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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

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

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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 1: Primary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 2 of 9)

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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 1: Primary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 8 of 9)

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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

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)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Bacterial Infections *S. pneumoniae* and other invasive bacteria.	• TMP-SMX 75/375 mg/m^2 body surface area per dose by mouth twice daily	• IVIG 400 mg/kg body weight every 2–4 weeks	Secondary Prophylaxis Indicated: • >2 serious bacterial infections in a 1-year period in children who are unable to take cART 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: • >2 serious bacterial infections in a 1-year period despite cART	November 6, 2013
Candidiasis	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	N/A	Secondary Prophylaxis Indicated: • Frequent or severe recurrences Criteria for Discontinuing Secondary Prophylaxis: • When CD4 count or percentage has risen to CDC immunologic Category 2 or 1 Criteria for Restarting Secondary Prophylaxis: • Frequent severe recurrences	November 6, 2013
Coccidioidomycosis	Fluconazole 6 mg/kg body weight (maximum 400 mg) by mouth once daily	Itraconazole 2–5 mg/kg body weight (maximum 200 mg) by mouth per dose twice daily	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 <250 cells/mm^3 or CD4 percentage <15%.	November 6, 2013
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 cART 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	November 6, 2013
Cryptosporidiosis	N/A	N/A	N/A	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 2: Secondary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 2 of 6)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
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 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 *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/mm^3 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/mm^3	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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 2: Secondary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 3 of 6)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Herpes Simplex Virus (HSV) Infections	Mucocutaneous Disease: • Acyclovir 20 mg/kg body weight/dose (maximum 800 mg/dose) by mouth BID Suppressive Therapy After Neonatal Skin, Eye, Mouth, or CNS Disease: • Acyclovir 300 mg/m^2 body surface area/dose by mouth TID for 6 months	Mucocutaneous Disease, For Adolescents Old Enough to Receive Adult Dosing: • Valacyclovir 500 mg by mouth BID, or • 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.	November 6, 2013
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 cART • Negative *Histoplasma* blood cultures • 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.	November 6, 2013
Human Papillomavirus (HPV)	N/A	N/A	N/A	November 6, 2013
Influenza	N/A	N/A	No role for secondary chemoprophylaxis	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 2: Secondary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 4 of 6)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
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. http://wwwnc.cdc.gov/travel/yellowbook/2012/chapter-3-infectious-diseases-related-to-travel/malaria.htm#1939	November 6, 2013
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 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	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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 2: Secondary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 5 of 6)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
***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 (max 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 cART • Completed ≥12 months MAC therapy • Asymptomatic for signs and symptoms of MAC • Aged 2 to <6 years with CD4 count >200 cells/ mm^3 for ≥6 consecutive months • Aged ≥6 years with CD4 count >100 cells/mm^3 for ≥6 consecutive months Criteria for Restarting Secondary 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
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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 2: Secondary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 6 of 6)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Syphilis	N/A	N/A	Secondary Prophylaxis Indicated: • N/A Criteria For Discontinuing Secondary Prophylaxis: • N/A Criteria For Restarting Secondary Prophylaxis: • N/A	November 6, 2013
Toxoplasmosis (Suppressive Therapy)	• Sulfadiazine 42.5–60 mg/kg body weight per dose twice daily* (maximum 2–4 g per day) by mouth, **plus** • 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 once every 3 days	• Clindamycin 7–10 mg/kg body weight per dose by mouth 3 times daily, plus • 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 once every 3 days Children Aged 1–3 Months and >24 Months: • Atovaquone 30 mg/kg body weight by mouth once daily • Leucovorin, 5 mg by mouth every 3 days • TMP-SMX, 150/750 mg/m^2 body surface area once daily by mouth 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 • TMP-SMX, 150/750 mg/m^2 body surface area once daily by mouth	Secondary Prophylaxis Indicated: • Prior toxoplasmic encephalitis **Note:** Alternate regimens with very limited data in children. TMP-SMX only to be used if patient intolerant to other regimens Criteria for Discontinuing Secondary Prophylaxis *If All of the Following Criteria are Fulfilled:* • Completed ≥6 months of cART, completed initial therapy for TE, asymptomatic for TE, **and** • Aged 1 to < 6 years; CD4 percentage ≥15% for >6 consecutive months • Aged ≥6 years; CD4 cell count >200 cells/mm^3 for >6 consecutive months Criteria For Restarting Secondary Prophylaxis: • Aged 1 to <6 years with CD4 percentage <15% • Aged ≥6 years with CD4 cell count <200 cells/mm^3	November 6, 2013
Varicella-Zoster Virus (VZV)	N/A	N/A	There is no indication for secondary prophylaxis	November 6, 2013

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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment 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 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Bacterial Infections Bacterial pneumonia *S. pneumoniae*; occasionally *S. aureus*, *H. influenzae*, *P. 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 (max 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-U flavored pastilles by mouth 4–5 times daily *Treatment Duration:* • 7 to 14 days Esophageal Disease: • Fluconazole 6–12 mg/kg body weight by mouth once daily (maximum dose: 600 mg)	Oropharyngeal (Fluconazole-Refractory): • Itraconazole oral solution 2.5 mg/kg body weight/dose by mouth twice daily (maximum 200–400 mg/day) Esophageal Disease: • Amphotericin B (deoxycholate) 0.3–0.7 g/kg body weight IV once daily *Echinocandins:* • Anidulafungin	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 HIV-infected children 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 HIV-uninfected immunocompromised children. Voriconazole Dosing in Pediatric Patients: • 9 mg/kg body weight/dose every 12 hours IV loading for day 1, followed by 8 mg/kg body weight/dose IV every 12	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 2 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Candidiasis, continued	• Itraconazole oral solution, 2.5 mg/kg body weight/dose by mouth twice daily *Treatment Duration:* • Minimum of 3 weeks and for at least 2 weeks following the resolution of symptoms	• 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 • Caspofungin • Infants aged <3 months, 25 mg/m^2 body surface area/dose daily IV • Aged 3 months–17 years, 70 mg/m^2/day IV loading dose followed by 50 mg/m^2/day IV (maximum 70 mg). **Note:** dosing based on surface area is recommended for children for caspofungin. • Aged ≥18 years, 70-mg loading dose IV, then 50 mg/dose daily IV • Micafungin **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. • Neonates, up to 10–12 mg/kg bodyweight/dose daily IV may be required to achieve therapeutic concentrations. • Infants, <15 kg body weight, 5–7 mg/kg body weight/dose daily IV • Children ≤40 kg body weight and aged 2–8 years, 3–4 mg/kg body weight/dose daily IV • Children ≤40 kg body weight and aged 9–17 years, 2–3 mg/kg body weight/dose daily IV • Children >40 kg body weight, 100 mg/dose daily IV • IV fluconazole • Children, 6–12 mg/kg body weight/dose daily for infants and children of all ages (maximum dose: 600 mg daily).	hours. • Conversion to oral voriconazole should be at 9 mg/kg body weight/dose orally every 12 hours. • Children aged ≥12 years and weighing at least 40 kg can use adult dosing (load 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.) Anidulafungin in Children Aged 2–17 Years • Loading dose of 3 mg/kg body weight/once daily followed by 1.5 mg/kg body weight/once daily (100 mg/day maximum). If a neonate's creatinine level is >1.2 mg/dL for >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 <1.2 mg/dL *Treatment Duration:* • Patients with esophageal candidiasis should be treated for a minimum of 3 weeks and for at least 2 weeks following resolution of symptoms. • Aged ≥18 years, 400 mg/dose once daily (6 mg/kg body weight once daily). *Treatment Duration:* • Patients with esophageal candidiasis should be treated for a minimum of 3 weeks and for at least 2 weeks following resolution of symptoms.	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 3 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed

Candidiasis, continued	Invasive Disease:
	Critically Ill
	Echinocandin Recommended:
	• Anidulafungin
	  • Aged 2–17 years, Load with 3 mg/kg body weight/daily dose and then maintenance at 1.5 mg/kg body weight once daily
	  • Aged ≥18 years, 200 mg loading dose, then 100 mg once daily
	• Caspofungin
	  • Infants aged <3 months, 25 mg/m^2 body surface area/dose once daily IV
	  • Aged 3 months–17 years, 70 mg/m^2 body surface area/day loading dose followed by 50 mg/m^2 once daily (maximum, 70 mg) (note: dosing based on surface area is recommended for children for caspofungin);
	  • Aged ≥18 years, 70-mg loading dose, then 50 mg once daily;
	• Micafungin
	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.
	  • Neonates, up to 10–12 mg/kg bodyweight/dose daily IV may be required to achieve therapeutic concentrations.
	  • Infants <15 kg body weight, 5–7 mg/kg/day
	  • Children ≤40 kg body weight and aged 2–8 years, 3–4 mg/kg body weight/dose daily IV
	  • Children ≤40 kg body weight and aged 9–17 years, 2–3 mg/kg body weight/dose daily
		Invasive Disease:
		• 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)
		• Lipid formulations of amphotericin B, 5 mg/kg body weight IV once daily
				November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 4 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Candidiasis, continued	• Children >40 kg body weight, 100 mg/dose daily IV *Not Critically Ill* *Fluconazole Recommended:* • 12 mg/kg body weight/dose daily (max dose: 600 mg) for infants and children of all ages • Avoid fluconazole for *C. krusei* and *C. glabrata*, avoid echinocandin for *C. parapsilosis*. *Treatment Duration:* • Based on presence of deep-tissue foci and clinical response; in patients with candidemia, treat until 2 weeks after last positive blood culture.			November 6, 2013
Coccidioido-mycosis	Severe Illness with Respiratory Compromise due to Diffuse Pulmonary or Disseminated Non-Meningitic Disease: • Amphotericin B deoxycholate 0.5–1.0 mg/kg body weight IV once daily, until clinical improvement. • 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). • 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.	Severe Illness with Respiratory Compromise Due to Diffuse Pulmonary or Disseminated Non-Meningitic Disease (If Unable to Use Amphotericin): • Fluconazole 12mg/kg body weight (maximum 800 mg) per dose IV or by mouth once daily • Treatment is continued for total of 1 year, followed by secondary prophylaxis.	Surgical debridement of bone, joint, and/or excision of cavitary lung lesions may be helpful. Itraconazole is the preferred azole for treatment of bone infections. Some experts initiate an azole during amphotericin B therapy; others defer initiation of the azole until after amphotericin B is stopped. For treatment failure, can consider voriconazole, caspofungin, or posaconazole (or combinations). However, experience is limited and definitive pediatric dosages have not been determined. Options should be discussed with an expert in the treatment of coccidioidomycosis. Chronic suppressive therapy (secondary prophylaxis) with fluconazole or itraconazole is routinely recommended following initial induction therapy for disseminated disease and is continued lifelong for meningeal disease. Therapy with amphotericin results In a more rapid clinical response in severe, non-meningeal disease.	November 6, 2013
	Meningeal Infection: • Fluconazole 12 mg/kg body weight (maximum 800 mg) IV or by mouth once daily followed by secondary lifelong prophylaxis.	Meningeal Infection (Unresponsive to Fluconazole): • IV amphotericin B plus intrathecal amphotericin B followed by secondary prophylaxis. **Note:** Expert consultation recommended.		

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 5 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Coccidioido-mycosis, continued	Mild-to-Moderate Non-Meningeal Infection (e.g., Focal Pneumonia): • Fluconazole 6–12 mg/kg body weight (maximum 400 mg) per dose IV or by mouth once daily.	Mild-to-Moderate Non-Meningeal Infection (e.g., Focal Pneumonia): • 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. • Duration of treatment determined by rate of clinical response.		November 6, 2013
Cryptococcosis	CNS Disease *Acute Therapy (Minimum 2-Week Induction Followed by Consolidation Therapy):* • 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 *Consolidation Therapy (Followed by Secondary Prophylaxis):* • 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	CNS Disease *Acute Therapy (Minimum 2-Week Induction Followed by Consolidation Therapy)* *If Flucytosine Not Tolerated or Unavailable:* • **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. *If Amphotericin B-Based Therapy Not Tolerated:* • 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 *Consolidation Therapy (followed by secondary prophylaxis):* • 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	In patients with meningitis, CSF culture should be negative prior to initiating consolidation therapy. Overall, *in vitro* resistance to antifungal agents used to treat cryptococcosis remains uncommon. Newer azoles (voriconazole, posaconazole, ravuconazole) are all very active *in vitro* against *C. neoformans*, but published clinical experience on their use for cryptococcosis is limited. Liposomal amphotericin and amphotericin B lipid complex are especially useful for children with renal insufficiency or infusion-related toxicity to amphotericin B deoxycholate. Liposomal amphotericin and amphotericin B lipid complex are **significantly more expensive than amphotericin B deoxycholate**. 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. Serum itraconazole concentrations should be monitored to optimize drug dosing. Amphotericin B may increase toxicity of flucytosine by increasing cellular uptake, or impair its renal	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 6 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Cryptococcus, continued	Localized Disease, Including Isolated Pulmonary Disease (CNS Not Involved)[b]: • 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 Disseminated Disease (CNS Not Involved) or Severe, Pulmonary Disease[b]: • Amphotericin B 0.7–1.0 mg/ kg body weight, or • Liposomal amphotericin, 3–5 mg/kg body weight, or • Amphotericin B lipid complex 5 mg/kg body weight IV once daily (± flucytosine)	200 mg/ dose; 600 mg/day). See comment on itraconazole under Other Options/Issues. Localized Disease Including Isolated Pulmonary Disease (CNS Not Involved)[b]: • Amphotericin B, 0.7–1.0 mg/kg body weight, or • Amphotericin liposomal 3–5 mg/kg body weight, or • Amphotericin lipid complex, 5 mg/kg body weight IV once daily Disseminated Disease (CNS Not Involved) or Severe, Pulmonary Disease[b]: • 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	excretion, or both. 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. [b] Duration of therapy for non-CNS disease depends on site and severity of infection and clinical response	November 6, 2013
Cryptospor-idiosis	Effective cART: • Immune reconstitution may lead to microbiologic and clinical response	There is no consistently effective therapy for cryptosporidiosis in HIV-infected individuals; optimized cART and a trial of nitazoxanide can be considered. Nitazoxanide (**BI**, HIV-Uninfected; **BII***, HIV-Infected in Combination with Effective cART): • 1–3 years: Nitazoxanide (20 mg/mL oral solution) 100 mg orally twice daily with food • 4–11 years: Nitazoxanide (20 mg/mL oral solution) 200 mg orally twice daily with food • ≥12 years: Nitazoxanide tablet 500 mg orally twice daily with food *Treatment Duration:* • 3–14 days	Supportive Care: • Hydration, correct electrolyte abnormalities, nutritional support Antimotility agents (such as loperamide) should be used with caution in young children.	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 7 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Cytomegalovirus (CMV)	Symptomatic Congenital Infection with Neurologic Involvement: • Ganciclovir 6 mg/kg body weight per dose IV every 12 hours for 6 weeks 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 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	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 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. • 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	• 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. • 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.	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 8 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed

Giardiasis	• Tinidazole, 50 mg/kg by mouth, administered as 1 dose given with food (maximum 2 g). **Note:** Based on data from HIV-uninfected children
	• Nitazoxanide. **Note:** Based on data from HIV-uninfected children
	  • 1–3 years: 100 mg by mouth every 12 hours with food for 3 days
	  • 4–11 years: 200 mg by mouth every 12 hours with food for 3 days
	  • ≥12 years: 500 mg by mouth every 12 hours with food for 3 days
		Metronidazole 5 mg/kg by mouth every 8 hours for 5-7 days.
		Note: Based on data from HIV-uninfected children
			Tinidazole is approved in the United States for children aged ≥3 years. It is available in tablets that can be crushed.
			Metronidazole has high frequency of gastrointestinal side effects. A pediatric suspension of metronidazole is not commercially available but can be compounded from tablets. It is not FDA-approved for the treatment of giardiasis.
			Supportive Care:
			• Hydration
			• Correction of electrolyte abnormalities
			• Nutritional support
			Antimotility agents (e.g., loperamide) should be used with caution in young children.
				November 6, 2013

Hepatitis B Virus (HBV)	Treatment of Only HBV Required (Child Does Not Require cART): • IFN-α 3 million units/m^2 body surface area SQ 3 times a week for 1 week, followed by dose escalation to 6 million units/m^2 body surface area (max 10 million units/dose), to complete a 24-week course, or • For children aged ≥12 years, adefovir 10 mg by mouth once daily for a minimum of 12 months (uncertain if risk of HIV resistance) Treatment of Both HIV And HBV Required (Child Not Already Receiving 3TC or FTC) • 3TC 4 mg/kg body weight (maximum 150 mg) per dose by mouth twice daily as part of a fully suppressive cART regimen • For children aged ≥2 years, include tenofovir as part of cART regimen with 3TC or FTC. For children aged ≥12, tenofovir dose is 300 mg once daily. For children aged <12 year, and 8 mg/kg body weight per dose once daily (maximum dose 300 mg)	• IFN-α 10 million units/m^2 body surface area SQ 3 times a week for 6 months (sometimes used for retreatment of failed lower-dose interferon therapy) • Alternative for 3TC: FTC 6 mg/kg body weight (maximum 200 mg) once daily	Indications for Treatment Include: • Detectable serum HBV DNA, irrespective of HBeAg status, for >6 months; and • Persistent (>6 months) elevation of serum transaminases (≥ twice the upper limit of normal); or • Evidence of chronic hepatitis on liver biopsy IFN-α is contraindicated in children with decompensated liver disease; significant cytopenias, severe renal, neuropsychiatric, or cardiac disorders; and autoimmune disease. Choice of HBV treatment options for HIV/HBV-co-infected children depends upon whether concurrent HIV treatment is warranted. 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. Tenofovir 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 <18 years. It should only be used for HBV in HIV/HBV-infected children as part of a cART regimen.	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 9 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Hepatitis B Virus (HBV), continued	Treatment of Both HIV and HBV Required (Child Already Receiving cART Containing 3TC or FTC, Suggesting 3TC/FTC Resistance): • For children aged ≥2 years, include tenofovir as part of cART regimen with 3TC or FTC. For children aged ≥12 years, tenofovir dose is 300 mg once daily. For children aged <12 years, 8 mg/kg body weight per dose once daily (maximum dose 300 mg) • For children aged ≥12 years, add adefovir 10 mg by mouth once daily or entecavir 0.5 mg by mouth once daily in addition to cART regimen. • For children aged <12 years, give 6-month course of IFN-α as above in addition to 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 tenofovir 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 >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 <16 years; a pharmacokinetic study is under way in HIV-uninfected children.	November 6, 2013

Hepatitis C Virus (HCV)	IFN-α Plus Ribavirin Combination Therapy:
	• Pegylated IFN-α: Peg-IFN 2a 180 μg/1.73 m^2 body surface area subcutaneously once per week (maximum dose 180 μg) OR Peg-IFN 2b 60 μg/m^2 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.
	  • >36 to 49 kg: 200 mg a.m.
		None	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 <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 >3 years in whom there are no contraindications to treatment
			For recommendations related to use of telaprevir or boceprevir in adults, including
				November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 10 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Hepatitis C Virus (HCV), continued	and 400 mg p.m. • >49 to 61 kg: 400 mg a.m. and p.m. • >61 to 75 kg: 400 mg a.m. and 600 mg p.m. • >75 kg: 600 mg a.m. and p.m. Treatment Duration: • 48 weeks, regardless of HCV genotype		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	November 6, 2013
Herpes Simplex Virus Infections (HSV)	Neonatal CNS or Disseminated Disease: • Acyclovir 20 mg/kg body weight IV/dose TID for ≥21 days Neonatal Skin, Eye, or Mouth Disease: • Acyclovir 20 mg/kg body weight IV/dose TID for 14 days CNS or Disseminated Disease in Children Outside the Neonatal Period: • Acyclovir 10 mg/kg body weight (up to 20 mg/kg body weight/dose in children <12 years) IV TID for 21 days Moderate to Severe Symptomatic Gingivostomatitis: • Acyclovir 5–10 mg/kg body weight/dose IV TID. Patients can be switched to oral therapy after lesions have begun to regress and therapy continued until lesions have completely healed.	• Valacyclovir is approved for immuno-competent 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	For Neonatal CNS Disease: • Repeat CSF HSV DNA PCR should be performed on days 19 to 21 of therapy; do not stop acyclovir until repeat CSF HSV DNA PCR is negative.	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 11 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Herpes Simplex Virus Infections (HSV), continued	Mild Symptomatic Gingivostomatitis: • Acyclovir 20 mg/kg body weight (maximum 400 mg/dose) dose by mouth QID for 7–10 days Recurrent Herpes Labialis: • Acyclovir 20 mg/kg body weight (maximum 400 mg/dose) dose by mouth QID for 5 days For First-Episode Genital Herpes (Adults and Adolescents): • Acyclovir 20 mg/kg body weight (maximim 400 mg/dose) dose by mouth TID for 7–10 days Recurrent Genital Herpes (Adults and Adolescents): • Acyclovir 20 mg/kg body weight (maximum 400 mg/dose) dose by mouth TID for 5 days Children with HSV Keratoconjunctivitis: • Often treated with topical trifluridine (1%) or acyclovir (3%) applied as 1–2 drops 5 times daily. Many experts add oral acyclovir to the topical therapy. 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	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. Acyclovir-Resistant HSV Infection: • Foscarnet 40 mg/kg body weight/dose given IV TID (or 60 mg/kg body weight/dose BID) should be administered slowly over the course of 2 hours (i.e., no faster than 1 mg/kg/minute).	• There is no pediatric preparation of valacyclovir (although crushed capsules can be used to make a suspension) and data on dosing in children are limited; can be used by adolescents able to receive adult dosing. • There is no pediatric preparation of famciclovir and data on dosing in children are unavailable; can be used by adolescents able to receive adult dosing. Alternative and Short-Course Therapy in Immunocompromised Adults with Recurrent Genital Herpes: • Acyclovir 800 mg per dose by mouth BID for 5 days • Acyclovir 800 mg per dose by mouth TID for 2 days **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.	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 12 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Histoplasmosis	Acute Primary Pulmonary Histoplasmosis: • 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 >20% or if aged ≥6, CD4 cell count >300 cells/mm^3), provided monitoring confirms clinical improvement and decreased urine antigen concentrations. Mild Disseminated Disease: • 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 Moderately Severe to Severe Disseminated Disease: *Acute Therapy (Minimum 2-Week Induction, Longer if Clinical Improvement is Delayed, Followed by Consolidation Therapy):* • Liposomal amphotericin B 3–5 mg/kg body weight, IV once daily (preferred) • Amphotericin B deoxycholate 0.7–1 mg/kg body weight IV once daily (alternative) *Consolidation Therapy (Followed by Chronic Suppressive Therapy):* • 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 Central Nervous System Infection *Acute Therapy (4–6 Weeks, Followed by Consolidation Therapy):* • Liposomal amphotericin B, 5 mg/kg body weight IV once daily	Acute Primary Pulmonary Histoplasmosis: • Fluconazole 3–6 mg/kg body weight (maximum 200 mg) by mouth once daily Mild Disseminated Disease: • 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 Moderately Severe to Severe Disseminated Disease: • 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	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. Urine antigen concentration should be assessed at diagnosis. If >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. 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.	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 13 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Histoplasmosis, continued	**(AII)** *Consolidation Therapy (Followed by Chronic Suppressive Therapy):* • 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			November 6, 2013
Human Papillomavirus (HPV)	• 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)** • 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)** • TCA or BCA (80%–90%) applied topically weekly for up to 3 to 6 weeks (provider applied) **(BIII)** • 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)** • Cryotherapy with liquid nitrogen or cryoprobe applied every 1–2 weeks **(BIII)** • Surgical removal either by tangential excision, tangential shave excision, curettage, or electrosurgery	• Intralesional IFN-α is generally not recommended because of high cost, difficult administration, and potential for systemic side effects **(CIII)** • 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)**. • 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.	Adequate topical anesthetics to the genital area should be given before caustic modalities are applied. Sexual contact should be limited while solutions or creams are on the skin. 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. cART has not been consistently associated with reduced risk of HPV-related cervical abnormalities in HIV-infected women. Laryngeal papillomatosis generally requires referral to a pediatric otolaryngologist. Treatment is directed at maintaining the airway, rather than removing all disease. For women who have exophytic cervical warts, a biopsy to exclude HSIL must be performed before treatment. Liquid nitrogen or TCA/BCA is recommended for vaginal warts. Use of a cryoprobe in the vagina is not recommended. Cryotherapy with liquid nitrogen or podophyllin resin (10%–25%) is recommended for urethral meatal warts. Cryotherapy with liquid nitrogen or TCA/BCA or surgical removal is recommended for anal warts. Abnormal Pap smear cytology should be referred to colposcopy for diagnosis and management.	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 14 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed

Influenza A and B	Oseltamivir for 5 days[e]:
	• Aged <3 months; 3 mg/kg/dose twice daily
	• Aged 3 months to <1 year; 3 mg/kg/dose twice daily
	• Aged ≥1 to 12 years; weight-band dosing
	  • ≤15 kg: 30 mg twice-daily
	  • >15 kg to 23 kg: 45 mg twice daily
	  • >23 kg to 40 kg: 60 mg twice daily
	  • >40 kg: 75 mg twice daily
	• Aged ≥13 years; 75 mg twice daily
	Zanamivir (aged ≥7 years) for 5 days:
	• 10 mg (2 inhalations) twice daily[f]
		None	[e]Oseltamivir is FDA-approved for treatment of influenza in children aged ≥2 weeks. The CDC recommends that clinicians who treat children ages ≥3 months to <1 year administer a dose of 3 mg/kg twice daily. A dose of 3 mg/kg/dose twice daily also is recommended for infants aged <3 months.
			Premature Infants: Current weight-based dosing recommendations for oseltamivir are not appropriate for premature infants: gestational age at delivery <38 weeks. See *J Infect Dis* 202 [4]:563-566, 2010 for dosing recommendations in premature infants.
			Oseltamivir treatment duration: Recommended duration for antiviral treatment is 5 days; longer treatment courses can be considered for patients who remain severely ill after 5 days of treatment.
			Renal insufficiency: A reduction in dose of oseltamivir is recommended for patients with creatinine clearance <30 mL/min.
			[f]**Zanamivir:** Zanamivir is not recommended for treatment in children aged <7 years.
				November 6, 2013

Influenza A (ONLY) *Oseltamivir-resistant, adamantane-sensitive strains*
(Based on CDC influenza surveillance www.cdc.gov/flu/weekly/fluactivitysurv.htm)
	Amantadine for 5 days[d]:
	• 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, 200 mg/day)
	Rimantadine for 5 days[d]:
	• Aged ≥13 years; 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.	

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 15 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed

Isosporiasis (Cystoisosporiasis)	TMP-SMX 5 mg/kg body weight of TMP component given twice daily by mouth for 10 days	Pyrimethamine 1 mg/kg body weight plus folinic acid 10-25 mg by mouth once daily for 14 days
		
		Second-Line Alternatives:
		• Ciprofloxacin 10–20 mg/kg body weight/day twice daily by mouth for 7 days
		• Nitazoxanide (see doses below) for 3 consecutive days
		  • Children 1–3 years: 100 mg by mouth every 12 hours
		  • Children 4–11 years: 200 mg by mouth every 12 hours
		  • Adolescents ≥12 years and adults: 500 mg by mouth every 12 hours
			If symptoms worsen or persist, the TMP-SMX dose may be increased to 5 mg/kg/day given 3–4 times daily by mouth for 10 days or the duration of treatment may be lengthened. Duration of treatment with pyrimethamine has not been well established.
			
			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	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
	
	Uncomplicated *P. Falciparum* OR Unknown Malaria Species From Chloroquine-Sensitive Region (See Comments for Link to Resistance Map):
	• 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
		N/A	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
			
			For sensitive and resistant malaria map: 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.	

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 16 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Malaria, continued	chloroquine phosphate [maximum 2500 mg] = 25 mg/kg body weight chloroquine base) *P. vivax, P. ovale, P. malariae, P. knowlesi* (All Areas Except Papua New Guinea, Indonesia; See Comments) *Initial Therapy (Followed by Anti-Relapse Therapy for P. Ovale and P. Vivax):* • 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) *Anti-Relapse Therapy for P. ovale, P. vivax:* • Primaquine 0.5 mg base/kg body weight (max 30 mg base) by mouth once daily for 14 days Uncomplicated *P. falciparum* or Unknown Malaria Species from Chloroquine-Resistant Areas (All Malaria Areas Except Those Listed as Chloroquine Sensitive) or Unknown Region: • Mefloquine (250-mg tablets only): 15 mg/kg body weight (maximum 750 mg) by mouth once, then 10 mg/kg body weight (maximum 500 mg) by mouth given 12 hours later • Quinine sulfate 10 mg/kg body weight (maximum 650 mg) per dose by mouth every 8 hours for 3 to 7 days, **plus** Clindamycin 7 mg/kg body weight per dose by mouth every 8 hours for 7 days, **or** doxycycline: 2.2 mg/kg body weight per dose (maximum 100 mg) given by mouth every 12 hours, **or** tetracycline 6–12.5 mg/kg body weight per dose by mouth given every 6 hours (maximum dose: 500 mg per dose given 4 times daily) for 7 days. • Artemether-lumefantrine: 1 tablet = 20 mg Artemether and 120 mg lumefantrine, a 3-day treatment schedule for a total of 6 doses. The		Treatment should be selected from one of the three following options: • Atovaquone-proguanil plus primaquine phosphate • Quinine sulfate plus **EITHER** doxycycline **OR** tetracycline **PLUS** primaquine phosphate. This regimen cannot be used in children aged <8 years. • Mefloquine plus primaquine phosphate	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 17 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Malaria, continued	second dose follows the initial dose 8 hours later, then 1 dose twice daily for the next 2 days. • 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			
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	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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 18 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Microsporidiosis	Effective ART Therapy: • 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 due to *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 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.	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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 19 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
***Mycobacterium avium* Complex (MAC)**	Initial Treatment (≥2 Drugs): • 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 For Severe Disease, Add: • Rifabutin 10–20 mg/kg body weight (maximum 300 mg/day) orally once daily	If Intolerant to Clarithromycin: • Azithromycin 10–12 mg/ kg body weight (maximum 500 mg/day) orally once daily 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: • Ciprofloxacin 10–15 mg/ kg orally twice daily (maximum 1.5 g/day), or • Levofloxacin 500 mg daily once daily, or • Amikacin 15–30 mg/kg body weight IV in 1 or 2 divided doses (maximum 1.5 g/day)	Combination therapy with a minimum of 2 drugs is recommended for at least 12 months. Clofazimine is associated with increased mortality in HIV-infected adults and should not be used. Children receiving ethambutol who are old enough to undergo routine eye testing should have monthly monitoring of visual acuity and color discrimination. Fluoroquinolones (e.g., ciprofloxacin and levofloxacin) are not labeled for use in children aged <18 years because of concerns regarding potential effects on cartilage; use in younger individuals requires an assessment of potential risks and benefits Chronic suppressive therapy (secondary prophylaxis) is recommended in children and adults following initial therapy.	November 6, 2013
Mycobacterium Tuberculosis	Intrathoracic Disease *Drug-Susceptible TB* *Intensive Phase (2 Months):* • Isoniazid, 10–15 mg/kg body weight (maximum 300 mg/day) by mouth once daily, **plus** • Rifampin 10–20 mg/kg body weight (maximum 600 mg/day) by mouth once daily, **plus** • Pyrazinamide 30–40 mg/kg body weight (maximum 2 g/day) by mouth once daily, **plus** • Ethambutol 15–25 mg/kg body weight (maximum 2.5 g/day) by mouth once daily *Continuation Phase (7 Months):* • Isoniazid 10–15 mg/kg body weight (maximum 300 mg/day) by mouth once daily, **plus** • Rifampin 10–20 mg/kg body weight (maximum 600 mg/day) by mouth once daily Extrathoracic Disease: **Note:** Depends on disease entity • Lymph node TB—treat as minimal intrathoracic disease	Alternative for Rifampin: • Rifabutin 10–20 mg/kg body weight (maximum 300 mg/day) by mouth once daily (same dose if 3 times a week) • Discuss with an expert. Alternative Continuation Phase *If Good Adherence and Treatment Response:* • Isoniazid 20–30 mg/kg body weight (maximum 900 mg/day) by mouth, plus • Rifampin 10–20 mg/kg body weight (maximum 600 mg/day) three times a week. • 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).	Only DOT. If cART-naive, start TB therapy immediately and initiate cART within 2–8 weeks. Already on cART; review to minimize potential toxicities and drug-drug interactions; start TB treatment immediately. Potential drug toxicity and interactions should be reviewed at every visit. Adjunctive Treatment: • Co-trimoxazole prophylaxis • 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. • Corticosteroids (2 mg/kg body weight per day of prednisone	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 20 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Mycobacterium Tuberculosis	• Bone or joint disease–consider extending continuation phase to 10 months (for total duration of therapy of 12 months). TB Meningitis: • 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) • Consider extending continuation phase to 10 months (for total duration of therapy of 12 months). • Discuss with an expert. *Drug-Resistant TB* *MDR-TB:* • Therapy should be based on resistance pattern of child (or of source case where child's isolate is not available); consult an expert. Treatment Duration: • 18–24 months after non-bacteriological diagnosis or after culture conversion; ≥12 months if minimal disease • Discuss with an expert.		[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. 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 levofloxacin 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.	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 21 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
***Pneumocystis* Pneumonia**	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)	If TMP-SMX-Intolerant or Clinical Treatment Failure After 5–7 Days of TMP-SMX Therapy *Pentamidine:* • 4 mg/kg body weight/dose IV/IM once daily is the first choice alternative regimen. **Note:** Pentamidine can be changed to atovaquone after 7–10 days IV therapy. *Atovaquone* *Daily Dosing:* • 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 *Twice-Daily Dosing*:* • Children aged ≥13 years: 750 mg/dose by mouth twice daily *Some experts use twice-daily dosing of atovaquone as alternative treatment for PCP in children aged <12 years: • Children aged 1–3 months and >24 months to 12 years: 15–20 mg/kg body weight /dose by mouth twice daily with food • Children aged 4–24 months: 22.5 mg/kg body weight/dose by mouth twice daily with food.	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). 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. Primaquine base 0.3 mg/kg body weight by mouth once daily (maximum 30 mg/day) **plus** clindamycin 10mg/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. Indications for Corticosteroids: • PaO_2 <70 mm Hg at room air or alveolar-arterial oxygen gradient >35 mm Hg *Prednisone Dose:* • 1 mg/kg body weight/dose by mouth twice daily for 5 days, then • 0.5–1 mg/kg body weight/dose by mouth twice daily for 5 days, then • 0.5 mg/kg body weight by mouth once daily for days 11 to 21. Alternative Corticosteroid Regimens Include: • 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 • 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. Chronic suppressive therapy (secondary prophylaxis) with TMP/SMX is recommended in children and adults following initial therapy (see Secondary Prophylaxis).	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 22 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Syphilis	Congenital *Proven or Highly Probable Disease:* • 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 • If diagnosed after 1 month of age, aqueous penicillin G 200,000–300,000 unit/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 days *Possible Disease:* • 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. Acquired: *Early Stage (Primary, Secondary, Early Latent):* • Benzathine penicillin 50,000 units/kg body weight (maximum 2.4 million units) IM for 1 dose *Late Latent:* • Benzathine penicillin 50,000 units/kg body weight (maximum 2.4 million units) IM once weekly for 3 doses *Neurosyphilis (Including Ocular):* • 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	Congenital *Proven or Highly Probable Disease (Less Desirable if CNS Involvement):* • Procaine penicillin G 50,000 units/kg body weight IM once daily for 10 days *Possible Disease:* • 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.	For treatment of congenital syphilis, repeat the entire course of treatment if >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.	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 23 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Toxoplasmosis	Congenital Toxoplasmosis: • 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, **plus** • Leucovorin (folinic acid) 10 mg by mouth or IM with each dose of pyrimethamine, **plus** • Sulfadiazine 50 mg/kg body weight by mouth twice daily *Treatment Duration:* • 12 months Acquired Toxoplasmosis *Acute Induction Therapy (Followed by Chronic Suppressive Therapy):* • 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, plus • Sulfadiazine 25–50 mg/kg body weight (maximum 1–1.5 g/dose) by mouth per dose 4 times daily, plus • Leucovorin 10–25 mg by mouth once daily, followed by chronic suppressive therapy Treatment Duration (Followed by Chronic Suppressive Therapy): • ≥6 weeks (longer duration if clinical or radiologic disease is extensive or response in incomplete at 6 weeks)	For Sulfonamide-Intolerant Patients: • 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	Congenital Toxoplasmosis: • For infants born to mothers with symptomatic *Toxoplasma* infection during pregnancy, empiric therapy of the newborn should be strongly considered irrespective of the mother's treatment during pregnancy. Acquired Toxoplasmosis: • Pyrimethamine use requires CBC monitoring at least weekly while on daily dosing and at least monthly while on less than daily dosing. • TMP-SMX—TMP 5 mg/kg body weight plus SMX 25 mg/kg body weight per dose IV or by mouth given twice daily has been used as an alternative to pyrimethamine-sulfadiazine in adults, but has not been studied in children. • Atovaquone (for adults, 1.5 g by mouth twice daily—double the prophylaxis dose) in regimens combined with pyrimethamine/leucovorin, with sulfadiazine alone, or as a single agent in patients intolerant to both pyrimethamine and sulfadiazine, has been used in adults, but these regimens have not been studied in children. • Azithromycin (for adults, 900–1,200 mg/day, corresponding to 20 mg/kg/day in children) has also been used in adults combined with pyrimethamine-sulfadiazine, but has not been studied in children. • Corticosteroids (e.g., prednisone, dexamethasone) have been used in children with CNS disease when CSF protein is very elevated (>1,000 mg/dL) or there are focal lesions with significant mass effects, with discontinuation as soon as clinically feasible. • Anticonvulsants should be administered to patients with a history of seizures and continued through the acute treatment; but should not be used prophylactically.	November 6, 2013

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 3: Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (page 24 of 24)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Varicella-Zoster Virus (VZV)	Chickenpox *Children with No or Moderate Immune Suppression (CDC Immunologic Categories 1 and 2) and Mild Varicella Disease:* • 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 *Children with Severe Immune Suppression (CDC Immunologic Category 3):* • Acyclovir 10 mg/kg body weight 500 mg/m^2/dose IV every 8 hours for 7–10 days and until no new lesions for 48 hours Zoster *Children with Uncomplicated Zoster:* • Acyclovir 20 mg/kg body weight/dose (max 800 mg/dose) by mouth QID for 7–10 days. *Children with Severe Immunosuppression (CDC Immunologic Category 3), Trigeminal or Sacral Nerve Involvement, Extensive Multidermatomal, or Disseminated Zoster:* • 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 *Children with Progressive Outer Retinal Necrosis:* • Ganciclovir 5 mg/kg body weight/dose IV every 12 hours, **plus** • foscarnet 90 mg/kg body weight/dose IV) every 12 hours, **plus** • ganciclovir 2 mg/0.05 mL intravitreal twice weekly and/or foscarnet 1.2 mg/0.05 mL intravitreal twice weekly *Children with ARN:* • Acyclovir 10–15 mg/kg body weight/dose IV every 8 hours daily for 10–14 days, **followed by** 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	Patients Unresponsive to Acyclovir: • 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	In children ≥1 year of age, some experts base IV acyclovir dosing on body surface area (500 mg/m^2 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.	November 6, 2013

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- = interferon-alfa; 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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

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)

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
Acyclovir (Zovirax)	Oral Suspension: • 40 mg/mL Capsules: • 200 mg Tablets: • 400 mg • 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	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.
Albendazole (Albenza)	Tablets: • 200 mg	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.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 2 of 22)

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
Amikacin	IV	More Frequent: • Nephrotoxicity • Neurotoxicity (including muscle twitching, seizures) • Ototoxicity, both auditory and vestibular Less Frequent: • Hypersensitivity (skin rash, redness, or swelling) Rare: • Neuromuscular blockade	N/A	Must be infused over 30 to 60 minutes to avoid neuromuscular blockade. Requires dose adjustment in patients with impaired renal function. Should monitor renal function and hearing periodically (e.g., monthly) in children on prolonged therapy. Therapeutic drug monitoring (TDM). indicated
Amphotericin B Deoxycholate (Fungizone)	IV	More Frequent: • Infusion-related reactions (fever/chills; nausea/vomiting; hypotension; anaphylaxis) • Anemia • Hypokalemia • Renal function impairment • Thrombophlebitis (at injection site) Less Frequent or Rare: • Blurred or double vision • Cardiac arrhythmias, usually with rapid infusions • Hypersensitivity (rash) • Leukopenia • Polyneuropathy • Seizures • Thrombocytopenia	• GI disturbance (nausea, vomiting, diarrhea, abdominal pain) • Headache	Monitor BUN, Cr, CBC, electrolytes, LFTs. Infuse over 1 to 2 hours; in patients with azotemia, hyperkalemia, or getting doses >1 mg/kg, infuse over 3 to 6 hours. Requires dose reduction in patients with impaired renal function. Avoid other nephrotoxic drugs, when possible,because nephrotoxicity is exacerbated with concomitant use of other nephrotoxic drugs; permanent nephrotoxicity is related to cumulative dose. Nephrotoxicity may be ameliorated by hydration with 0.9% saline IV over 30 minutes prior to the amphotericin B infusion. Infusion-related reactions less frequent in children than adults; the onset is usually 1 to 3 hours after infusion, duration <1 hour; frequency decreases over time. Pre-treatment with acetaminophen and/or diphenhydramine may alleviate febrile reactions.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 3 of 22)

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
Amphotericin B Lipid Complex (Abelcet)	IV	More Frequent: • Infusion-related reactions (fever/chills, nausea/vomiting; headache, nausea and vomiting) Less Frequent: • Anemia • Leukopenia • Respiratory distress • Thrombocytopenia • Renal function impairment	• GI disturbance (loss of appetite, nausea, vomiting, diarrhea, abdominal pain)	Monitor BUN, Cr, CBC, electrolytes, and LFTs. Infuse diluted solution at rate of 2.5 mg/kg/hour. In-line filters should not be used. 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.
Amphotericin B Liposome (AmBisome)	IV	More Frequent: • Fever, chills • Hypokalemia Less Frequent: • Back pain • Chest pain • Dark urine • Dyspnea • Infusion-related reaction (fever/chills, headache) • Jaundice • Renal function impairment Rare: • Anaphylactic reaction	• GI disturbance (nausea, vomiting, diarrhea, abdominal pain) • Headache • Skin rash	Monitor BUN, Cr, CBC, electrolytes, and LFTs. Infuse over 2 hours. Consider dose reduction in patients with impaired renal function.
Artesunate	IV: • Only available from CDC Malaria Hotline; telephone: (770) 488-7788	Rare: • Anaphylactic reaction • Neutropenia • Bradycardia	• GI disturbance (nausea, vomiting) • Headache • Skin rash	Monitor CBC, LFTs, and electrolytes. ~40% less mortality than with quinidine use in severe malaria 50% lower incidence of hypoglycemia than quinidine
Atovaquone (Mepron)	Oral Suspension: • 150 mg/mL	Frequent: • Fever • Skin rash	Frequent: • GI disturbances (nausea, vomiting, diarrhea) • Headache • Cough • Insomnia	Should be administered with a meal to enhance absorption; bioavailability increases 3-fold when administered with high-fat meal.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

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

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
Atovaquone/ Proguanil (Malarone)	Tablets: • Pediatric tablets; 62.5 mg/ 25 mg • Adult tablets; 250 mg/100 mg	Less frequent: • Vomiting • Pruritus	N/A	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 <30 mL/min.
Azithromycin (Zithromax)	Oral Suspension: • 20 mg/mL • 40 mg/mL Tablets: • 250 mg • 500 mg • 600 mg IV	More Frequent: • Thrombophlebitis (IV form) Rare: • Acute interstitial nephritis • Allergic reactions/ anaphylaxis (dyspnea, hives, rash) • Pseudomembranous colitis	• GI disturbances (abdominal discomfort or pain, diarrhea, nausea, vomiting) • Dizziness, headache	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.
Capreomycin (Capastat)	IM	More Frequent: • Nephrotoxicity Less Frequent: • Hypersensitivity (rash, fever) • Hypokalemia • Neuromuscular blockade • Ototoxicity, both auditory and vestibular • Injection site pain, sterile abscess	N/A	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.
Caspofungin (Cancidas)	IV	More Frequent: • Histamine-mediated symptoms (fever, facial swelling, pruritus, bronchospasm) Rare: • Hypokalemia • Anaphylactic reaction	• GI disturbances (nausea, vomiting, diarrhea) • Headache • Skin rash, facial flushing • Elevated liver transaminases • Thrombophlebitis	Requires dose adjustment in moderate-to-severe hepatic insufficiency. IV infusion over 1 hour in normal saline (do not use diluents containing dextrose)

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 5 of 22)

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
Chloroquine Phosphate (Aralen)	Tablets: • 500 mg • 250 mg	More Frequent: • Pruritus: Common in individuals of black race (25%–33%) Less Frequent, but More Severe: • Auditory toxicity • Ocular toxicity • Neuropsychiatric disorders • QT prolongation • Hepatitis • Bone marrow suppression • Peripheral neuropathy	• Psoriasis exacerbations • GI disturbances (nausea, vomiting, diarrhea) • Visual disturbances including photosensitivity • Tinnitus • Muscle weakness	Store in child-proof containers and protect from light. Can be toxic in overdose. Bitter tasting, so consider administering with foods that can mask the taste. Solution available worldwide, but not in United States. Caution in patients with G6PD deficiency or seizure disorder. Monitor CBC; periodic neurologic and ophthalmologic exams in patients on prolonged therapy.
Cidofovir (Vistide)	IV	More Frequent: • Nephrotoxicity • Neutropenia Less Frequent: • Fever and allergic reactions Rare: • Vision changes due to ocular hypotony • Metabolic acidosis	• GI disturbances (anorexia, diarrhea, nausea, vomiting) • Headache • Asthenia • Proteinuria	Infuse over 1 hour. Should not be used in patients with severe renal impairment. 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. Concurrent use of other nephrotoxic drugs should be avoided. Monitor renal function, urinalysis, electrolytes, and CBC and perform ophthalmologic exams.
Ciprofloxacin (Cipro)	Oral Suspension: • 50 mg/mL • 100 mg/mL Tablets: • 100 mg • 250 mg • 500 mg • 750 mg XR Tablets *Cipro XR:* • 500 mg • 1000 mg *Proquin XR:* • 500 mg IV	Less Frequent: • Phototoxicity Rare: • CNS stimulation • Hepatotoxicity • Hypersensitivity reactions (rash, pruritus, and exfoliative skin disorders including SJS, dyspnea, and vasculitis) • Interstitial nephritis • Phlebitis (at injection sites) • Pseudomembranous colitis • Tendonitis or tendon rupture • QT interval prolongation	More Frequent: • GI disturbances (abdominal discomfort or pain, diarrhea, nausea, vomiting) • CNS toxicity (dizziness, headache, insomnia, drowsiness) Less Frequent: • Change in taste • Photosensitivity	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. IV infusions should be over 1 hour. Do not split, crush, or chew extended-release tablets.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

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

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
Clarithromycin (Biaxin)	Oral Suspension: • 25 mg/mL • 50 mg/mL Tablets: • 250 mg • 500 mg	Rare: • Hepatotoxicity • Hypersensitivity reaction (rash, pruritus, dyspnea) • Pseudomembranous colitis • Thrombocytopenia • QT interval prolongation	More Frequent: • GI disturbances (abdominal discomfort or pain, diarrhea, nausea, vomiting) Less Frequent: • Abnormal taste sensation • Headache • Rash	Requires dose adjustment in patients with impaired renal function. Can be administered without regard to meals. Reconstituted suspension should not be refrigerated. Potential drug interactions
Clindamycin (Cleocin)	Oral Solution: • 15 mg/mL Capsules: • 75 mg, 150 mg, 300 mg IV	More Frequent: • Pseudomembranous colitis Less Frequent: • Hypersensitivity (skin rash, redness, pruritus) • Neutropenia • Thrombocytopenia	More Frequent: • GI disturbances (abdominal pain, nausea, vomiting, diarrhea) Less Frequent: • Fungal overgrowth, rectal and genital areas	IV preparation contains benzyl alcohol, not recommended for use in neonates. IV preparation must be diluted prior to administration. Capsule formulation should be taken with food or a full glass of water to avoid esophageal irritation. Reconstituted oral solution should not be refrigerated.
Cycloserine (Seromycin)	Capsules: • 250 mg	More Frequent: • CNS toxicity (including confusion, anxiety) Less Frequent: • Hypersensitivity (skin rash) • Peripheral neuropathy • Seizures • Psychosis Rare: • Cardiac arrhythmias	• Headache, dizziness, drowsiness, confusion Rare: • Photosensitivity	Take with food to minimize gastric irritation. Neurotoxicity is related to excessive serum concentrations; serum concentrations should be maintained at 25–30 mcg/mL. Requires dose adjustment in patients with impaired renal function. Do not administer to patients with severe renal impairment (because of increased risk of neurotoxicity). Should monitor serum levels, if possible. Should administer pyridoxine at the same time. Monitor renal function, LFTs, and CBC.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 7 of 22)

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
Dapsone	Syrup (available under Compassionate Use IND): • 2 mg/mL Tablets: • 25 mg • 100 mg	More Frequent: • Hemolytic anemia (especially if G6PD deficiency) • Methemoglobinemia • Skin rash Rare: • Blood dyscrasias • Exfoliative skin disorders (including SJS) • Hepatic toxicity • Mood or other mental changes • Peripheral neuritis • Hypersensitivity reaction (fever, rash, jaundice, anemia)	• CNS toxicity (headache, insomnia, nervousness) • GI disturbances (anorexia, nausea, vomiting) • Photosensitivity reactions	Protect from light; dispense syrup in amber glass bottles. Monitor CBC and LFTs.
Doxycycline (Vibramycin)	Tablets and Capsules: • 20 mg • 50 mg • 75 mg • 100 mg Oral Suspension and Syrup: • 5 mg/mL oral suspension • 10 mg/mL oral syrup IV	More Frequent: • GI irritation, pill esophagitis • Photosensitivity Less frequent: • May cause increased intracranial pressure, photosensitivity, hemolytic anemia, rash, and hypersensitivity reactions. • *Clostridium difficile*-associated diarrhea • Pseudotumor cerebri	• Staining of teeth a concern for individuals aged <8 years • Photo-onycholysis • GI disturbances (nausea, vomiting, abdominal cramps)	Swallow with adequate amounts of fluids Avoid antacids, milk, dairy products, and iron for 1 hour before or 2 hours after administration of doxycycline. Use with caution in hepatic and renal disease. IV doses should be infused over 1 to 4 hours. Patient should avoid prolonged exposure to direct sunlight (skin sensitivity). Generally not recommended for use in children aged <8 years because of risk of tooth enamel hypoplasia and discoloration, unless benefit outweighs risk. Monitor renal function, CBC, and LFTs if prolonged therapy.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 8 of 22)

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
Erythromycin	Erythromycin-Base Tablet: • 250 mg • 333 mg • 500 mg Delayed-Release Tablet: • 250 mg • 333 mg • 500 mg Delayed-Release Capsule: • 250 mg Erythromycin Ethyl Succinate *Suspension:* • 200 mg • 400 mg/5 mL *Oral Drops:* • 100 mg/2.5 mL *Chewable Tablet:* • 200 mg *Tablet:* • 400 mg Erythromycin Estolate *Suspension:* • 125 mg • 250 mg/5 mL Erythromycin Stearate *Tablet:* • 250 mg • 500 mg Erythromycin Gluceptate: • IV Erythromycin Lactobionate: • IV	Less Frequent: • Estolate may cause cholestatic jaundice, although hepatotoxicity is uncommon (2% of reported cases). Rare: • QT prolongation • Hypersensitivity reactions (rash, exfoliative skin disorders including SJS)	• GI disturbances (nausea, vomiting, abdominal cramps) • Rash, urticaria • Increased LFTs	Use with caution in liver disease. Oral therapy should replace IV therapy as soon as possible. Give oral doses after meals. Parenteral administration should consist of a continuous drip or slow infusion over 1 hour or longer. Adjust dose in renal failure. 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. High potential for interaction with many ARVs and other drugs.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 9 of 22)

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
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, leucopenia, 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.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 10 of 22)

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
Flucytosine (Ancobon)	Capsules: • 250 mg • 500 mg Oral Liquid: • Extempo-raneous preparation	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 Rare: • 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 (Foscavir)	IV	More Frequent: • Nephrotoxicity • Serum electrolyte abnormalities (hypocalcaemia, hypophosphatemia, hypomagnesemia, hypokalemia) Less Frequent: • Hematologic toxicity (anemia, granulocytopenia) • Neurotoxicity (muscle twitching, tremor, seizures, tingling around mouth) • Cardiac abnormalities secondary to electrolyte changes • Phlebitis (at site of injection) Rare: • Sores or ulcers mouth or throat	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).

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 11 of 22)

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
Ganciclovir (Cytovene)	Capsules: • 250 mg • 500 mg IV	More Frequent: • Granulocytopenia • Thrombocytopenia Less Frequent: • Anemia • CNS effects (confusion, headache) • Hypersensitivity (fever, rash) • Elevated transaminase enzymes • Increase in creatinine, BUN • Phlebitis (at injection sites) Rare: • Retinal detachment • Seizures • Psychosis • Cardiac (hypertension, chest pain)	• 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.
Interferon-alfa-2B (IFN-α-2B; Intron)	Parenteral (SQ or IV use)	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: • Abnormality 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	Severe adverse effects less common in children than adults. Toxicity dose-related, with significant reduction over the first 4 months of therapy. 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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 12 of 22)

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
Interferon-alfa-2B (IFN-α-2B; Intron), continued				(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.
Isoniazid (Nydrazid)	Oral Syrup: • 10 mg/mL Tablets: • 100 mg • 300 mg IM	More Frequent: • Hepatitis prodromal syndrome (anorexia, weakness, vomiting) • Hepatitis • Peripheral neuritis Rare: • Blood dyscrasias • Hypersensitivity (fever, rash, joint pain) • Neurotoxicity (includes seizure) • Optic neuritis	• GI disturbances (abdominal pain, nausea, vomiting, diarrhea) • Elevated liver transaminases • Pyridoxine deficiency	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.
Itraconazole (Sporanox)	Oral Solution: • 10 mg/mL Capsules: • 100 mg IV	Less frequent: • Hypersensitivity (fever, chills, skin rash) • Hypokalemia (can be associated with cardiac arrhythmias) Rare: • Hepatotoxicity • Hematologic abnormalities (thrombocytopenia, leukopenia)	More Frequent: • GI disturbances (abdominal pain, constipation, diarrhea, anorexia, nausea, vomiting) Less Frequent: • CNS effects (dizziness, drowsiness, headache) • Rash	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.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 13 of 22)

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
Kanamycin	IV IM	More Frequent: • Nephrotoxicity • Neurotoxicity (including muscle twitching, seizures) • Ototoxicity, both auditory and vestibular Less Frequent: • Hypersensitivity (skin rash, redness or swelling) Rare: • Neuromuscular blockade	N/A	Must be infused over 30 to 60 minutes to avoid neuromuscular blockade. Requires dose adjustment in patients with impaired renal function. Should monitor renal function and hearing periodically (e.g., monthly) in children on prolonged therapy. Monitor serum concentrations (TDM). Monitor renal function; conduct, hearing exams for patients receiving prolonged therapy.
Ketoconazole (Nizoral)	Tablets: • 200 mg Topical: • Shampoo • Cream • Gel • Foam Suspension: • Extempo-raneous preparation	Less Frequent: • Hypersensitivity (fever, chills, skin rash) Rare: • Hepatotoxicity (including hepatic failure)	Frequent: • GI disturbances (abdominal pain, constipation, diarrhea, anorexia, nausea, vomiting) Less Frequent: • CNS effects (dizziness, drowsiness, headache) Rare: • Gynecomastia • Impotence • Menstrual irregularities • Photophobia	Adverse GI effects occur less often when administered with food. Drugs that decrease gastric acidity or sucralfate should be administered ≥2 hours after ketoconazole. Disulfiram-like reactions have occurred in patients ingesting alcohol. 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 >40 years, but cases reported in children. High-dose ketoconazole suppresses corticosteroid secretion, lowers serum testosterone concentration (reversible). Multiple potential drug interactions. Monitor LFTs.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 14 of 22)

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
Mefloquine (Lariam)	Tablets: • 250 mg	More Frequent: • CNS (psychosis, depression, hallucinations, paranoia, seizures) Rare: • Blood dyscrasias • Cholestasis, elevated bilirubin	• Rash • GI disturbances (abdominal pain, constipation, diarrhea, anorexia, nausea, vomiting) • CNS (dizziness, vivid dreams, insomnia) • Tinnitus, blurred vision	Side effects less prominent in children. Administer with food and plenty of water. Tablets can be crushed and added to food; bitter tasting so administer with foods that can mask the taste Monitor LFTs.
Nitazoxanide (Alinia)	Oral Suspension: • 20 mg/mL Tablets: • 500 mg	N/A	More Frequent: • GI disturbances (abdominal pain, nausea, vomiting) • Headache Rare: • Scleral icterus • Rash	Should be given with food. Shake suspension well prior to dosing.
P-Aminosalicyclic Acid (Paser)	Delayed Release Granules: • 4 g per packet	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	• GI disturbances (abdominal pain, nausea, vomiting, diarrhea)	Should not be administered to patients with severe renal disease. Drug should be discontinued at first sign of hypersensitivity reaction (rash, fever, and GI symptoms typically precede jaundice). Vitamin B12 therapy should be considered in patients receiving for >1 month. Administer granules by sprinkling on acidic foods such as applesauce or yogurt or a fruit drink like tomato or orange juice. Maintain urine at neutral or alkaline pH to avoid crystalluria. The granule soft "skeleton" may be seen in the stool. Monitor CBC and LFTs.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 15 of 22)

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
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 (Pegintron)	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.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 16 of 22)

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
Pegylated Interferon Alfa-2B (Pegintron), continued		Rare: • Abnormality or loss of vision • Allergic reaction (rash, hives) • Hypothyroidism • Development of antinuclear antibodies	transaminases, serum creatinine and BUN, glucose, triglycerides	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.
Pentamidine (Pentam)	IV Aerosol	IV *More Frequent:* • Nephrotoxicity • Hypoglycemia • Hyperglycemia or diabetes mellitus • Elevated liver transaminases • Hypotension • Leukopenia or neutropenia • Thrombocytopenia *Less Frequent:* • Anemia • Cardiac arrhythmias • Hypersensitivity (skin rash, fever) • Pancreatitis • Phlebitis • Sterile abscess (at site injection) Aresol *More Frequent:* • Sneezing • Cough	IV *More Frequent:* • GI disturbances (anorexia, nausea, vomiting, diarrhea) *Less Frequent:* • Unpleasant metallic taste Aresol *More Frequent:* • Bronchospasm	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.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 17 of 22)

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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 18 of 22)

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
Quinidine	IV	Serious: • Cardiac arrhythmias • QT interval prolongation • Hypoglycemia • Hemolytic anemia (with G6PD deficiency) • Hepatotoxicity	Very Frequent: • Cinchonism—syndrome of tinnitus, reversible high-frequency hearing loss, deafness, vertigo, blurred vision, diplopia, photophobia, headache, confusion, and delirium; dose dependent	EKG monitoring is standard of care. Do not give by bolus infusion. If EKG changes observed, slow infusion rate. Monitor CBC and LFTs.
Ribavirin Virazole *Powder for solution for nebulization* Rebetol *Oral capsules and oral solution* Copegus, Ribasphere, Ribapak *Oral tablets and capsules*	Powder for Solution for Nebulization: • Reconstituted product contains 20 mg/mL Oral Solution: • 40 mg/mL Capsules: • 200 mg Tablets: • 200 mg • 400 mg • 600 mg	• Hemolytic anemia (with associated potential for increase in unconjugated bilirubin and uric acid) Less Frequent: • Neutropenia, thrombocytopenia, anemia • Pancreatitis	• CNS effects (fatigue, headache, insomnia, depression) • GI disturbances (abdominal pain, nausea, vomiting) • Skin rash • Myalgia, arthralgia, weakness	Should not be used in patients with severe renal impairment. Should not be used as monotherapy for treatment of hepatitis C, but used in combination with IFN-α. Intracellular phosphorylation of pyrimidine nucleoside analogues (zidovudine, stavudine, zalcitabine) decreased by ribavirin, may have antagonism; use with caution. Enhances phosphorylation of didanosine; use with caution because of increased risk of pancreatitis/mitochondrial toxicity. Oral solution contains propylene glycol. Teratogenic/embryocidal. Contraindicated in pregnant women and their male partners. Avoid pregnancy for additional 6 months after treatment. Monitor CBC, renal function, LFTs, and thyroid function. Perform pregnancy tests regularly while on therapy.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 19 of 22)

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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 20 of 22)

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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in HIV-Infected Children: Preparations and Major Toxicities (page 21 of 22)

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention if Persistent or Bothersome	
Valacyclovir (Valtrex)	Tablets: • 500 mg • 1 g **Note:** An oral suspension formulation 50 mg/mL can be prepared in Ora-Sweet or Syrpalta syrups)	Rare: • Renal failure • Bone marrow suppression • Thrombotic microangiopathy/hemolytic uremic syndrome • CNS (psychosis, seizures, delirium)	More Frequent: • Headache, nausea Less Frequent: • Arthralagia • Dizziness, fatigue • GI disturbances (diarrhea or constipation, anorexia, abdominal pain, vomiting) • Dysmenorrhea	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.
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	• 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.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

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

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

[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- = 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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (Last updated November 6, 2013; last reviewed November 6, 2013)

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.aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/32/drug-interactions/

http://www.drugs.com/drug_interactions.html

http://hivinsite.ucsf.edu/InSite?page=ar-00-02

http://www.nynjaetc.org/clinical_support.html

http://www.clinicaloptions.com/inPractice.aspx

http://epocrates.com

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections
(page 1 of 9)

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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections
(page 2 of 9)

Drug Name	Overlapping Toxicities	Recommendation
*** The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).**		
Cidofovir	Overlapping Toxicities: • Antibacterial drugs: aminoglycosides • Antiviral drugs: foscarnet • Nephrotoxic drugs	Monitor for toxicities of these drugs.
Ciprofloxacin	Decreases Ciprofloxacin Absorption: • ARV drugs: didanosine • Minerals: ferrous sulfate, zinc • Gastrointestinal drugs: antacids, sucralfate, magnesium-containing laxatives	Give oral ciprofloxacin 2 hours before or 6 hours after drugs that may interfere with absorption.
	Overlapping Toxicities: • Artemether/lumefantrine, clarithromycin, quinine	Caution advised.
Clarithromycin	Increases Clarithromycin Concentrations: • ARV drugs: atazanavir/ritonavir, lopinavir/ritonavir • Antifungals: itraconazole (itraconazole concentrations also increased)	Caution advised. Concern for QTc prolongation. Decrease clarithromycin dose or consider switching to azithromycin, which has less potential for drug interactions.
	Increases Concentration of Other Medications: • ARV drugs: etravirine	Consider alternative agent.
	Decreases Clarithromycin Concentrations: • ARV drugs: efavirenz, etravirine, nevirapine • Antimycobacterial drugs: rifampin, rifabutin (rifabutin concentrations also increased)	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.
Clindamycin	Decreases Clindamycin Antibacterial Efficacy: • Antibacterial drugs: chloramphenicol, erythromycins	Avoid concomitant use.
Cycloserine	Overlapping Toxicities: • Antimycobacterial drugs: ethionamide, isoniazid	Caution advised.
Dapsone	Decreases Dapsone Concentrations: • Antimycobacterial drugs: rifampin	Co-administration should be avoided if possible. Consider alternatives for dapsone or use rifabutin.
	Decreases Dapsone Absorption: • ARV drugs: didanosine suspension • Gastrointestinal drugs: antacids	For co-administration with antacids or didanosine suspension, give dapsone 1 hour before or 4 hours after the other medication.
	Overlapping Toxicities: • Bone marrow suppressant drugs or drugs associated with hemolysis	Caution advised.
Doxycycline	Decreases Doxycycline Concentrations: • Anticonvulsant drugs: phenytoin, carbamazepine • Antimycobacterial drugs: rifampin	Potential for decreased doxycycline efficacy. Monitor for therapeutic failure.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 3 of 9)

Drug Name	Overlapping Toxicities	Recommendation
*** The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).**		
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 tipranivir 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.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections
(page 4 of 9)

Drug Name	Overlapping Toxicities	Recommendation
*** The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).**		
Interferon-Alfa	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)	Use with caution.
	Decreases Isoniazid Absorption: • Gastrointestinal drugs: antacids	Caution advised.
	Increases Concomitant Drug Concentrations: • Diazepam	Caution advised.
	Decreases Concomitant Drug Concentrations: • Antifungal drugs: ketoconazole, itraconazole	Co-administration should be avoided, if possible.
	Overlapping Toxicities: • Antimycobacterial 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	Monitor itraconazole concentration. Co-administration of efavirenz should be avoided if possible.
	• Anticonvulsant drugs: carbamazepine, (fos)phenytoin	Monitor itraconazole concentration.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 5 of 9)

Drug Name	Overlapping Toxicities	Recommendation
*** The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).**		
Itraconazole, continued	• Antimycobacterial drugs: rifampin, rifabutin, rifapentine, isoniazid	Co-administration with rifampin should be avoided. Co-administration with rifabutin should be avoided, if possible. Monitor for toxicities. Monitor itraconazole concentration.
	Decreases Itraconazole Absorption: • ARV drugs: didanosine • Gastrointestinal drugs: antacids, anticholinergics/antispasmodics, histamine H_2-receptor antagonists, omeprazole, sucralfate	Monitor itraconazole concentration.
Lumefantrine	Increases Concomitant Drug Levels: • ARV drugs: nevirapine	Monitor for nevirapine toxicity.
	Overlapping Toxicities: • ARV drugs: protease inhibitors • Antibacterial drugs: macrolides, fluoroquinolones • Antifungal drugs: fluconazole, voriconazole • Antimalarial drugs: quinine, quinidine • Psychotropic drugs: quetiapine, tricyclic antidepressants	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).
Mefloquine	Decreases Mefloquine Concentrations: • Antimalarial drugs: quinine • Antimycobacterial: rifampin	Monitor for decreased mefloquine efficacy. Co-administration of rifampin should be avoided, if possible; use rifabutin instead.
	Decreases Concomitant Drug Concentrations: • ARV drugs: ritonavir, possibly other protease inhibitors	Monitor for virologic failure of protease inhibitor-containing ART regimen.
	Overlapping Toxicities: • Anti-malarial drugs: quinine • Other drugs that can cause prolonged QT	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.
Nitazoxanide	Increases Concomitant Drug Concentrations: • Phenytoin	Potential for interaction with other medications that are highly protein bound. Use with caution as interaction will increase concentrations of concomitant medication.
Paromomycin	Overlapping Toxicities: • Neuromuscular blocking drugs	Use with caution.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 6 of 9)

Drug Name	Overlapping Toxicities	Recommendation
*** The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).**		
Pentamidine	Overlapping Toxicities: • Antiviral drugs: foscarnet	Co-administration should be avoided, if possible. Monitor for toxicities (hypocalcaemia, QT prolongation).
	• ARV drugs: protease inhibitors, didanosine	Co-administration should be avoided, if possible. Monitor for toxicities (QT prolongation with protease inhibitors; pancreatitis for didanosine).
	• Bone marrow suppressant drugs	Monitor for toxicities.
	• Nephrotoxic drugs	Monitor for toxicities.
	• Other drugs that can cause prolonged QT	Monitor for toxicities. Avoid co-administration, if possible.
Posaconazole	Decreases Posaconazole Drug Concentrations: • ARV drugs: efavirenz, fosamprenavir, rilpivirine	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.
	• Anticonvulsant drugs: phenytoin	Co-administration should be avoided, if possible. If co-administered, monitor posaconazole concentrations and adjust dose accordingly.
	• Antimycobacterial drugs: rifabutin, rifampin	Co-administration should be avoided, if possible. If co-administered, monitor posaconazole concentrations and adjust dose accordingly.
	Increases Concomitant Drug Concentrations: • ARV drugs: atazanavir, saquinavir, lopinavir, etravirine, and ritonavir	Co-administration should be avoided, if possible. Monitor for toxicities. Consider monitoring concentrations and adjust dose as necessary.
	• Antibacterial drugs: erythromycin, clarithromycin	Co-administration should be avoided.
	• Anticonvulsant drugs: phenytoin	Co-administration should be avoided.
	• Sedatives/hypnotics: midazolam, alprazolam, diazepam	Co-administration should be avoided, if possible. Monitor for toxicities.
	• Antimycobacterial drugs: rifabutin	Co-administration should be avoided.
	• 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.
	• Antimalarials: Quinidine, quinine, mefloquine, lumefantrine, halofantrine	Co-administration should be avoided.
	Decreases Concomitant Drug Concentrations: • ARV drugs: fosamprenavir	Co-administration should be avoided.
	• Other drugs that can cause prolonged QT	Use with caution. Monitor for toxicities.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 7 of 9)

Drug Name	Overlapping Toxicities	Recommendation
*** The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).**		
Proguanil	Decreases Proguanil Concentrations: • Atazanavir/ritonavir, lopinavir/ritonavir, efavirenz	Use with caution.
Pyrazinamide	Overlapping Toxicities: • Antimycobacterial drugs: rifampin, ethionamide • Hepatotoxic drugs	Use with caution. Monitor for hepatotoxicity.
Quinidine	Increases Quinidine Concentrations: • Protease inhibitors	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.
	• Itraconazole, posaconazole, voriconazole	Co-administration should be avoided. Increased risk of arrhythmia.
	Decreases Quinidine Concentrations: • Etravirine	Use with caution. Monitor quinidine levels.
	Increases Concomitant Drug Concentrations: • Tricyclic antidepressants	Co-administration should be avoided, if possible. Monitor for toxicities.
	Overlapping Toxicities: • Other drugs that can prolong QT interval	Co-administration should be avoided, if possible. Monitor for toxicities (QT prolongation).
Ribavirin	Increases Concentrations Of Concomitant Drug: • ARV drugs: didanosine	Co-administration should be avoided. Potential for increased risk of pancreatitis and mitochondrial toxicity.
	Decreases Concentrations of Concomitant Drug: • Zidovudine, stavudine	Co-administration should be avoided, if possible.
	Overlapping Toxicities: • Zidovudine, all NRTIs	Co-administration should be avoided, if possible. Monitor for toxicities (anemia for zidovudine; lactic acidosis for all NRTIs).
Rifabutin	Increases Rifabutin Concentrations: • HIV protease inhibitors	Use with caution. Monitor for rifabutin toxicity. Reduce rifabutin dose if co-administered with PIs.
	• Fluconazole	Use with caution. Monitor for rifabutin toxicity. Consider rifabutin dose reduction.
	• Voriconazole, itraconazole, posaconazole	Co-administration should be avoided, if possible. If co-administered, consider TDM and monitor for rifabutin toxicities (and azole clinical efficacy).
	• Clarithromycin	Co-administration should be avoided, if possible. Monitor for rifabutin toxicity. Consider rifabutin dose reduction or using azithromycin instead.
	Increases Concomitant Drug Concentrations: • Didanosine	Use with caution. Monitor for didanosine toxicity.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections (page 8 of 9)

Drug Name	Overlapping Toxicities	Recommendation
*** The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).**		
Rifabutin, continued	Decreases Rifabutin Concentrations: • Efavirenz, etravirine	Use with caution. Higher rifabutin dose required when efavirenz co-administered. Consider TDM.
	Decreases Concomitant Drug Concentrations: • ARV drugs: rilpivirine	Co-administration should be avoided.
	• ARV drugs: saquinavir, etravirine, maraviroc	Co-administration should be avoided, if possible.
	• Antibacterial drugs: dapsone, atovaquone	Use with caution. Monitor for dapsone treatment failure.
	• Antifungal drugs: azoles (except for fluconazole)	Co-administration should be avoided, if possible. If co-administered, consider TDM and monitor for rifabutin toxicities (and azole clinical efficacy).
	• Contraceptives: oral	Oral contraceptives less effective. Additional non-hormonal contraceptive or alternative recommended.
Rifampin	Decreases Concomitant Drug Concentrations: • Contraceptives: oral	Oral contraceptives less effective. Additional non-hormonal contraceptive or alternative recommended.
	• ARV drugs: PIs ± ritonavir, nevirapine, raltegravir, rilpivirine	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.
	• Antimicrobial: atovaquone, dapsone, clarithromycin, doxycycline	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.
	• Antifungal drugs: azoles, caspofungin	Increase in dose of caspofungin is recommended when co-administered with CYP450 inducers. Azoles: Monitor for efficacy. May need to increase antifungal dose
	• Other: corticosteroids, methadone	Caution advised with corticosteroids (decreased efficacy). Methadone: Monitor for efficacy and/or opiate withdrawal symptoms with methadone.
	Overlapping Toxicities: • Bone marrow suppressant drugs • Hepatotoxic drugs	Monitor for toxicities of these drugs.
Streptomycin	Potential for Increased Toxicity Due to Overlapping Toxicity: • Nephrotoxic drugs • Neuromuscular blocking drugs	Monitor for toxicities of these drugs.

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017

Table 5: Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections
(page 9 of 9)

Drug Name	Overlapping Toxicities	Recommendation
*** The drug interactions included in this table were selected on the basis of their potential clinical significance and are not inclusive of all potential drug interactions (see drug label and the drug interaction websites listed for complete information on drug interactions).**		
Telaprevir	Please see Adult OI guidelines for information about drug interactions, including warnings about interactions between telaprevir and HIV protease inhibitors. Caution advised.	
Trimethoprim-Sulfamethoxazole	Overlapping Toxicities: • Folate antagonists • Bone marrow suppressant drugs	Monitor for toxicities of these drugs.
Valacyclovir	Potential For Increased Concentrations (of Both Drugs) and Overlapping Toxicity: • Antivirals: acyclovir, valganciclovir, ganciclovir, cidofovir • ARVs: tenofovir	Monitor for toxicities of these drugs.
Valganciclovir	Potential for Increased Concentrations (of Both Drugs) and Overlapping Toxicity: • Antivirals: valacyclovir, acyclovir, ganciclovir, cidofovir • ARVs: tenofovir	Monitor for toxicities of these drugs.
Voriconazole	Decreases Voriconazole Concentrations: • Anticonvulsant drugs: carbamazepine, long-acting barbiturates	Caution advised.
	• Antimycobacterial drugs: rifabutin, rifampin	Rifabutin and Rifampin co-administration should be avoided.
	• ARV drugs: efavirenz, nevirapine, PIs boosted with ritonavir	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.
	Increases Voriconazole Concentrations: • ARV drugs: etravirine	Monitor voriconazole concentrations to reduce toxicity.
	Increases Concomitant Drug Concentrations: • Antimycobacterial drugs: rifabutin	Caution advised.
	• ARV drugs: protease inhibitors boosted with ritonavir, efavirenz, etravirine	Caution advised.
	• Statins: simvastatin, lovastatin, atorvastatin	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.
	• Sedatives/hypnotics: midazolam, alprazolam, triazolam	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

Downloaded from http://aidsinfo.nih.gov/guidelines on 2/1/2017