dose of 200 mg/day)		[d] **Adamantanes:** Because of resistance in currently circulating influenza A virus strains, amantadine and rimantadine are not currently recommended for chemoprophylaxis or treatment (adamantanes are not active against influenza B virus). However, potential exists for emergence of oseltamivir-resistant, adamantane-sensitive circulating influenza A strains. Therefore, verification of antiviral sensitivity of circulating influenza A strains should be done using the CDC influenza surveillance website: http://www.cdc.gov/flu/weekly/fluactivitysurv.htm If administered based on CDC antiviral sensitivity surveillance data, both amantadine and rimantadine are recommended for chemoprophylaxis of influenza A in children aged ≥1 yr. For treatment, rimantadine is only approved for use in adolescents aged ≥13 years. Rimantadine is preferred over amantadine because of less frequent adverse events. Some pediatric influenza specialists may consider it appropriate for treatment of children aged >1 year. **Renal insufficiency:** A reduction in dose of amantadine is recommended for patients with creatinine clearance <30 mL/min.	November 6, 2013
Isosporiasis **(Cystoisosporiasis)**	There are no U.S. recommendations for primary prophylaxis of isosporiasis.	N/A	Initiation of cART to avoid advanced immunodeficiency may reduce incidence; TMP-SMX prophylaxis may reduce incidence.	November 6, 2013

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Table 1: Primary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 4 of 9)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Malaria	For Travel To Chloroquine-Sensitive Areas: • 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 • Atovaquone/proguanil once daily started 1–2 days before travel, for duration of stay, and then for 1 week after returning home • 11–20 kg; 1 pediatric tablet (62.5 mg/25 mg) • 21–30 kg, 2 pediatric tablets (125 mg/50 mg) • 31–40 kg; 3 pediatric tablets (187.5 mg/75 mg) • >40 kg; 1 adult tablet (250 mg/100 mg) • 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 • Mefloquine 5 mg/kg body weight orally given once weekly (max 250 mg) For Areas with Mainly P. Vivax: • 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 For Travel to Chloroquine-Resistant Areas: • Atovaquone/proguanil once daily started 1–2 days before travel, for duration of stay, and then for 1 week after returning home • 11–20 kg; 1 pediatric tablet (62.5 mg/25 mg) • 21–30 kg; 2 pediatric tablets (125 mg/50 mg) • 31–40 kg; 3 pediatric tablets (187.5 mg/75 mg) • >40 kg; 1 adult tablet (250 mg/100 mg) • 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 • Mefloquine 5 mg/kg body weight orally given once weekly (maximum 250 mg)	N/A	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: http://www.cdc.gov/malaria/ 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. G6PD screening must be performed prior to primaquine use. Chloroquine phosphate is the only formulation of chloroquine available in the United States; 10 mg of chloroquine phosphate = 6 mg of chloroquine base. For travel to chloroquine-resistant areas, preferred drugs are atovaquone/proguanil, doxycycline (for children aged ≥8 years) or mefloquine.	November 6, 2013
Microsporidiosis	N/A	N/A	Not recommended	December 15, 2016

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Table 1: Primary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 5 of 9)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed

***Mycobacterium avium* Complex (MAC)**	• Clarithromycin 7.5 mg/kg body weight (maximum 500 mg) by mouth orally twice daily, **or**
	• Azithromycin 20 mg/kg body weight (maximum 1200 mg) orally once weekly
		• Azithromycin 5 mg/kg body weight (maximum 250 mg) orally once daily
		• Children aged >5 years: rifabutin 300 mg orally once daily with food
			Primary Prophylaxis Indicated for Children:
			• Aged <1 year with CD4 count <750 cells/mm^3
			• Aged 1 to <2 years with CD4 count <500 cells/mm^3;
			• Aged 2 to <6 years with CD4 count <75 cells/mm^3
			• Aged ≥6 years with CD4 count <50 cells/mm^3
			Criteria for Discontinuing Primary Prophylaxis:
			• Do not discontinue in children age <2 years.
			• After ≥6 months of cART and:
			  • Aged 2 to <6 years with CD4 count >200 cells/mm3 for >3 consecutive months
			  • 1Aged ≥6 years with CD4 count >100 cells/mm^3 for >3 consecutive months
			Criteria for Restarting Primary Prophylaxis:
			• Aged 2 to <6 years with CD4 count <200 cells/mm^3
			• Aged ≥6 years with CD4 count <100 cells/mm^3
				November 6, 2013

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Table 1: Primary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 6 of 9)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Mycobacterium Tuberculosis (post-exposure)	Source Case Drug Susceptible: • Isoniazid 10–15 mg/kg body weight (maximum 300 mg/day) by mouth daily for 9 months Source Case Drug Resistant: • Consult expert and local public health authorities.	• 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 • 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	Drug-drug interactions with cART should be considered for all rifamycin containing alternatives. 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.	November 6, 2013

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Table 1: Primary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 7 of 9)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
***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/ mm^3 or CD4 percentage <15%; HIV-infected children aged 6–12 years with CD4 count <200 cells/ mm^3 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/mm^3 for >3 consecutive months, or • Aged ≥6 years, CD4 percentage ≥15% or CD4 count is ≥200 cells/ mm^3 for >3 consecutive months Criteria for Restarting Primary Prophylaxis: • Aged 1 to < 6 years with CD4 percentage <15 or CD4 count <500 cells/mm^3 • Aged ≥6 years with CD4 percentage <15% or CD4 count <200 cells/mm^3	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

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Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Toxoplasmosis	TMP-SMX 150/750 mg/m^2 body surface area once daily by mouth	For Children Aged ≥1 Month: • Dapsone 2 mg/kg body weight or 15 mg/m^2 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/m^2 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/m^2 body surface area per dose once daily by mouth 3 times weekly on 3 consecutive days per week • TMP-SMX 75/375 mg/m^2 body surface area per dose twice daily by mouth every day • TMP-SMX 75/375 mg/m^2 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/mm^3 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/mm^3 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/mm^3	November 6, 2013

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Table 1: Primary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 9 of 9)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Varicella-Zoster Virus (VZV) Pre-Exposure Prophylaxis	Varicella vaccine	N/A	See Figures 1 and 2 for detailed vaccine recommendations.	November 6, 2013
Varicella-Zoster Virus (VZV) Primary (Post-Exposure) Prophylaxis	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 (BIII). • 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. [a] CDC. Revised classification system for human immunodeficiency virus infection in children less than 13 years of age. Official authorized addenda: human immunodeficiency virus infection codes and official guidelines for coding and reporting ICD-9-CM. *MMWR Morb Mortal Wkly Rep*. 1994;43:1-19. Available at http://www.cdc.gov/mmwr/PDF/rr/rr4312.pdf.	November 6, 2013

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

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