Guidelines for the Prevention and Treatment of Opportunistic Infections in Children With and Exposed to HIV

Developed by the HHS Panel on Opportunistic Infections in Children With and Exposed to HIV—A Working Group of the NIH Office of AIDS Research Advisory Council (OARAC) and in collaboration with the National Institutes of Health, the HIV Medicine Association of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the American Academy of Pediatrics

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It is emphasized that concepts relevant to HIV management evolve rapidly. The Panels have a mechanism to update recommendations on a regular basis, and the most recent information is available on the Clinicalinfo website (https://clinicalinfo.hiv.gov/).

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Updated: April 23, 2026
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Indication	First Choice	Alternative	Comments/Special Issues
Bacterial Infections (*S. pneumoniae* and other invasive bacteria)	• Pneumococcal, meningococcal, and Hib vaccines • IVIG 400 mg/kg body weight every 2–4 weeks (only in cases of hypogammaglobulinemia, IgG <400 mg/dL)	TMP-SMX, 75/375 mg/m^2 BSA per dose by mouth twice daily	See CDC website for detailed immunization schedule. Criteria for Discontinuing IVIG • Resolution of hypogammaglobulinemia Criteria for Restarting IVIG • Relapse of hypogammaglobulinemia
Candida Infections	Not routinely recommended	N/A	N/A
Coccidioidomycosis	N/A	N/A	Primary prophylaxis is not routinely indicated in children.
COVID-19	COVID-19 vaccines and updated vaccines	Pemivibart (Pemgarda) *Aged ≥12 Years and ≥40 kg* • Pemivibart injection solution: 4,500 mg administered as a single IV infusion	COVID-19 Vaccination Indicated for— • All children with HIV aged ≥6 months regardless of CD4 cell count or viral load • Household members and close contacts of children with HIV aged ≥6 months For up-to-date vaccine guidance, see CDC's Use of COVID-19 Vaccines in the United States webpage. Children with HIV may qualify for additional doses of COVID-19 vaccines if they have stage 3 HIV infection, history of an AIDS-defining illness without immune reconstitution, clinical manifestations of symptomatic HIV, or untreated HIV infection.

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Indication	First Choice	Alternative	Comments/Special Issues
			Pemivibart Indicated for— • Adults and adolescents aged ≥12 years and who weigh ≥40 kg with moderate-to-severe immunocompromise (including those with advanced or untreated HIV infection) who are unlikely to have an adequate response to COVID-19 vaccination.
Cryptococcosis	Not recommended	Not recommended	N/A
Cryptosporidiosis	ARV therapy to avoid advanced immune deficiency	N/A	N/A
Cytomegalovirus Infection (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 to 16 years, valganciclovir oral solution 50 mg/mL at dose in milligrams = 7 x BSA x CrCl (up to maximum CrCl of 150 mL/min/1.73 m^2) orally once daily with food (maximum dose 900 mg/day)	N/A	Primary Prophylaxis Can Be Considered for— • CMV antibody positivity and severe immunosuppression (i.e., CD4 count <50 cells/mm^3 in children age ≥6 years; CD4 percentage <5% in children age <6 years). Criteria for Discontinuing Primary Prophylaxis • Age ≥6 years with CD4 count >100 cells/mm^3 • Age <6 years with CD4 percentage >10% Criteria for Considering Restarting Primary Prophylaxis • Age ≥6 years with CD4 count <50 cells/mm^3 • Age <6 years with CD4 percentage <5%
Giardiasis	ART to avoid advanced immunodeficiency	N/A	N/A

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Hepatitis B Virus Infection (HBV)	All Children • HepB vaccine Infants Born to Women With HBV • HepB vaccine plus HBIG	HBIG following exposure	See Figure 1. Recommended Immunization Schedule for detailed vaccine recommendations. Primary Prophylaxis Indicated for— • All individuals who are not infected with HBV Criteria for Discontinuing Primary Prophylaxis • N/A Criteria for Restarting Primary Prophylaxis • N/A
Hepatitis C Virus Infection (HCV)	N/A	N/A	N/A
Herpes Simplex Virus Infection (HSV)	N/A	N/A	Primary prophylaxis not indicated
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
Human Papillomavirus Disease (HPV)	HPV vaccine	N/A	See Figure 1. Recommended Immunization Schedule for detailed vaccine recommendations.
Isosporiasis (Cystoisosporiasis)	There are no U.S. recommendations for primary prophylaxis of isosporiasis.	N/A	Initiation of ART to avoid severe immunodeficiency may reduce incidence; TMP-SMX prophylaxis may reduce incidence.

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Indication	First Choice	Alternative	Comments/Special Issues
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 o 11–20 kg; one pediatric tablet (62.5 mg/25 mg) o 21–30 kg, two pediatric tablets (125 mg/50 mg) o 31–40 kg; three pediatric tablets (187.5 mg/75 mg) o >40 kg; one 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: https://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.

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Indication	First Choice	Alternative	Comments/Special Issues
	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 o 11–20 kg; one pediatric tablet (62.5 mg/25 mg) o 21–30 kg; two pediatric tablets (125 mg/50 mg) o 31–40 kg; three pediatric tablets (187.5 mg/75 mg) o >40 kg; one 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)		

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Indication	First Choice	Alternative	Comments/Special Issues
Microsporidiosis	N/A	N/A	Not recommended
Mycobacterium avium Complex (MAC)	• Clarithromycin 7.5 mg/kg (maximum 500 mg/dose) PO twice daily, *or* • Azithromycin 20 mg/kg (maximum 1,200 mg) PO once weekly Note: Careful monitoring of drug–drug interactions is critical when using clarithromycin in children on ARVs.	• Azithromycin 5 mg/kg (maximum 250 mg) PO once daily • For children who cannot tolerate azithromycin or clarithromycin, rifabutin (5 mg/kg/daily, maximum dose 300 mg) is an alternative prophylactic agent for MAC, although drug interactions and a lack of efficacy data in children limit its use.	Primary Prophylaxis Indicated for Children With HIV Who Have Advanced Immunosuppression, as Defined by CD4 Count Below, and Who Are Not on a Fully Suppressive ARV Regimen • *Aged <1 Year:* CD4 count <750 cells/mm^3 • *Aged 1 to 5 Years:* CD4 count <500 cells/mm^3 • *Aged ≥6 Years:* CD4 count <200 cells/mm^3 Criteria for Discontinuing Primary Prophylaxis • Do not discontinue in children aged <2 years. • After ≥6 months of ART, *and* o *Aged 2 to <6 Years:* CD4 count >200 cells/mm^3 for >3 consecutive months o *Aged ≥6 Years:* CD4 count >100 cells/mm^3 for >3 consecutive months Criteria for Restarting Primary Prophylaxis • *Aged 2 to <6 Years:* CD4 count ≤200 cells/mm^3 • *Aged ≥6 Years:* CD4 count ≤100 cells/mm^3

Table 1. Primary Prophylaxis of Opportunistic Infections in Children With and Exposed to HIV—Summary of Recommendations

Indication	First Choice	Alternative	Comments/Special Issues
Mycobacterium tuberculosis Treatment of LTBI, Also Known as TB Preventive Therapy	Source Case Drug Susceptible • Age 2 to <12 years o 12 weekly doses of isoniazid (25 mg/kg for children aged 2–12 years) and rifapentine (10–14.0 kg: 300 mg; 14.1–25.0 kg: 450 mg; 25.1–32.0 kg: 600 mg; 32.1–49.9 kg: 750 mg; ≥50.0 kg: 900 mg maximum) • Age ≥12 years o 12 doses of weekly isoniazid (15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum) and rifapentine (10–14.0 kg: 300 mg; 14.1–25.0 kg: 450 mg; 25.1–32.0 kg: 600 mg; 32.1–49.9 kg: 750 mg; ≥50.0 kg: 900 mg maximum) Source Case Drug Resistant • For isoniazid-resistant source cases, daily rifampin 15–20 mg/kg (maximum 600 mg/day) for 4 months is recommended. • For isoniazid- and rifampin-resistant (i.e., MDR-TB) source cases, consult a TB expert and local public health authorities.	• Rifampin 15–20 mg/kg (max 600 mg) daily for 4 months duration, *or* • Isoniazid 10–15 mg/kg (max 300 mg) daily and rifampin 15–20 mg/kg (maximum 600 mg/day) for 3 months duration, *or* • Isoniazid 10–15 mg/kg (max 300 mg) daily for 6–9 months	Indications • Positive TST (TST ≥5 mm in children with HIV) or IGRA without previous TB treatment • Close contact with any infectious TB case (repeated exposures warrant repeated post-exposure prophylaxis) Considerations • TB disease must be excluded before starting treatment for latent TB infection. • Drug–drug interactions with ART should be considered for all rifamycin-containing alternatives. Criteria for Discontinuing Prophylaxis • Only with documented severe adverse event, such as hepatotoxicity, hypersensitivity, or other adverse drug reactions, which are rare in children and adolescents. 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 children with HIV; and pregnant girls and women.

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Pneumocystis Pneumonia	• TMP-SMX: 5–10 mg/kg/DAY (TMP component) • Maximum individual dose: 160 mg/DOSE (TMP component). • Several dosing regimens have been used successfully: o 3 days per week on consecutive or alternate days in divided doses every 12 hours o Daily as a single dose o Administration 2 days per week on consecutive or alternate days in doses divided every 12 hours has been used successfully in pediatric oncology patients.	Dapsone and atovaquone are both first-line alternatives (see text for relative risks and benefits), followed by aerosolized pentamidine as second line and IV pentamidine as third line. Dapsone • *Children Aged ≥1 Month:* 2 mg/kg/dose (maximum: 100 mg/dose) PO once daily or 4 mg/kg/dose (maximum 200 mg/dose) PO once weekly Atovaquone • *Children Aged 1–3 Months or >24 Months to 12 Years:* 30–40 mg/kg/dose PO once daily with food (maximum: 1,500 mg/dose) • *Children Aged 4–24 Months:* 45 mg/kg/dose PO once daily with food (maximum: 1,500 mg/dose) • *Children Aged ≥13 Years:* 1,500 mg PO once daily	Primary Prophylaxis Indicated for— • All infants with HIV or in whom HIV infection cannot be presumptively excluded beginning from age 4–6 weeks to 12 months, regardless of CD4 count or percentage • Children With Stage 3 CD4 Count (see HIV Infection Stage Table for more information): o *Children Aged 1 Year to <6 Years:* <500 cells/mm^3 or <22% o *Children Aged ≥6 Years:* <200 cells/mm^3 or <14% Criteria for Discontinuing Primary Prophylaxis • *Children Aged <1 Year:* Continue primary prophylaxis in children with HIV throughout the first year of life • Children Aged 1 Year and Older on ART for ≥6 Months With CD4 Count Above Age-Specific Stage 3 Cutoff for >3 Consecutive Months: o *Children Aged 1 Year to <6 Years:* ≥500 cells/mm^3 or ≥22% o *Children Aged ≥6 Years:* ≥200 cells/mm^3 or ≥14% • Discontinuation can be considered in children ≥6 Years if on ART for ≥6 months with undetectable viral load and CD4 count 101–200 cells/mm^3 if intolerant of prophylaxis medications Criteria for Restarting Primary Prophylaxis • CD4 count below age-specific stage 3 cutoff (see above)

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		Aerosolized Pentamidine Via Respirgard II Nebulizer *For Children Able to Comply With Its Use:* • *Children Aged <5 Years:* Limited data regarding dosing. 9 mg/kg/dose or 150 mg/dose every month have been suggested. • *Children Aged ≥5 Years:* 300 mg every month IV Pentamidine • 4 mg/kg/dose every 3–4 weeks; maximum dose: 300 mg/dose • Limited data regarding dosing frequency; based on use in oncology patients	
Syphilis	N/A	Same as for primary prophylaxis.	Primary Prophylaxis Indicated for— • N/A Criteria for Discontinuing Primary Prophylaxis • N/A Criteria for Restarting Primary Prophylaxis • N/A
Toxoplasmosis	TMP-SMX 150/750 mg/m^2 BSA once daily PO	**For Children Aged ≥1 Month:** • Dapsone 2 mg/kg body weight or 15 mg/m^2 BSA (maximum 25 mg) PO once daily, *plus*	Primary Prophylaxis Indicated for— *Children With IgG Antibody to Toxoplasma and Severe Immunosuppression Who Are:* • Aged <1 year with CD4% ≤26% or CD4 ≤750 cells/mm^3, *or*

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Indication	First Choice	Alternative	Comments/Special Issues
		• Pyrimethamine 1 mg/kg body weight or 15 mg/m^2 BSA (maximum 25 mg) PO once daily, *plus* • Leucovorin 5 mg PO every 3 days (continued for 1 week after pyrimethamine completed due to long half-life) For Children Aged 1–3 Months and >24 Months: • Atovaquone 30 mg/kg body weight (maximum 1,500 mg) PO once daily with food For Children Aged 4–24 Months: • Atovaquone 45 mg/kg body weight (maximum 1,500 mg) PO once daily with food, *with or without* • Pyrimethamine 1 mg/kg body weight or 15 mg/m^2 BSA (maximum 25 mg) PO once daily, *plus* leucovorin 5 mg PO every 3 days Acceptable Alternative Dosage Schedules for TMP-SMX • TMP-SMX 150/750 mg/m^2 BSA per dose PO three times weekly on 3 consecutive days per week • TMP-SMX 75/375 mg/m^2 BSA per dose twice daily PO every day	• Aged 1–5 years with CD4% ≤22% or CD4 ≤500 cells/mm^3, *or* • Aged ≥6 years with CD4 count ≤100 cells/mm^3 Criteria for Discontinuing Primary Prophylaxis Note: Do not discontinue in children aged <1 year. • Aged 1–5 years with CD4 count >500 cells/mm^3 for >3 consecutive months *or* • Aged ≥6 years with CD4 count >200 cells/mm^3 for >3 consecutive months Criteria for Restarting Primary Prophylaxis: • Aged 1–5 years with CD4 count <500 cells/mm^3 *or* • Aged ≥6 years with CD4 count <200 cells/mm^3

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Indication	First Choice	Alternative	Comments/Special Issues
		• TMP-SMX 75/375 mg/m^2 BSA per dose twice daily PO three times weekly on alternate days	
Varicella-Zoster Virus Disease (VZV) Pre-exposure Prophylaxis	VAR (Varivax) vaccine 2-dose series	N/A	VAR is indicated for children aged ≥12 months with HIV stage 1 or 2. VAR is **not recommended** for children with HIV stage 3. See the Varicella Vaccine section of Figure 1. Recommended Immunization Schedule for detailed vaccine recommendations information.
Varicella-Zoster Virus Disease (VZV) Primary (Post-exposure) Prophylaxis	Varicella-zoster immune globulin (human [VariZIG]) administered IM, ideally within 96 hours (up to 10 days) after exposure Dosing Based on Body Weight • ≤2 kg: 62.5 international units • 2.1–10 kg: 125 international units • 10.1–20 kg: 250 international units • 20.1–30 kg: 375 international units • 30.1–40 kg: 500 international units • ≥40.1 kg: 625 international units	If VariZIG Is Not Available • IGIV 400 mg/kg actual body weight administered ideally within 96 hours (up to 10 days) after exposure If Passive Immunization Is Not Possible • Consider acyclovir 20 mg/kg/dose (max: 800 mg/dose) PO four times daily OR valacyclovir 20 mg/kg/dose (max: 1,000 mg/dose) PO three times daily for 7 days, beginning 7 days after exposure.	Primary (Post-exposure) Prophylaxis Is Indicated for— • Children with HIV stage 1 or 2 and substantial exposure to varicella or HZ with no verified history of prior infection, no evidence of vaccination, or who are seronegative for VZV on a sensitive and specific antibody assay; *or* • Children with HIV stage 3 and substantial exposure to varicella or HZ, regardless of immunity history to varicella Note: VariZIG is commercially available in the United States from a broad network of specialty distributors. Varicella vaccine should be administered 5 months after receipt of VariZIG in eligible children. Some experts start acyclovir upon first appearance of rash in children with HIV, rather than providing acyclovir as prophylaxis.

Key to Acronyms: ART = antiretroviral therapy; ARV = antiretroviral; BSA = body surface area; CD4 = CD4 T lymphocyte; CDC = Centers for Disease Control and Prevention; CMV = cytomegalovirus; CrCl = creatinine clearance; HBIG = hepatitis B immune globulin; HBV = hepatitis B virus; HepB = hepatitis B [vaccine]; Hib = *Haemophilus influenzae* type b; HPV = human papillomavirus; IgG = immunoglobulin G; IGRA = interferon-gamma release assay; IM = intramuscular; IV = intravenous; IVIG = intravenous immunoglobulin; LTBI = latent TB infection; MDR-TB = multidrug-resistant tuberculosis; PO = orally; TB = tuberculosis; TMP-SMX = trimethoprim-sulfamethoxazole; TST = tuberculin skin test; VZV = varicella-zoster virus

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

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

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

Indication	First Choice	Alternative	Comments/Special Issues
Cryptosporidiosis	N/A	N/A	N/A
Cytomegalovirus Infection (CMV)	• Ganciclovir 5 mg/kg body weight IV once daily; *or* • For older children who can receive adult dose (based on their BSA), valganciclovir tablets 900 mg orally once daily with food; *or* • For children aged 4 months to 16 years, valganciclovir oral solution 50 mg/mL at dose in milligrams = 7 x BSA x CrCl (up to maximum CrCl of 150 mL/min/1.73 m^2) orally once daily with food; *or* • Foscarnet 90–120 mg/kg body weight IV once daily	• Cidofovir 5 mg/kg body weight per dose IV every other week. Must be given with probenecid and IV hydration.	Secondary Prophylaxis Indicated for— • Prior disseminated disease, retinitis, neurologic disease, or GI disease with relapse. Criteria for Discontinuing Secondary Prophylaxis (All of the Following Criteria Must Be Fulfilled) • Completed ≥6 months of ART • Age <6 years with CD4 percentage ≥15% for >6 consecutive months • Age ≥6 years with CD4 count >100 cells/mm^3 for >6 consecutive months • Consultation with ophthalmologist (if retinitis) o Routine (i.e., every 3–6 months) ophthalmological follow-up is recommended for early detection of relapse or immune restoration uveitis. Criteria for Restarting Secondary Prophylaxis • Age <6 years with CD4 percentage <15% • Age ≥6 years with CD4 count <100 cells/mm^3
Giardiasis	N/A	N/A	N/A
Hepatitis B Virus Infection (HBV)	HepA vaccine	N/A	Secondary Prophylaxis Indicated for— • Individuals with chronic HBV infection to prevent further liver injury. Criteria for Discontinuing Secondary Prophylaxis • N/A

Indication	First Choice	Alternative	Comments/Special Issues
			Criteria for Restarting Secondary Prophylaxis • N/A
Hepatitis C Virus Infection (HCV)	N/A	N/A	N/A
Herpes Simplex Virus (HSV) Infection	Mucocutaneous Disease • Acyclovir 20 mg/kg body weight/dose (maximum 800 mg/dose) by mouth twice daily Suppressive Therapy After Neonatal HSV Disease (Skin, Eye, Mouth, CNS, or Disseminated Disease) • Acyclovir 300 mg/m^2 BSA/dose by mouth three times daily for 6 months	Mucocutaneous Disease, for Adolescents Old Enough to Receive Adult Dosing • Valacyclovir 500 mg by mouth twice daily, *or* • Famciclovir 500 mg by mouth twice daily	Secondary Prophylaxis Indicated • Suppressive secondary prophylaxis can be considered for children with severe and recurrent mucocutaneous (oral or genital) disease. Criteria for Discontinuing Secondary Prophylaxis • After a prolonged period (e.g., 1 year) of prophylaxis, consider suspending prophylaxis and determine with the patient whether additional prophylaxis is necessary. Although level of immune reconstitution is a consideration, no specific CD4 threshold has been established.
Histoplasmosis (Suppressive Therapy)	Itraconazole oral solution 5–10 mg/kg body weight (maximum 200 mg) per dose by mouth daily	Fluconazole 3–6 mg/kg body weight (maximum 200 mg) by mouth once daily	Secondary Prophylaxis Indicated • Documented histoplasmosis in a patient with impaired immune function Criteria for Discontinuing Secondary Prophylaxis *If All of the Following Criteria Are Fulfilled* • CD4 percentage >15% at any age; or CD4 cell count >150 cells/mm^3 aged ≥6 years • Received ≥1 year itraconazole maintenance therapy • Established (e.g., ≥6 months) adherence to effective ART • Negative *Histoplasma* blood cultures

Indication	First Choice	Alternative	Comments/Special Issues
			• Serum Histoplasma antigen <2 ng/mL Use same initial itraconazole dosing for capsules as for solution. Itraconazole solution is preferred to the capsule formulation because it is better absorbed; solution can achieve serum concentrations 30% higher than those achieved with the capsules.
Human Papillomavirus Disease (HPV)	N/A	N/A	N/A
Isosporiasis (Cystoisosporiasis)	If Severe Immunosuppression— • TMP-SMX 2.5 mg/kg body weight of the TMP component (maximum 80 mg TMP) twice daily by mouth three times per week	Pyrimethamine 1 mg/kg body weight (maximum 25 mg) ***plus*** folinic acid, 5–15 mg by mouth once daily. Second-Line Alternative • Ciprofloxacin, 10–20 mg/kg body weight (maximum 500 mg) by mouth three times per week	Consider discontinuing secondary prophylaxis in patients without evidence of active *Isospora* infection who have sustained improvement in immunologic status (from CDC immunologic category 3 to CD4 values that fall within category 1 or 2) for >6 months in response to ART. In adults, the dose of pyrimethamine for secondary prophylaxis (25 mg daily) is lower than the dose for treatment (50–75 mg daily), but no data exist for dosing in children. Thus, the recommended dose for secondary prophylaxis in children is pyrimethamine 1 mg/kg (maximum 25 mg) by mouth once daily. Ciprofloxacin is not a drug of choice in children because of increased incidence of adverse events, including events related to joints and/or surrounding tissues.
Malaria	For *P. vivax* or *P. ovale* • Primaquine 0.5 mg/kg base (0.8mg/kg salt) up to adult dose orally, daily for 14 days after departure from the malarious area	N/A	This regimen, known as PART, is recommended only for individuals who have resided in a malaria-endemic area for an extended period of time. Adult dose: 30 mg base (52.6 mg salt) orally, daily for 14 days after departure from the malarious area. http://wwwnc.cdc.gov/travel/yellowbook/2012/chapter-3-infectious-diseases-related-to-travel/malaria.htm#1939

Indication	First Choice	Alternative	Comments/Special Issues
Microsporidiosis	Disseminated, Non-ocular Infection or GI Infection Caused by Microsporidia Other Than *E. bieneusi* or *V. corneae* • Albendazole 7.5 mg/kg body weight (maximum 400 mg/dose) by mouth twice daily Ocular Infection • Topical fumagillin bicyclohexylammonium (Fumidil B) 3 mg/mL in saline (fumagillin 70 µg/mL) eye drops: 2 drops every 2 hours for 4 days, then 2 drops four times a day (investigational use only in United States) *plus*, for infection attributed to microsporidia other than *E. bieneusi* or *V. corneae*, *albendazole* 7.5 mg/kg body weight (maximum 400 mg/dose) by mouth twice daily for management of systemic infection	N/A	Criteria for Discontinuing Secondary Prophylaxis • After initiation of ART, resolution of signs and symptoms and sustained immune reconstitution (more than 6 months at CDC immunologic category 1 or 2)
Mycobacterium avium Complex (MAC) (Chronic Suppressive Therapy)	• Clarithromycin[a] 7.5 mg/kg body weight (maximum 500 mg/dose) PO twice daily, *plus* • Ethambutol 15–25 mg/kg body weight (maximum 2.5 g/day) PO once daily, with or without food • *For Children Aged ≥6 Years Who Received Rifabutin as Part of Initial Treatment:* rifabutin[a] 5 mg/kg	• Azithromycin 5 mg/kg body weight (maximum 250 mg) orally once daily, *plus* • Ethambutol 15–25 mg/kg body weight (maximum 2.5 g) orally once daily, with or without food • *For Children Aged ≥6 Years Who Received Rifabutin as Part of Initial Treatment:* rifabutin[a] 5 mg/kg	Secondary Prophylaxis Indicated • Prior disease Criteria for Discontinuing Secondary Prophylaxis • Children with a history of disseminated MAC and continued immunosuppression should receive lifelong prophylaxis to prevent recurrence. • There are limited data to recommend discontinuation of secondary prophylaxis in children aged <2 years. However, if continuation of secondary prophylaxis for

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

Indication	First Choice	Alternative	Comments/Special Issues
	o Administration 2 days per week on consecutive or alternate days in doses divided every 12 hours has been used successfully in pediatric oncology patients.	Atovaquone • *Children Aged 1–3 Months or >24 Months to 12 Years:* 30–40 mg/kg/dose PO once daily with food (maximum: 1,500 mg/dose) • *Children Aged 4–24 Months:* 45 mg/kg/dose PO once daily with food (maximum: 1,500 mg/dose) • *Children Aged ≥13 Years:* 1,500 mg PO once daily Aerosolized Pentamidine Via Respirgard II Nebulizer *For Children Able to Comply With Its Use* • *Children Aged <5 Years:* Limited data regarding dosing. 9 mg/kg/dose or 150 mg/dose every month have been suggested. • *Children Aged ≥5 Years:* 300 mg every month IV Pentamidine • 4 mg/kg/dose every 3 to 4 weeks; maximum dose: 300 mg/dose • Limited data regarding dosing frequency; based on use in oncology patients	o *Children Aged ≥6 Years:* ≥200 cells/mm^3 or ≥14% • Discontinuation can be considered in children ≥6 Years if on ART for ≥6 months with undetectable viral load and CD4 count 101–200 cells/mm^3 if intolerant of prophylaxis medications Criteria for Restarting Secondary Prophylaxis • CD4 count below age-specific stage 3 cutoff (see above)

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

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

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

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

Table 3. Treatment of Opportunistic Infections in Children With and Exposed to HIV—Summary of Recommendations

Updated: April 23, 2026
Reviewed: April 23, 2026

Indication	First Choice	Alternative	Comments/Special Issues
Bacterial Infections Bacterial pneumonia; *S. pneumoniae;* occasionally *S. aureus, H. influenzae,* *P. aeruginosa*	• Amoxicillin 90 mg/kg/dose orally divided every 8 or 12 hours (max 1 g/dose) for outpatient management, *or* • Ampicillin 200–400 mg/kg/day divided every 6 hours (max 2 g/dose) (use higher dose if *S. pneumoniae* MIC ≥4 mcg/mL), *or* • 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)	• Ceftazidime 200–300 mg/kg/day divided every 8 hours IV or IM (max 12 g/day), *or* • Cefepime 50 mg/kg/dose every 8 hours IV or IM (max 2 g/dose)	Alternative treatment should be determined based on local antimicrobial susceptibility patterns or that of the bacterial isolate, if available. For children who are receiving combination ART, have mild or no immunosuppression, and have mild-to-moderate community-acquired pneumonia, oral therapy option would be amoxicillin 45 mg/kg/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.

Indication	First Choice	Alternative	Comments/Special Issues
Candida Infections	Oropharyngeal *Uncomplicated Infection* • Clotrimazole troches, 10-mg troche PO four or five times daily • Nystatin suspension 4–6 mL PO four times daily, *or* one or two 200,000-unit flavored pastilles by mouth four or five times daily *Moderate to Severe OPC* • Fluconazole 3–6 mg/kg/dose PO once daily (maximum dose: 400 mg/day) *Treatment Duration* • 7 to 14 days	Oropharyngeal (Fluconazole-Refractory) • Itraconazole oral solution 2.5 mg/kg body weight/dose PO twice daily (maximum 200–400 mg/day) for 7–14 days • Posaconazole PowderMix for delayed-release oral suspension in children age ≥2 years and in the weight band for 7–14 days: o *10 kg to <12 kg*: 90 mg PO twice daily on Day 1, followed by 90 mg PO once daily o *12 kg to <17 kg:* 120 mg PO twice daily on Day 1, followed by 120 mg PO once daily o *17 kg to <21 kg:* 150 mg PO twice daily on Day 1, followed by 150 mg PO once daily o *21 kg to <26 kg:* 180 mg PO twice daily on Day 1, followed by 180 mg PO once daily o *26 kg to <36 kg:* 210 mg PO twice daily on Day 1, followed by 210 mg PO once daily o *36–40 kg:* 240 mg PO twice daily on Day 1, followed by 240 mg PO once daily • Posaconazole delayed-release *tablets* in children ≥2 years old and >40 kg body weight: 300 mg PO twice daily on	Itraconazole oral solution **should not** be used interchangeably with itraconazole capsules. Itraconazole capsules are generally ineffective for treatment of esophageal disease. Central venous catheters should be removed, when feasible, in children with HIV with fungemia. In uncomplicated catheter-associated *C. albicans* candidemia, an initial course of amphotericin B followed by fluconazole to complete treatment can be used (use invasive disease dosing). Voriconazole has been used to treat esophageal candidiasis in a small number of immunocompromised children without HIV. Voriconazole Dosing in Pediatric Patients • Voriconazole 9 mg/kg body weight/dose every 12 hours IV loading for Day 1, followed by voriconazole 8 mg/kg body weight/dose IV every 12 hours. • Conversion to oral voriconazole should be at 9 mg/kg body weight/dose orally every 12 hours. • Children aged ≥12 years and weighing ≥40 kg can use adult dosing (load voriconazole 6 mg/kg body weight/dose every 12 hours IV on Day 1, followed by 4 mg/kg body weight/dose every 12 hours IV. Conversion to oral therapy at 200 mg every 12 hours by mouth). 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).

Indication	First Choice	Alternative	Comments/Special Issues
		Day 1, followed by 300 mg PO once daily for 7–14 days • Posaconazole oral suspension: 6 mg/kg/dose three times daily for 7–14 days • Posaconazole IV: 6 mg/kg/dose (maximum 300 mg) IV twice daily on Day 1, followed by 6 mg/kg/dose (maximum 300 mg) IV once daily for 7–14 days • *Alternative:* Voriconazole: Dosing as per esophageal disease below • *Alternative:* Echinocandins: Dosing as per esophageal disease below • *Alternative:* Lipid formulation amphotericin B 3–4 mg/kg daily. Note: Low-dose lipid formulation amphotericin B dosing has not been established. • *Alternative:* Amphotericin B (deoxycholate) 0.3–0.5 mg/kg body weight IV once daily	Fluconazole Dosing Considerations • 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 • *Aged ≥18 Years*: 400 mg/dose once daily (6 mg/kg body weight once daily)
	Esophageal Disease • Fluconazole 6 mg/kg/day PO once on Day 1, then 3–6 mg/kg/dose PO once daily (maximum dose: 12 mg/kg/day, 400 mg/day) *Treatment Duration* • 14–21 days	Esophageal Disease (Intolerance of Oral Therapy) • Fluconazole 6 mg/kg/day IV once on Day 1, then 3–6 mg/kg/dose IV once daily (maximum dose: 12 mg/kg/day, 400 mg/day) for 14–21 days *Echinocandins* • Anidulafungin	N/A

Indication	First Choice	Alternative	Comments/Special Issues
		o *Aged 1 Month to 17 Years*: Loading dose of 3 mg/kg body weight/daily and then maintenance at 1.5 mg/kg body weight/dose daily IV (maximum 100 mg/day) • Caspofungin o Infants Aged <*3 Months*: 25 mg/m^2 BSA/dose daily IV o *Aged 3 Months to 17 Years*: 70 mg/m^2/day IV loading dose followed by 50 mg/m^2/day IV (maximum 70 mg). Note: Dosing of caspofungin for children should be based on BSA. • Micafungin o Note: In the United States, optimal dosing for infants younger than 4 months is not yet established. Studies indicate linear PK; age and clearance are inversely related (see recommended doses below). o *Neonates*: Up to 10–12 mg/kg body weight/dose daily IV may be required to achieve therapeutic concentrations. o *Ages ≥4 Months and Weight ≤30 kg:* 3 mg/kg body weight/dose IV daily o *Ages ≥4 Months and Weight >30 kg:* 2.5 mg/kg body weight/dose IV daily (maximum dose: 150 mg/day)	

Indication	First Choice	Alternative	Comments/Special Issues
		• Lipid formulation amphotericin B 3–4 mg/kg daily. Note: Low-dose lipid formulation amphotericin B dosing has not been established. • Amphotericin B (deoxycholate) 0.3–0.5 mg/kg body weight IV once daily Esophageal Disease (Fluconazole-Refractory) • Itraconazole oral solution 2.5 mg/kg body weight/dose PO twice daily • Voriconazole o *Ages 2 Years to <12 Years:* 4 mg/kg body weight/dose IV every 12 hours. Consider switch to 9 mg/kg/dose (maximum 350 mg) PO every 12 hours only after significant clinical improvement. o *Ages 12–14 Years and Weight <50 kg:* 4 mg/kg body weight/dose IV every 12 hours. Consider switch to 9 mg/kg/dose (maximum 350 mg) PO every 12 hours only after significant clinical improvement. o *Ages 12–14 Years and Weight ≥50 kg:* 200 mg PO/IV every 12 hours o *Ages ≥15 Years and Weight <40 kg:* 100 mg PO/IV every 12 hours o *Ages ≥15 Years and Weight ≥40 kg:* 200 mg PO/IV every 12 hours • *Alternative:* Echinocandins: Dosing as above	

Indication	First Choice	Alternative	Comments/Special Issues
		• *Alternative:* Lipid formulation amphotericin B: Dosing as above • *Alternative:* Amphotericin B (deoxycholate): Dosing as above • *Alternative:* Posaconazole: Dosing as above • *Alternative:* Isavuconazonium sulfate IV (372 mg/vial) o *Ages 1 Year to <3 Years and Weight <18 kg:* 15 mg/kg body weight/dose every 8 hours IV loading for six doses (48 hours), followed by 15 mg/kg once daily o *Ages 3 Years to <18 Years and Weight <37 kg:* 10 mg/kg every 8 hours IV loading for six doses (48 hours), followed by 10 mg/kg once daily IV o *Ages 3 Years to <18 Years and Weight ≥37 kg:* 372 mg (total dose) every 8 hours IV loading for six doses (48 hours), followed by 372 mg (total dose) once daily IV • *Alternative:* Isavuconazonium sulfate capsules (74.5 mg/capsule) o *Ages 6 Years to <18 Years and Weight 16 kg to <25 kg:* 149 mg (2 capsules) PO every 8 hours loading for six doses (48 hours), followed by 149 mg (2 capsules) PO once daily o *Ages 6 Years to <18 Years and Weight 18 kg to <25 kg:* 223.5 mg	

Indication	First Choice	Alternative	Comments/Special Issues
		(3 capsules) PO every 8 hours loading for six doses (48 hours), followed by 223.5 mg (3 capsules) PO once daily o *Ages 6 Years to <18 Years and Weight 25 kg to <32 kg:* 298 mg (4 capsules) PO every 8 hours loading for six doses (48 hours), followed by 298 mg (4 capsules) PO once daily o *Ages 6 Years to <18 Years and Weight ≥32 kg:* 372 mg (5 capsules) PO every 8 hours loading for six doses (48 hours), followed by 372 mg (5 capsules) PO once daily *Treatment Duration* • 14–21 days	
	Invasive Disease: Moderately Severe to Severely Ill *Echinocandin Recommended* • Anidulafungin o *Aged 1 Month–17 Years*: Load with 3 mg/kg body weight/daily dose IV and then maintenance dose at 1.5 mg/kg body weight once daily (maximum 100 mg/day) • Caspofungin: o *Infants Aged <3 Months*: 25 mg/m^2 BSA/dose once daily IV	Invasive Disease • Fluconazole 25 mg/kg body weight/dose once IV/PO loading for Day 1, followed by 12 mg/kg body weight IV/PO once daily (maximum 600 mg/day) for minimum 2 weeks after last positive blood culture (if uncomplicated candidemia) o For infants aged ≤3 months and gestational age <30 weeks, maintenance dosing is 9 mg/kg/dose IV/PO daily • Lipid formulations of amphotericin B, 3–5 mg/kg body weight IV once daily	Central venous catheters should be removed, when feasible, in children with HIV with fungemia. The preferred treatment for invasive disease in children with HIV depends on severity of disease, previous azole exposure, and *Candida* isolate obtained (if known). If a child with uncomplicated invasive candidiasis is initiated on an intravenous antifungal agent, such as an echinocandin or an amphotericin B formulation, step-down therapy to an oral agent such as fluconazole can be considered when the patient is clinically improved, has isolates susceptible to the oral agent, and have negative repeat blood cultures following initiation of antifungal therapy.

Indication	First Choice	Alternative	Comments/Special Issues
	o *Aged 3 Months–17 Years:* 70 mg/m^2 BSA/day loading dose followed by 50 mg/m^2 once daily (maximum 70 mg). Note: Dosing of caspofungin in children should be based on BSA. • Micafungin: o Note: In the United States, optimal dosing for infants younger than 4 months is not yet established. Studies indicate linear PK; age and clearance are inversely related (see recommended doses below). o *Neonates*: Up to 10–12 mg/kg body weight/dose daily IV may be required to achieve therapeutic concentrations. o *Infants <15 kg Body Weight:* 5–7 mg/kg/day o *Children ≤40 kg Body Weight and Aged 2–8 Years*: 3–4 mg/kg body weight/dose daily IV o *Children ≤40 kg Body Weight and Aged 9–17 Years:* 2–3 mg/kg body weight/dose daily o *Children >40 kg Body Weight:* 100 mg/dose daily IV *Treatment Duration* • Based on presence of deep-tissue foci and clinical response; in those	• Amphotericin B deoxycholate, 1 mg/kg body weight IV once daily in the neonatal period • Voriconazole: o *Ages 2 Years to <12 Years:* 9 mg/kg body weight/dose every 12 hours IV loading for two doses, followed by voriconazole 8 mg/kg body weight/dose IV every 12 hours. Conversion to oral voriconazole should be at 9 mg/kg/dose (maximum 350 mg) PO every 12 hours. o *Ages 12–14 Years and Weight <50 kg:* 9 mg/kg body weight/dose every 12 hours IV loading for two doses, followed by voriconazole 8 mg/kg body weight/dose IV every 12 hours. Conversion to oral voriconazole should be at 9 mg/kg/dose (maximum 350 mg) PO every 12 hours. o *Ages 12–14 Years and Weight ≥50 kg:* Load voriconazole 6 mg/kg body weight/dose every 12 hours IV for two doses, followed by 3–4 mg/kg body weight/dose IV every 12 hours. Conversion to oral therapy should be at 200 mg PO every 12 hours. If response is inadequate, may increase to 300 mg PO every 12 hours. o *Ages ≥15 Years and Weight <40 kg:* Load voriconazole 6 mg/kg body	Voriconazole can be used in situations in which mold coverage is also warranted.

Indication	First Choice	Alternative	Comments/Special Issues
	with candidemia, treat until 2 weeks after last positive blood culture. Invasive Candidiasis: Mildly to Moderately Ill *Fluconazole Recommended* • Fluconazole 25 mg/kg body weight/dose once IV/PO loading for Day 1, followed by 12 mg/kg body weight/dose IV/PO daily (maximum dose: 600 mg) • For infants aged ≤3 months and gestational age <30 weeks, fluconazole maintenance dosing is 9 mg/kg/dose IV daily. • Avoid fluconazole for *C. krusei* and *C. glabrata.* See dosing for echinocandins above. • Use caution with echinocandins for *C. parapsilosis*. *Treatment Duration* • Based on presence of deep-tissue foci and clinical response; in those with candidemia, treat until 2 weeks after last positive blood culture.	weight/dose every 12 hours IV for two doses, followed by 3–4 mg/kg body weight/dose IV every 12 hours. Conversion to oral therapy should be at 100 mg PO every 12 hours. If response is inadequate, may increase to 150 mg PO every 12 hours. o *Ages ≥15 Years and Weight ≥40 kg:* Load voriconazole 6 mg/kg body weight/dose every 12 hours IV for two doses, followed by 3–4 mg/kg body weight/dose IV every 12 hours. Conversion to oral therapy should be at 200 mg PO every 12 hours. If response is inadequate, may increase to 300 mg PO every 12 hours. *Treatment Duration* • Based on presence of deep-tissue foci and clinical response; in those with candidemia, treat until 2 weeks after last positive blood culture.	
	Invasive Disease: CNS *Neonates* • *Initial:* Amphotericin B deoxycholate 1 mg/kg body weight/dose IV daily,	Invasive Disease: CNS *Neonates* • Amphotericin B deoxycholate 1 mg/kg body weight/dose IV daily, *or* liposomal	Infected CNS devices should be removed if possible. For patients in whom a ventricular device cannot be removed, amphotericin B deoxycholate could be administered through the device into the ventricle. Intrathecal neonatal doses have ranged from 0.5 mg/day in 2 mL of D5W to 0.6 mg/day in 0.5 mL of

Indication	First Choice	Alternative	Comments/Special Issues
	or liposomal amphotericin B 5 mg/kg body weight/dose IV daily • *Step-Down (If Fluconazole-Susceptible):* Fluconazole 25 mg/kg body weight/dose once IV/PO loading for Day 1, followed by 12 mg/kg body weight/dose IV/PO daily *Children* • *Initial:* Liposomal amphotericin B 5 mg/kg body weight/dose IV daily +/- flucytosine 25 mg/kg body weight/dose PO four times daily • *Step-Down (If Fluconazole-Susceptible):* Fluconazole 25 mg/kg body weight/dose once IV/PO loading for Day 1, followed by 12 mg/kg body weight/dose IV/PO daily (maximum dose: 800 mg) *Treatment Duration* • ≥1 month until all signs, symptoms, and CSF and radiographic abnormalities have resolved	amphotericin B 5 mg/kg body weight/dose IV daily, *and* • Flucytosine 25 mg/kg body weight/dose PO four times daily as salvage therapy *Children* • *Initial:* Amphotericin B deoxycholate 0.7–1 mg/kg body weight/dose IV daily IV daily (maximum 1.5 mg/kg/day) +/- flucytosine 25 mg/kg body weight/dose PO four times daily • *Step-Down (If Fluconazole-Susceptible):* Fluconazole 25 mg/kg body weight/dose once IV/PO loading for Day 1, followed by 12 mg/kg body weight/dose IV/PO daily (maximum dose: 800 mg)	D5W (total doses were 0.15 mg to 8.6 mg); doses of 0.125 to 0.25 mg have been administered to children via an Ommaya reservoir. Lipid formulations of amphotericin may not adequately penetrate the kidneys and should only be used with caution in neonates when urinary tract involvement is suspected or confirmed. Fluconazole dosing for CNS candidiasis is unknown but based on dosing for *Candida* invasive disease and maximums from cryptococcal meningitis. In neonates with CNS candidiasis, micafungin 10–15 mg/kg/dose IV daily may be considered as alternative therapy in special circumstances, such as salvage therapy or situations in which toxicity or drug resistance (e.g., *C. glabrata*) preclude the use of the preferred agents.
Coccidioidomycosis	Severe Illness With Respiratory Compromise Due to Diffuse Pulmonary or Disseminated Non-Meningitic Disease • Liposomal amphotericin B preparation at a dose of 5 mg/kg body weight IV once daily (dose can be increased to as much as	Severe Illness With Respiratory Compromise Due to Diffuse Pulmonary or Disseminated Non-Meningitic Disease *If Unable to Use Amphotericin B—* • Fluconazole 12 mg/kg body weight (maximum 800–1,200 mg) per dose IV or by mouth once daily	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. Fluconazole can be used as an alternative agent.

Indication	First Choice	Alternative	Comments/Special Issues
	10 mg/kg body weight IV once daily for life-threatening infections) • Amphotericin B deoxycholate 0.5–1.0 mg/kg body weight IV once daily until clinical improvement. • Liposomal amphotericin B is the treatment of choice with similar efficacy and fewer adverse events. • 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.	• Treatment is continued for a total of 1 year, followed by secondary prophylaxis.	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, isavuconazole, caspofungin, or posaconazole (or combinations). However, experience is limited in children. 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. Therapy with amphotericin B results in a more rapid clinical response in severe, non-meningeal disease.
	Mild-to-Moderate Non-Meningeal Coccidioidal Infection • Fluconazole 6–12 mg/kg body weight (maximum 400 mg) per dose IV or by mouth once daily for 6–12 months and clinical improvement	Mild-to-Moderate Non-Meningeal Coccidioidal Infection • Itraconazole 2–5 mg/kg body weight (maximum dose 200 mg) per dose IV or PO three times daily for 3 days, then 2–5 mg/kg body weight (maximum dose 200 mg) PO per dose twice daily thereafter for 6–12 months and clinical improvement • *Age ≥13 Years:* Posaconazole oral (delayed-release tablets), 300 mg twice daily for two doses, followed by 300 mg daily for 6–12 months and clinical improvement	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. Fluconazole can be used as an alternative agent. For treatment failure, can consider voriconazole, isavuconazole, caspofungin, or posaconazole (or combinations). However, experience is limited in children. Options should be discussed with an expert in the treatment of coccidioidomycosis. Secondary prophylaxis should be considered after treatment of milder disease if CD4 count remains <250 cells/mm^3 or CD4 percentage <15%.

Indication	First Choice	Alternative	Comments/Special Issues
	Coccidioidal Meningitis • Lifelong fluconazole 12 mg/kg body weight (maximum 800–1,200 mg) per dose IV or PO once daily	Coccidioidal Meningitis • IV liposomal amphotericin B plus intrathecal amphotericin B deoxycholate followed by secondary prophylaxis	For treatment failure, can consider posaconazole, isavuconazole, or voriconazole. Chronic suppressive therapy (secondary prophylaxis) with fluconazole is continued lifelong for meningeal disease. Options for treatment and secondary prophylaxis should be discussed with an expert in the treatment of coccidioidomycosis in children.
COVID-19	Non-hospitalized Children at High Risk of Progression to Severe COVID-19 *Aged ≥28 Days to <12 Years* • Remdesivir (Veklury) o ≥3 to <40 kg: Lyophilized powder only; IV loading dose: 5 mg/kg/dose on Day 1, followed by 2.5 mg/kg/dose once daily on Days 2 and 3 o ≥40 kg: Injection solution or lyophilized powder; IV loading dose: 200 mg on Day 1, followed by 100 mg once daily on Days 2 and 3 *Aged ≥12 Years and ≥40 kg* • Nirmatrelvir 300 mg and ritonavir 100 mg, administered together (Paxlovid), twice daily for 5 days Hospitalized Children • Remdesivir (Veklury) o ≥3 to <40 kg: Lyophilized powder only; IV loading dose:	Non-hospitalized Children at High Risk of Progression to Severe COVID-19 *Aged ≥28 Days to <12 Years* • N/A *Aged ≥12 Years* • Remdesivir (Veklury) o ≥3 to <40 kg: Lyophilized powder only, IV: loading dose: 5 mg/kg/dose on Day 1, followed by 2.5 mg/kg/dose once daily on Days 2 and 3	Remdesivir is administered intravenously. When given to non-hospitalized patients, duration is for 3 days. When given to hospitalized patients, duration is generally 5 days or until hospital discharge, whichever is first, but may extend to up to 10 days based on clinical response. Remdesivir should be started within 7 days of symptom onset but could be considered if presenting with >7 days of symptoms in children with severe immunosuppression. Ritonavir-boosted nirmatrelvir is an oral PI that may be administered with other ARVs, including those that contain ritonavir or cobicistat, without any interruption or modification to the usual ART. However, there is potential for significant drug–drug interactions with other medications, requiring dose or frequency adjustment or avoidance. Consult a drug interactions database, such as the University of Liverpool COVID-19 Drug–Drug Interaction website, for further guidance. Ritonavir-boosted nirmatrelvir should be started within 5 days of symptom onset. Renal and hepatic function should be evaluated prior to initiating ritonavir-boosted nirmatrelvir, and doses should be adjusted if needed. Dexamethasone has potential for drug–drug interactions, including with NNRTIs. Providers should

Indication	First Choice	Alternative	Comments/Special Issues
	5 mg/kg/dose on Day 1, followed by 2.5 mg/kg/dose once daily on Days 2 through 5 o ≥40 kg: Injection solution or lyophilized powder; IV loading dose: 200 mg on Day 1, followed by 100 mg once daily on Days 2 through 5 • Dexamethasone 0.15 mg/kg (with a maximum dose of 6 mg), oral or IV, once daily for up to 10 days		consult a drug interactions resource, such as the University of Liverpool COVID-19 Drug–Drug Interaction website, for further guidance. Alternative corticosteroids, such as hydrocortisone or methylprednisolone, may be considered if dexamethasone is not available or if alternative corticosteroids are being administered for another indication.
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— o 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.	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

Indication	First Choice	Alternative	Comments/Special Issues
		• If Amphotericin B-Based Therapy Not Tolerated— o 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) o Itraconazole 5–10 mg/kg body weight by mouth given once daily, or 2.5–5 mg/kg body weight given twice daily (maximum 200 mg/dose) for a minimum of 8 weeks. A loading dose (2.5–5 mg/kg body weight per dose 3 times daily) is given for the first 3 days (maximum 200 mg/dose; 600 mg/day). See comment on itraconazole under Other Options/Issues.	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 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. [a] Duration of therapy for non-CNS disease depends on site and severity of infection and clinical response
	Localized Disease, Including Isolated Pulmonary Disease (CNS Not Involved)[a] • 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	Localized Disease Including Isolated Pulmonary Disease (CNS Not Involved)[a] • 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	

Indication	First Choice	Alternative	Comments/Special Issues
	Disseminated Disease (CNS Not Involved) or Severe, Pulmonary Disease[a] • 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)	Disseminated Disease (CNS Not Involved) or Severe, Pulmonary Disease[a] • 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	
Cryptosporidiosis	Effective ART • Immune reconstitution might lead to parasitologic and clinical response	There is no consistently effective therapy for cryptosporidiosis in patients with HIV infection; optimized ART and a trial of nitazoxanide should be considered. Nitazoxanide • 1–3 years of age: Nitazoxanide (20 mg/mL oral solution) 100 mg orally twice daily with food • 4–11 years of age: Nitazoxanide (20 mg/mL oral solution) 200 mg orally twice daily with food • ≥12 years of age: 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.
Cytomegalovirus Infection (CMV)	Symptomatic Congenital Infection With Neurologic Involvement • Ganciclovir 6 mg/kg body weight per dose IV every 12 hours for 6 weeks, *or*		Data on valganciclovir dosing in young children for treatment of retinitis are unavailable, but consideration can be given to transitioning from IV

Indication	First Choice	Alternative	Comments/Special Issues
	• Valganciclovir 16 mg/kg body weight per dose orally twice daily for 6 months		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 ART. 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.
	Disseminated Disease and Retinitis *Induction 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) *Chronic Maintenance Therapy* • Ganciclovir 5 mg/kg body weight once daily for 5–7 days	Disseminated Disease and Retinitis *Induction 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 for 14–21 days *Chronic Maintenance Therapy* • Foscarnet 90–120 mg/kg body weight IV once daily *Alternative Therapy for Retinitis (Followed by Chronic Maintenance Therapy; See Cytomegalovirus Row in Secondary Prophylaxis Table)* • Valganciclovir tablets 900 mg per dose orally twice daily for 14–21 days, followed by chronic suppressive therapy (see above). o Note: This is an option in older children who can receive the adult dose (based on their BSA) and in patients with mild disease. • 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 who are intolerant to	

Indication	First Choice	Alternative	Comments/Special Issues
		other therapies. Induction dosing in adults is 5 mg/kg body weight IV once weekly for 2 weeks, followed by chronic suppressive therapy (see Cytomegalovirus row in Secondary Prophylaxis table); however, data on dosing in children are unavailable. Must be given with probenecid and IV hydration.	
	Central Nervous System Disease *Induction Therapy* • 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 *Chronic Maintenance Therapy* • See Cytomegalovirus row in Secondary Prophylaxis table		
Giardiasis	• Tinidazole, 50 mg/kg by mouth, administered as 1 dose given with food (maximum 2 g). Note: Based on data from children who are HIV-negative • Nitazoxanide o *1–3 years*: 100 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 children who are HIV-negative	Tinidazole is FDA-approved in the United States for children aged ≥3 years. It is available in tablets that can be crushed. Metronidazole has a high frequency of gastrointestinal side effects. A pediatric suspension of metronidazole is not commercially available but can be compounded from tablets. Metronidazole is not FDA-approved for the treatment of giardiasis. Supportive Care • Hydration

Indication	First Choice	Alternative	Comments/Special Issues
	o *4–11 years*: 200 mg by mouth every 12 hours with food for 3 days o ≥*12 years*: 500 mg by mouth every 12 hours with food for 3 days Note: Based on data from children who are HIV-negative		• Correction of electrolyte abnormalities • Nutritional support Antimotility agents (e.g., loperamide) should be used with caution in young children.
Hepatitis B Virus Infection (HBV)	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 ART regimen • For children aged ≥2 years, TAF as part of ART regimen with 3TC or FTC • For children ≥14 kg to <25 kg, FTC 120 mg/TAF 15 mg FDC once daily • For children ≥25 kg, FTC 200 mg/TAF 25 mg FDC once daily, or 3TC 300 mg plus 25 mg TAF daily • Note: For children weighing <35 kg, FTC/TAF combination should not be used with protease inhibitors for HIV therapy	Alternative for 3TC: FTC 6 mg/kg bodyweight (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 Choice of HBV treatment options for children with HIV/HBV infection 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. TAF is approved for use in treatment of HIV infection in children aged ≥2 years but is not approved for treatment of HBV infection in children aged <12 years. It should only be used for HBV in children with HIV/HBV coinfection as part of an ART regimen. Entecavir is approved for use in children without HIV ≥2 years of age for treatment of chronic HBV. It should only be used for HBV in children with HIV/HBV

Indication	First Choice	Alternative	Comments/Special Issues
	Child Already Receiving ART Containing 3TC or FTC, Suggesting 3TC/FTC Resistance • For children aged ≥2 years, include TDF or TAF as part of ART regimen with 3TC or FTC o For children aged <12 years, TDF 8 mg/kg body weight per dose once daily (maximum dose 300mg) o For children aged ≥12 years, TAF 25 mg once daily • For children aged ≥12 years, add entecavir 0.5 mg by mouth once daily in addition to ART regimen		coinfection who also receive an HIV-suppressive ART regimen but cannot use or access tenofovir. IRIS may be manifested by dramatic increase in transaminases as CD4 counts rise within the first 6-12 weeks of ART. It may be difficult to distinguish between drug-induced hepatotoxicity and other causes of hepatitis and IRIS. In children receiving TDF or TAF 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 >12 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.
Hepatitis C Virus Infection (HCV)	For detailed dosing recommendations for HCV antiviral therapy in children and adolescents, refer to the section on HCV in Children.	For detailed dosing recommendations for HCV antiviral therapy in children and adolescents, refer to the section on HCV in Children.	The American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) have developed a web-based process for the rapid formulation and dissemination of evidence-based, expert-developed recommendations for hepatitis C virus (HCV) management. See the AASLD/IDSA HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C for more details. For more information on other important considerations in the management of HCV in children and adolescents with HIV—such as drug–drug interactions, alternate therapies, dose adjustment, and

Indication	First Choice	Alternative	Comments/Special Issues
			extra monitoring—refer to the section on Patients With HIV/HCV Coinfection.
Herpes Simplex Virus Infection (HSV)	Neonatal CNS or Disseminated Disease • Acyclovir 20 mg/kg body weight IV/dose every 8 hours for ≥21 days Neonatal Skin, Eye, or Mouth Disease • Acyclovir 20 mg/kg body weight IV/dose every 8 hours for 14 days CNS or Disseminated Disease in Children Outside the Neonatal Period • Acyclovir 10 mg/kg body weight (up to 15 mg/kg body weight/dose in children <12 years) IV every 8 hours for 21 days		For Neonatal CNS Disease— • Repeat CSF HSV DNA PCR should be performed on days 19 to 21 of therapy. If the repeat CSF HSV DNA PCR is positive, continue IV acyclovir for an additional week, repeating the CSF HSV DNA PCR again near the end of extended treatment. Acyclovir should not be stopped until a repeat CSF HSV DNA PCR is negative.
	Moderate to Severe Symptomatic Gingivostomatitis • Acyclovir 5–10 mg/kg body weight/dose IV every 8 hours. Patients can be switched to oral therapy after lesions have begun to regress and therapy continued until lesions have completely healed. Mild Symptomatic Gingivostomatitis • Acyclovir 20 mg/kg body weight (maximum 400 mg/dose) dose by mouth four times a day for 7–10 days Recurrent Herpes Labialis	• Valacyclovir is approved for immunocompetent adults and adolescents with first-episode mucocutaneous HSV at a dose of 1 g/dose by mouth twice daily for 7–10 days; also approved for recurrent herpes labialis in children ≥12 years using two, 2 g doses by mouth separated by 12 hours as single-day therapy. • Recurrent genital HSV can be treated with valacyclovir 500 mg twice daily for 3 days or 1 g by mouth daily for 5 days.	

Indication	First Choice	Alternative	Comments/Special Issues
	• Acyclovir 20 mg/kg body weight (maximum 400 mg/dose) dose by mouth four times a day for 5 days For First-Episode Genital Herpes (Adults and Adolescents)— • Acyclovir 20 mg/kg body weight (maximum 400 mg/dose) dose by mouth three times a day for 7–10 days	• Immunocompetent adults with recurrent herpes labialis can be treated with famciclovir, 1 g/dose by mouth twice daily for 1 day. • Famciclovir is approved to treat primary genital HSV in immunocompetent adults at a dose of 250 mg/dose by mouth three times daily for 7–10 days. • Recurrent genital HSV is treated with famciclovir 1 g/dose by mouth twice daily 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 twice daily for 7 days.	
	Recurrent Genital Herpes (Adults and Adolescents) • Acyclovir 20 mg/kg body weight (maximum 400 mg/dose) dose by mouth three times daily for 5 days Children With HSV Keratoconjunctivitis • Often treated with topical trifluridine (1%) or ganciclovir (0.15%) 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		Alternative and Short-Course Therapy in Immunocompromised Adults With Recurrent Genital Herpes • Acyclovir 800 mg per dose by mouth twice daily for 5 days • Acyclovir 800 mg per dose by mouth three times daily 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.

Indication	First Choice	Alternative	Comments/Special Issues
	body weight/dose IV every 8 hours for 10–14 days, followed by oral valacyclovir 1 g/dose three times daily for 4–6 weeks • As an alternative, oral acyclovir 20 mg/kg body weight/dose four times daily for 4–6 weeks after IV acyclovir for 10–14 days		
		Acyclovir-Resistant HSV Infection • Foscarnet 40 mg/kg body weight/dose given IV every 8 hours or 60 mg/kg body weight/dose IV every 12 hours should be administered slowly over the course of 2 hours (i.e., no faster than 1 mg/kg/minute).	
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.	Acute Primary Pulmonary Histoplasmosis • Fluconazole 3–6 mg/kg body weight (maximum 200 mg) by mouth once daily	Use same initial itraconazole dosing for capsules as for solution. Itraconazole solution is preferred to the capsule formulation because it is better absorbed; solution can achieve serum concentrations 30% higher than those achieved with the capsules. 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.
	Mild Disseminated Disease	Mild Disseminated Disease	

Indication	First Choice	Alternative	Comments/Special Issues
	• 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	• 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	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.
	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	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	
	Central Nervous System Infection *Acute Therapy (4–6 Weeks, Followed by Consolidation Therapy)*		

Indication	First Choice	Alternative	Comments/Special Issues
	• Liposomal amphotericin B, 5 mg/kg body weight IV once daily (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		
Human Papillomavirus Disease (HPV)	Monitoring for spontaneous resolution is a reasonable option; 30% resolve spontaneously within 6 months and 90% within several years. Patient- or Parent-Applied Treatment Options • Imiquimod (3.75% or 5%) cream applied topically at night and washed off in the morning for 3 nonconsecutive nights a week for up to 16 weeks (BII) • Podofilox (0.5%) solution/gel applied topically two times daily for 3 consecutive days a week. Withhold treatment for 4 days and repeat the cycle weekly up to four times (BIII). • Sinecatechins (15%) ointment applied three times daily for up to	Patient- or Parent-Applied Treatment Options • Cidofovir topical gel (1%) is an experimental therapy studied in adults with HIV that is commercially available through compounding pharmacies and has very limited use in children; systemic absorption can occur with potential for renal toxicity (CIII). Provider-Applied Treatment Options • Intralesional IFN-α and 5-FU/ epinephrine gel implant are generally not recommended because of high cost, difficult administration, potential for systemic side effects, and lack of testing in children (CIII).	When choosing treatment options, parent and child comfort in application should be considered. Children have a low pain threshold and, generally, sensitive skin. Adequate topical anesthetics to the genital area should be given before caustic modalities are applied. For young children, these approaches are poorly tolerated due treatment-related and postoperative pain, and as a result may require general anesthesia. Therefore, these should be mainly reserved for children with extensive lesions. Many of these agents are contraindicated in pregnancy and have potential teratogenic effect. When treatment options are considered, the potential for pregnancy should be discussed and proper precautions during pregnancy explained.

Indication	First Choice	Alternative	Comments/Special Issues
	16 weeks, until warts are cleared completely and not visible (BIII) Provider-Applied Treatment Options • TCA (80% to 90%) applied topically weekly for up to 3 to 6 weeks (BIII). • Cryotherapy with liquid nitrogen or cryoprobe applied every 1–2 weeks up to four times (BIII). • Surgical removal either by tangential excision, tangential shave excision, curettage, or electrosurgery (BIII)	Note: These alternative therapies should include consultation with infectious disease and dermatological specialists.	
Isosporiasis (Cystoisosporiasis)	TMP-SMX 5 mg/kg body weight of the TMP component (maximum 160 mg TMP) twice daily by mouth for 10 days	Pyrimethamine 1 mg/kg body weight (maximum 25 mg) plus folinic acid 5–15 mg by mouth once daily for 14 days Second-Line Alternatives • Ciprofloxacin 10–20 mg/kg body weight (maximum 500 mg) by mouth twice daily for 7 days • Nitazoxanide (see doses below) for 3 consecutive days *Children Aged 1 Year–3 Years* • Nitazoxanide 100 mg by mouth every 12 hours *Children Aged 4 Years–11 Years* • Nitazoxanide 200 mg by mouth every 12 hours *Adolescents Aged ≥12 Years and Adults* • Nitazoxanide 500 mg by mouth every 12 hours	If symptoms worsen or persist, the TMP-SMX dose (5 mg/kg/dose of the TMP component) may be given more frequently (e.g., 3–4 times daily by mouth for 10 days) and/or the duration of treatment may be increased to 3–4 weeks. The optimal duration of treatment with pyrimethamine has not been established. Ciprofloxacin is not a drug of choice in children because of increased incidence of adverse events, including events related to joints and/or surrounding tissues.

Indication	First Choice	Alternative	Comments/Special Issues
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: o 5–8 kg; 2 pediatric tablets for 3 days; o 9–10 kg; 3 pediatric tablets for 3 days; o 11–20 kg; 4 pediatric tablets or 1 adult tablet for 3 days; o 21–30 kg; 2 adult tablets for 3 days; o 31–40 kg; 3 adult tablets for 3 days; o >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 1,000 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	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: https://www.cdc.gov/malaria/travelers/country_table/a.html High treatment failure rates due to chloroquine-resistant *P. vivax* have been documented in Papua New Guinea and Indonesia. 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

Indication	First Choice	Alternative	Comments/Special Issues
	[maximum 2,500 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 1,000 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 2,500 mg] = 25 mg/kg body weight chloroquine base) *Anti-Relapse Therapy for* P. ovale *and* 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		

Indication	First Choice	Alternative	Comments/Special Issues
	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 second dose follows the initial dose 8 hours later, then 1 dose twice daily for the next 2 days. o 5 to <15 kg; 1 tablet per dose o 15 to <25 kg; 2 tablets per dose o 25 to <35 kg; 3 tablets per dose o >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	N/A	Quinidine gluconate is a class 1a anti-arrhythmic agent not typically stocked in pediatric hospitals. When regional supplies are unavailable, the CDC

Indication	First Choice	Alternative	Comments/Special Issues
	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)		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. Investigational New Drug: 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

Indication	First Choice	Alternative	Comments/Special Issues
			• Use quinidine with caution with other protease inhibitors.
Microsporidiosis	Effective ART • Immune reconstitution may lead to microbiologic and clinical response. For Disseminated (Not Ocular) and Intestinal Infection Attributed to Microsporidia Other than *E. bieneusi* or *V. corneae*— • Albendazole 7.5 mg/kg body weight (maximum 400 mg/dose) by mouth twice daily (in addition to ART) *Treatment Duration* • Continue until sustained immune reconstitution (longer than 6 months at CDC immunologic category 1 or 2) after initiation of ART and resolution of signs and symptoms For *E. bieneusi* or *V. corneae* Infections— • Fumagillin (where available) adult dose 20 mg by mouth 3 times daily, *or* • TNP-470 (a synthetic analogue of fumagillin; where available) recommended for treatment of infections caused by *E. bieneusi* in HIV-infected adults (in addition to ART) For Ocular Infection—	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.

Indication	First Choice	Alternative	Comments/Special Issues
	• Topical fumagillin bicyclohexylammonium (Fumidil B) 3 mg/mL in saline (fumagillin 70 µg/mL) eye drops: 2 drops every 2 hours for 4 days, then 2 drops four times daily (investigational use only in United States) **plus**, for microsporidial infection other than *E. bieneusi* and *V. corneae*, albendazole 7.5 mg/kg body weight (maximum 400 mg/dose) by mouth twice daily for management of systemic infection in systemic infection (in addition to ART) *Treatment Duration* • Continue until sustained immune reconstitution (longer than 6 months at CDC immunologic category 1 or 2) after initiation of ART and resolution of signs and symptoms.		
Mycobacterium avium Complex (MAC)	**Initial Treatment (≥2 Drugs):** • Clarithromycin[a] 7.5–15 mg/kg (maximum 500 mg/dose) PO twice daily, *plus* • Ethambutol 15–25 mg/kg (maximum 2.5 g/day) PO once daily followed by chronic suppressive therapy *If Experiencing Severe Disease (Extensive End Organ Involvement, Prolonged Symptoms, Slow Response to Therapy)*	**If Intolerant to Clarithromycin** • Azithromycin 10–12 mg/kg (maximum 500 mg/day) PO once daily, plus ethambutol **For Children With Severe Symptoms or Disseminated Disease Who Need a Rifabutin Alternative or a Fourth Drug to Supplement a Macrolide/ Ethambutol/Rifabutin Regimen** • Amikacin[b] 15–30 mg/kg (maximum 1.5 g/day) IV in one or two divided doses. Therapeutic drug monitoring (peak and trough levels) is required, *or*	Susceptibility testing is recommended prior to treatment initiation. Combination therapy with a minimum of two drugs is recommended for ≥12 months. Careful monitoring for drug–drug interactions is advised. Clofazimine is associated with increased mortality in adults with HIV 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.

Indication	First Choice	Alternative	Comments/Special Issues
	• Add rifabutin[a] 10–20 mg/kg (maximum 300 mg/day) PO once daily	• Linezolid 10 mg/kg/dose PO every 8 hours for age 1 month to <12 years (maximum 600 mg/dose) and 10 mg/kg/dose PO every 12 hours (maximum 600 mg) for age ≥12 years, *or* • Moxifloxacin 7.5–10 mg/kg (maximum dose 400 mg daily) PO once daily, *or* • Levofloxacin 15-20 mg/kg/dose PO once daily (maximum dose 750 mg), *or* • Ciprofloxacin 10–15 mg/kg (maximum 1.5 g/day) PO twice daily, *or* • Bedaquiline for children aged ≥5 years weighing ≥15 kg (based on MDR-TB regimens): o *Weeks 1–2:* 400 mg once daily o *Weeks 3–24:* 200 mg three times weekly • For therapy beyond 24 weeks, consider consultation with a pediatric infectious disease/HIV expert.	Fluoroquinolones (e.g., ciprofloxacin and moxifloxacin) are used with caution in children aged <18 years because of concerns regarding potential effects on cartilage; use in children aged <18 years requires an assessment of potential risks and benefits. Chronic suppressive therapy (secondary prophylaxis) is recommended in children and adults following initial therapy. Limited data for bedaquiline in adults with NTM.
Mycobacterium tuberculosis	Intrathoracic Disease *Drug-Susceptible TB* • Intensive Phase (2 Months) o Isoniazid 10–15 mg/kg body weight (maximum 300 mg/day) by mouth once daily, plus	Alternative for Rifampin • Rifabutin 10–20 mg/kg body weight (maximum 300 mg/day) by mouth once daily (same dose if three times a week) • Discuss with an expert. Alternative Continuation Phase With Three Times Weekly Dosing (4 Months)	Treatment for TB disease should always be provided by DOT. If ART-naive, start TB therapy immediately and initiate ART within 2–8 weeks. If already on ART, review regimen to minimize potential toxicities and drug interactions; start TB treatment immediately.

Indication	First Choice	Alternative	Comments/Special Issues
	○ Rifampin 15–20 mg/kg body weight[a] (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 1 g/day) by mouth once daily ○ In children with minimal disease with fully drug-susceptible TB, some experts recommend a three-drug intensive phase regimen excluding ethambutol. • Continuation Phase (4 Months) ○ Isoniazid 10–15 mg/kg body weight (maximum 300 mg/day) by mouth once daily, plus ○ Rifampin 15–20 mg/kg body weight[a] (maximum 600 mg/day) by mouth once daily Extrathoracic Disease Note: Depends on disease entity • Lymph node TB—treat as minimal intrathoracic disease • Bone or joint disease—consider extending the continuation phase to 10 months (for total duration of therapy of 12 months). TB Meningitis	*If Good Adherence and Treatment Response* • Isoniazid 20–30 mg/kg body weight (maximum 900 mg/day) by mouth three times per week, plus • Rifampin 15–20 mg/kg body weight (maximum 600 mg/day) three times per week • In children with minimal disease with fully drug-susceptible TB, some experts recommend a continuation phase of 4 months (total duration of therapy of 6 months)	Potential drug toxicity and interactions should be reviewed at every visit. Drug interactions with ART should be considered for all rifamycin-containing alternatives. Adjunctive Treatment • Co-trimoxazole prophylaxis • Pyridoxine 1–2 mg/kg body weight/day (maximum 25–50 mg/day) with isoniazid or cycloserine/terizidone, 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 children with HIV; and pregnant girls and women. • Corticosteroids (2 mg/kg body weight per day of prednisone [maximum 60 mg/day] or its equivalent for 4–6 weeks followed by tapering) with TB meningitis; may be considered with pleural effusions, pericarditis, severe airway compression, or severe IRIS. Second-Line Drug Doses • Consult with an expert as dosing guidelines continue to evolve with emerging data. [a] Some experts recommend using a daily rifampin dose of 20–30 mg/kg/day for infants and toddlers.

Indication	First Choice	Alternative	Comments/Special Issues
	• As an alternative to ethambutol, 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 two doses until well tolerated. • Many experts recommend rifampin doses of 20–30 mg/kg daily for treatment of TB meningitis. See the AAP Red Book and WHO Operational Handbook on Tuberculosis for more information. • Consider extending the continuation phase to 10 months (for a total duration of therapy of 12 months). • Discuss with an expert. Drug-Resistant TB • Therapy should be based on the resistance pattern of the child (or of the source case where the child's isolate is not available); consult an expert.		
Pneumocystis Pneumonia	TMP-SMX 15–20 mg/kg/day (TMP component) in divided doses every 6–8 hours IV or PO 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/dose IV/IM once daily is the first-choice alternative regimen for severe disease.	After acute pneumonitis resolved in mild-to-moderate PCP, IV TMP-SMX can be transitioned to oral formulations. For oral administration, total daily dose of TMP-SMX can also be administered in three divided doses (every 8 hours). The following regimens have been used in adults, but data in children are limited:

Indication	First Choice	Alternative	Comments/Special Issues
		• Note: Close electrolyte and glucose monitoring required. Pentamidine can be changed to atovaquone after 7–10 days IV therapy. Atovaquone can be considered for initial therapy in mild-to-moderate disease. *Atovaquone* • Daily Dosing o *Children Aged 1–3 Months and >24 Months to 12 Years:* 30–40 mg/kg/dose PO once daily with food o *Children Aged 4–24 Months:* 45 mg/kg/dose PO once daily with food • Twice-Daily Dosing o *Children Aged ≥13 Years:* 750 mg/dose PO twice daily o 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/dose PO twice daily with food ▪ *Children Aged 4–24 Months:* 22.5 mg/kg/dose PO twice daily with food	• Dapsone 2 mg/kg/dose PO once daily (maximum 100 mg/day) **plus** trimethoprim 5 mg/kg/dose PO every 8 hours • Primaquine base 0.3 mg/kg/dose PO once daily (maximum 30 mg/day) **plus** clindamycin 10mg/kg/dose IV or PO (maximum 600 mg/dose given IV and 300–450 mg/dose given orally) every 6 hours Chronic suppressive therapy (secondary prophylaxis) with TMP-SMX is recommended in children and adults following initial therapy (see Secondary Prophylaxis). Corticosteroids Adjunctive Therapy *Indication* • PaO_2 <70 mmHg at room air or alveolar-arterial oxygen gradient ≥35 mmHg *Prednisone Dose* • Days 1–5: 1 mg/kg/dose PO twice daily, then • Days 6–10: 0.5–1 mg/kg/dose PO twice daily, then • Days 11–21: 0.5 mg/kg/dose PO once daily. *Alternative Corticosteroid Regimens* • Adult Dosage of Prednisone o Days 1–5: 40 mg/dose PO twice daily, then o Days 6–10: 40 mg/dose PO once daily, then o Days 11–21: 20 mg/dose PO once daily • Methylprednisolone IV

Indication	First Choice	Alternative	Comments/Special Issues
			o Days 1–7: 1 mg/kg/dose every 6 hours, then o Days 8–9: 1 mg/kg/dose twice daily, then o Days 10–11: 0.5 mg/kg/dose twice daily, then o Days 12–16: 1 mg/kg/dose once daily
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	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.

Indication	First Choice	Alternative	Comments/Special Issues
	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		

Indication	First Choice	Alternative	Comments/Special Issues
Toxoplasmosis	Congenital Toxoplasmosis • Pyrimethamine loading dose of 1 mg/kg body weight PO twice daily for 2 days, then 1 mg/kg body weight PO once daily for 2–6 months, then 1 mg/kg body weight PO three times weekly thereafter, *plus* • Leucovorin (folinic acid) 10 mg PO or IM three times weekly, *plus* • Sulfadiazine 50 mg/kg body weight PO twice daily *Treatment Duration* • 12 months Acquired Toxoplasmosis *Acute Induction Therapy (Followed by Chronic Suppressive Therapy)* • Pyrimethamine loading dose of 1 mg/kg body weight (maximum 50 mg) PO twice daily for 3 days, then 1 mg/kg body weight (maximum 25 mg) PO once daily, *plus* • Sulfadiazine 25–50 mg/kg body weight (maximum 1–1.5 g/dose) PO per dose four times daily, *plus* • Leucovorin 10–20 mg PO once daily, continued for one week after stopping pyrimethamine *Treatment Duration (Followed by Chronic Suppressive Therapy)*:	For Sulfonamide-Intolerant Patients: • Pyrimethamine loading dose of 1 mg/kg body weight PO twice daily for 2 days, then 1 mg/kg body weight PO once daily for 2–6 months, then 1 mg/kg body weight PO three times weekly thereafter, *plus* • Leucovorin (folinic acid) 10 PO or IM three times weekly, *plus* • Clindamycin 5–7.5 mg/kg body weight PO or IV (maximum 600 mg/dose) per dose four times daily	Congenital Toxoplasmosis • For infants born mothers with symptomatic *Toxoplasma* infection during pregnancy, empiric therapy of the newborn should be strongly considered irrespective of 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. • The following regimens are used in adults but have not been studied in children: o TMP-SMX 5/25 mg/kg body weight per dose IV or PO given twice daily as an alternative to pyrimethamine-sulfadiazine o Atovaquone 1,500 PO twice daily administered— ▪ with pyrimethamine and leucovorin, *or* ▪ with sulfadiazine, *or* ▪ alone, for those with pyrimethamine and sulfadiazine intolerance o Azithromycin 900–1,200 mg daily (corresponding to 20 mg/kg daily, maximum 1,000 mg in children) administered with pyrimethamine-leucovorin • Corticosteroids (e.g., prednisone, dexamethasone) have been used in children with CNS disease when CSF protein is very elevated (>1,000 mg/dL) or when focal lesions with significant mass effects are

Indication	First Choice	Alternative	Comments/Special Issues
	• ≥6 weeks (longer duration if clinical or radiologic disease is extensive or response in incomplete at 6 weeks)		present, with discontinuation as soon as clinically feasible. • Anticonvulsants should be administered to people with a history of seizures and continued through the acute treatment but should not be used prophylactically. • Sulfadiazine may be given as two to four equal doses per day as long as the total daily dose is 85–120 mg/kg body weight. • Consider screening for G6PD deficiency before starting sulfadiazine or TMP-SMX in people from regions with high prevalence of severe G6PD deficiency.
Varicella-Zoster Virus Disease (VZV)	Varicella *Children With Severe Immunosuppression (HIV Stage 3) or Severe Varicella Disease (see* Treating Disease *in text)* • Acyclovir 10 mg/kg/dose or 500 mg/m^2/dose IV every 8 hours for at least 7 days and until no new lesions appear for 48 hours *Children With No or Moderate Immunosuppression (HIV Stage 1 and 2) and Mild Varicella Disease* • If age ≥3 months: o Valacyclovir 20 mg/kg/dose (max: 1,000 mg/dose) PO three times daily for 7–14 days	*Children Unresponsive to Acyclovir When Resistance Is Suspected* • Foscarnet: 120–180 mg/kg/day IV divided every 8–12 hours for at least 7 days and until no new lesions appear for 48 hours *Children in Whom IV Acyclovir Is Indicated, in the Setting of a National Shortage of IV Acyclovir* • Foscarnet: 120–180 mg/kg/day IV divided every 8–12 hours for at least 7 days and until no new lesions appear for 48 hours, *or* • Ganciclovir 5 mg/kg/dose IV every 12 hours for at least 7 days and until no new lesions appear for 48 hours	For children aged <2 years, the dose of IV acyclovir is 10 mg/kg/dose every 8 hours. For children aged ≥2 years, some health care providers administer the same dose or base the dose on body surface area (500 mg/m^2/dose IV every 8 hours). When children treated with IV acyclovir show signs of clinical improvement with no new lesions for 48 hours, completion of antiviral therapy with an oral agent may be considered. Renal dose adjustments listed below are only applicable for IV acyclovir: • CrCl >50 mL/minute/1.73 m^2: No dose adjustment necessary • CrCl 25 to 50 mL/minute/1.73 m^2: Administer the usual recommended dose every 12 hours

Indication	First Choice	Alternative	Comments/Special Issues
	• If age <3 months OR unable to obtain valacyclovir suspension: o Acyclovir 20 mg/kg/dose (max: 800 mg/dose) PO four times daily for 7–14 days		• CrCl 10 to <25 mL/minute/1.73 m^2: Administer the usual recommended dose every 24 hours • CrCl <10 mL/minute/1.73 m^2: Administer 50% of the usual recommended dose every 24 hours (e.g., if the usual recommended dose is 10 mg/kg/dose every 8 hours, then administer 5 mg/kg/dose every 24 hours) • Intermittent hemodialysis: 5 mg/kg/dose IV every 24 hours; administer after hemodialysis on dialysis days • Peritoneal dialysis: 5 mg/kg/dose IV every 24 hours; no supplemental dose needed • Continuous renal replacement therapy: 10 mg/kg/dose IV every 12 hours For patients with renal impairment on PO acyclovir, the Panel recommends consultation with a pediatric pharmacist and extrapolation of dose adjustments used for adults with renal impairment. In children receiving acyclovir, it is important to maintain adequate hydration to avoid crystallization of the drug in the renal tubules. Valacyclovir doses should be adjusted for renal impairment; however, no formal pediatric renal dosing guidelines exist for valacyclovir. The Panel recommends consultation with a pediatric pharmacist and extrapolation of dose adjustments used for adults with renal impairment (see package insert). There is no pediatric preparation of valacyclovir, although 500 mg caplets can be extemporaneously compounded to make a suspension.

Indication	First Choice	Alternative	Comments/Special Issues
			For patients with renal impairment on IV foscarnet, the Panel recommends consultation with a pediatric pharmacist and extrapolation of dose adjustments used for management of cytomegalovirus.
	Herpes Zoster *Children With Severe Immunosuppression (HIV Stage 3), Trigeminal or Sacral Nerve Involvement, Visceral Involvement, Extensive Multidermatomal, or Disseminated HZ* • Acyclovir 10 mg/kg/dose or 500 mg/m^2/dose IV every 8 hours for 10–14 days *Children With No or Moderate Immunosuppression (HIV Stage 1 and 2) and Uncomplicated HZ* • If age ≥3 months: o Valacyclovir 20 mg/kg/dose (max: 1,000 mg/dose) PO three times daily for 7–14 days If age <3 months or unable to obtain valacyclovir suspension: • Acyclovir 20 mg/kg/dose (max: 800 mg/dose) PO four times daily for 7–14 days	*Children Unresponsive to Acyclovir When Resistance Is Suspected* • Foscarnet IV: 120–180 mg/kg/day divided every 8–12 hours for at least 7 days and until no new lesions appear for 48 hours Famciclovir is approved for use in adults (age ≥18 years) with HZ at a dose of 500 mg/dose PO three times daily for 7–14 days; however, data are insufficient to support the use of famciclovir for HZ in children with HIV.	For most cases, oral treatment (as opposed to IV) for HZ is considered safe because the risk of disseminated, life-threatening disease is lower with HZ than with varicella. For renal dose adjustment and other administration considerations with acyclovir, valacyclovir, and foscarnet, see Varicella above.

Indication	First Choice	Alternative	Comments/Special Issues
	Children With Progressive Outer Retinal Necrosis • Acyclovir 10 mg/kg/dose or 500 mg/m^2/dose IV every 8 hours OR ganciclovir 5 mg/kg/dose IV every 12 hours, *plus* • Foscarnet 90 mg/kg/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 Acute Retinal Necrosis* • Acyclovir 10 mg/kg/dose or 500 mg/m2/dose IV every 8 hours for 10–14 days, **followed by** valacyclovir 20 mg/kg/dose (max: 1,000 g/dose) PO three times daily for 4–6 weeks OR acyclovir 20 mg/kg/dose (max: 800 mg/dose) PO four times daily for 4–6 weeks		Involvement of an ophthalmologist with experience in managing HZ ophthalmicus and its complications in children **is strongly recommended** when ocular involvement is evident. Optimal management of progressive outer retinal necrosis has not been defined.

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

[b] Amikacin levels for therapeutic drug monitoring: peak (C_{max}) 30–40 mg/L and trough (C_{min}) <5 mg/L for once daily dosing; C_{max} 65–80 mg/L for thrice weekly dosing

Key: 3TC = lamivudine; 5-FU = 5-fluorouracil; AAP = American Academy of Pediatrics; ARN = acute retinal necrosis; ART = antiretroviral therapy; ARV = antiretroviral; BSA = body surface area; CBC = complete blood count; CMV = cytomegalovirus; CNS = central nervous system; CSF = cerebrospinal fluid; D5W = 5% dextrose in water; DOT = directly observed therapy; FDA = U.S. Food and Drug Administration; FDC = fixed-dose combination; FTC = emtricitabine; G6PD = glucose-6-phosphate dehydrogenase; GI = gastrointestinal; HBeAg = hepatitis B e antigen; HBV = hepatitis B virus; HCV = hepatitis C virus; HSV = herpes simplex virus; HZ = herpes zoster; ICP = intracranial pressure; IFN-α = interferon-alfa; IGRA = interferon-gamma release assay; IM = intramuscular; IRIS = immune reconstitution inflammatory syndrome; IV = intravenous; LIP = lymphocytic interstitial pneumonia; MIC = minimum inhibitory concentration; NNRTI = non-nucleoside reverse transcriptase inhibitors; OPC = oropharyngeal; PCP = *Pneumocystis* pneumonia; PCR = polymerase chain reaction; PI = protease inhibitor; PK = pharmacokinetic; PO = orally; TAF = tenofovir alafenamide; TB = tuberculosis; TCA = trichloroacetic acid; TDF = tenofovir disproxil fumarate; TMP = trimethoprim; TMP-SMX = trimethoprim-sulfamethoxazole; WHO = World Health Organization

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Updated: June 05, 2025
Reviewed: June 05, 2025

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Acyclovir	Oral Suspension • 40 mg/mL Capsules • 200 mg Tablets • 400 mg • 800 mg IV • 500 mg	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)	More Frequent • GI disturbances (anorexia, diarrhea, nausea, vomiting) • Headache, lightheadedness • Malaise Less Frequent (More Common in Adults Than Children) • Agitation • Alopecia • Dizziness • Myalgia, paresthesia • Somnolence	Requires dose adjustment in children with renal impairment. Avoid other nephrotoxic drugs. To avoid renal tubular damage related to crystalluria, administer IV preparation by slow IV infusion over at least 1 hour at a final concentration not to exceed 7 mg/mL. This must be accompanied by adequate hydration. Use caution with IV preparation in children with underlying neurological conditions, serious hepatic or electrolyte abnormalities, or substantial hypoxia.

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Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
		Parenteral and Oral Forms • Rash (urticarial, exfoliative skin disorders including SJS) • Anaphylaxis • Seizures • Elevated ALTs and ASTs • Fever • Hallucinations • Leukopenia • Lymphadenopathy • Peripheral edema • Visual abnormalities		
Albendazole	Tablet • 200 mg	More Frequent • Abnormal ALTs and ASTs 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. Recommend giving with a high-fat meal to increase absorption. May crush or chew tablets and give with water. Monitor CBC and LFTs prior to each cycle and every 2 weeks during therapy. Pregnancy tests may be administered.

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Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Amikacin	IV • 500 mg • 1,000 mg	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 children with impaired renal function. Should monitor renal function and hearing periodically (e.g., monthly) in children on prolonged therapy. TDM indicated. Use with caution in children on ECMO; PK may be altered. Dose adjustment with close monitoring necessary.
Amphotericin B Deoxycholate	IV • 50 mg	More Frequent • Infusion-related reactions (fever/chills, hypotension, anaphylaxis) • Anemia • Hypokalemia • Renal function impairment • Thrombophlebitis (at injection site) Less Frequent or Rare • Blurred or double vision	• GI disturbance (nausea, vomiting, diarrhea, abdominal pain) • Headache	Monitor BUN, Cr, CBC, electrolytes, LFTs, fluid status and input/output, signs of hypokalemia. Infuse over 1 to 2 hours; in children with azotemia, hyperkalemia, or getting doses >1 mg/kg, infuse over 3 to 6 hours. Requires dose reduction in children with impaired renal function.

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Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
		• Cardiac arrhythmias, usually with rapid infusions • Hypersensitivity (rash) • Leukopenia • Polyneuropathy • Seizures • Thrombocytopenia		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 are less frequent in children than adults; the onset is usually 1 to 3 hours after infusion, duration <1 hour; frequency decreases over time. Addition of heparin to infusion solution may reduce phlebitis. Flush line with dextrose; NS may cause precipitate. Pre-treatment with acetaminophen and/or diphenhydramine may alleviate febrile reactions.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

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	IV • 100 mg	More Frequent: • Infusion-related reactions (fever/chills, and headache) 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 a rate of 2.5 mg/kg/hour. To minimize immediate infusion-related reactions, premedicate with the following 30 to 60 minutes prior to administration: acetaminophen, diphenhydramine, and/or hydrocortisone. Adequate hydration and pre-infusion administration of NS may decrease risk of nephrotoxicity. In-line filters should not be used. Do not dilute with saline solutions or mix with other drugs or electrolytes (compatibility has not been established). Use with caution with bone marrow suppressants or other nephrotoxic drugs; renal toxicity is dose-dependent, but less renal toxicity than seen with conventional amphotericin B. Consider dose reduction in children with impaired renal function.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Amphotericin B Liposome	IV • 50 mg	More Frequent • Fever, chills • Hypokalemia Less Frequent • Back pain • Chest pain • Dark urine • Dyspnea • Infusion-related reaction (headache) • Jaundice • Renal function impairment Rare • Anaphylactic reaction	• GI disturbance (nausea, vomiting, diarrhea, abdominal pain) • Headache • Rash	Monitor BUN, Cr, CBC, electrolytes, and LFTs. Infuse over 2 hours. Do not use in-line filter less than 1 micron to administer. Consider dose reduction in children with impaired renal function. Flush line with D5W before and after infusion.
Artesunate	IV • Please refer to the AMIVAS website.	Rare • Anaphylactic reaction • Neutropenia • Bradycardia	• GI disturbance (nausea, vomiting) • Headache • Rash	Monitor CBC, LFTs, and electrolytes. Artesunate is preferred over quinidine for severe malaria because of decreased mortality. Monitor signs and symptoms of hemolytic anemia, Hb, and renal function for 4 weeks after therapy.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Atovaquone	Oral Suspension • 150 mg/mL	Frequent • Fever • Rash	Frequent • GI disturbances (nausea, vomiting, diarrhea) • Headache • Cough • Insomnia	Should be administered with a meal to enhance absorption; bioavailability increases threefold when administered with a high-fat meal. Avoid suspension in neonates due to benzyl alcohol. Monitor CBC with differential, liver enzymes, bilirubin, serum electrolytes, and serum amylase.
Atovaquone/ Proguanil	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. Atovaquone taken with a high-fat meal significantly increases the rate and extent of absorption. Side effects requiring discontinuation in ~1% to 2% of people.[b] Not recommended for prophylaxis in children with CrCl <30 mL/min.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Azithromycin	Oral Suspension • 20 mg/mL • 40 mg/mL Tablets • 250 mg • 500 mg • 600 mg Oral Powder Packet • 1,000 mg IV • 500 mg	More Frequent • Thrombophlebitis (IV form) Rare • Acute interstitial nephritis • Allergic reactions/anaphylaxis (dyspnea, hives, rash) • Pseudomembranous colitis • Prolonged QT interval • Syncope • Torsades de pointes • Ventricular tachycardia	• 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 a concentration of 1 mg/mL over a 3-hour period, or 2 mg/mL over a 1-hour period; IV should not be administered as a bolus. Use with caution in children with hepatic function impairment; biliary excretion is the main route of elimination. Potential drug interactions. See Table 5. Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections and the Drug–Drug Interactions section of the Adult and Adolescent Antiretroviral Guidelines for more information.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Bedaquiline	Tablets • 20 mg • 100 mg	Less Frequent • Chest pain • Hemoptysis Rare • Prolonged QT interval on ECG • Hepatotoxicity	More Frequent • Arthralgia • Nausea Less Frequent • Anorexia • Rash Rare • Increased serum amylase	Monitor serum potassium, calcium, and magnesium at baseline. Monitor ALT, AST, alkaline phosphatase, and bilirubin at baseline and monthly during treatment. Monitor EKG at baseline and monthly during treatment. Give with food (standard meal approximately 22 g of fat and 558 calories) to increase bioavailability twofold.
Capreomycin	IV/IM • 1,000 mg	More Frequent • Nephrotoxicity Less Frequent • Hypersensitivity (rash, fever) • Hypokalemia • Neuromuscular blockade • Ototoxicity, both auditory and vestibular • Injection site pain, sterile abscess	N/A	Rarely used in the United States because of efficacy concerns. Administer only by deep IM injection into large muscle mass (superficial injections may result in sterile abscess). Requires dose adjustment in children with impaired renal function. Monitor renal function and hearing periodically (e.g., monthly) in children on prolonged therapy. Monitor LFTs and electrolytes.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Caspofungin	IV • 50 mg • 70 mg	More Frequent • Histamine-mediated symptoms (fever, facial swelling, pruritus, bronchospasm) Rare • Hypokalemia • Anaphylactic reaction	• GI disturbances (nausea, vomiting, diarrhea) • Headache • Rash, facial flushing • Elevated ALTs and ASTs • Thrombophlebitis	Requires dose adjustment in moderate-to-severe hepatic insufficiency. Administer IV infusion over 1 hour in normal saline (do not use diluents containing dextrose). Higher doses (150 mg or greater) should be infused over at least 2 hours.
Chloroquine Phosphate	Tablets • 500 mg • 250 mg	More Frequent • Pruritus: Common in individuals of Black race 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 • Muscle weakness	Store in child-proof containers and protect from light. Overdose can be toxic. Chloroquine phosphate is bitter tasting, so consider administering with foods such as chocolate syrup that can mask the taste. Use with caution in children with G6PD deficiency or seizure disorder. Genetic testing is recommended.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
				Monitor CBC; periodic neurologic and ophthalmologic exams are recommended in children on prolonged therapy. Monitor EKG at baseline and as clinically indicated in children with elevated risk of QT prolongation.
Cidofovir	IV • 370 mg	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 children with severe renal impairment. Nephrotoxicity risk is decreased with prehydration with IV NS 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. Perform ophthalmologic exams and monitor renal function, urinalysis, electrolytes, and CBC.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Ciprofloxacin	Oral Suspension • 50 mg/mL • 100 mg/mL Tablets • 100 mg • 250 mg • 500 mg • 750 mg XR Tablets • 500 mg • 1,000 mg IV • 200 mg • 400 mg	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 taking sucralfate, 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 XR tablets. QT prolongation is concentration-dependent and occurs with use of two or more medications that prolong QT interval.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Clarithromycin	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 children with impaired renal function. Can be administered without regard to meals. Reconstituted suspension should not be refrigerated. Potential drug interactions exist. See Table 5. Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections and Drug-Drug Interactions section of the Adult and Adolescent Antiretroviral Guidelines for more information.
Clindamycin	Oral Solution • 15 mg/mL Capsules • 75 mg • 150 mg • 300 mg IV/IM • 300 mg	More Frequent • Pseudomembranous colitis Less Frequent • Hypersensitivity (rash, redness, pruritus) • Neutropenia • Thrombocytopenia	More Frequent • GI disturbances (abdominal pain, nausea, vomiting, diarrhea) Less Frequent • Fungal overgrowth in rectal and genital areas	IV preparation not recommended for use in neonates because of benzyl alcohol. IV preparation must be diluted prior to administration. Do not exceed 600 mg in a single IM injection.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
	• 600 mg • 900 mg			Capsule formulation should be taken with food or a full glass of water to avoid esophageal irritation. Reconstituted oral solution should not be refrigerated. Some products may contain tartrazine and can cause allergic reactions. Allergic reactions are frequently observed in people who also have aspirin hypersensitivity.
Cycloserine	Capsule • 250 mg	More Frequent • CNS toxicity (including confusion, anxiety) Less Frequent • Hypersensitivity (skin rash) • Peripheral neuropathy • Seizures • Psychosis Rare • Cardiac arrhythmias	More Frequent • Headache, dizziness, drowsiness 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. Monitor serum levels if possible. Requires dose adjustment in children with impaired renal function. Do not administer to children with severe renal impairment (because of increased risk of neurotoxicity).

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
				Should coadminister pyridoxine at the same time. May increase Vitamin B12 and folic acid requirements. Monitor renal function, LFTs, and CBC.
Dapsone	Oral Suspension (extemporaneously prepared from 25 mg tablets) • 2 mg/mL Tablets • 25 mg • 100 mg	More Frequent • Hemolytic anemia (especially with 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. Use with caution in children with G6PD deficiency, Hb M deficiency, and methemoglobin reductase deficiency.
Doxycycline	Tablets and Capsules • 20 mg	More Frequent • GI irritation, pill esophagitis	• Staining of teeth possible for individuals aged <8 years	Swallow with adequate amounts of fluids.

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Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
	• 50 mg • 75 mg • 100 mg Oral Suspension and Syrup • 5 mg/mL oral suspension • 10 mg/mL oral syrup IV • 100 mg	• Photosensitivity Less Frequent • Increased intracranial pressure • Photosensitivity • Hemolytic anemia • Rash and hypersensitivity reactions • Clostridium difficile-associated diarrhea • Pseudotumor cerebri	• Photo-onycholysis • GI disturbances (nausea, vomiting, abdominal cramps)	Avoid antacids, milk, dairy products, and iron for 1 hour before and 2 hours after administration of doxycycline. Avoid high-fat meals that can reduce doxycycline serum levels. Use with caution in hepatic and renal disease. IV doses should be infused over 1 to 4 hours. Children should avoid prolonged exposure to direct sunlight (skin sensitivity). Monitor renal function, CBC, and LFTs if therapy is prolonged.
Erythromycin	Erythromycin-Base Tablet • 250 mg • 333 mg • 500 mg DR Tablet • 250 mg	Less Frequent • Estolate may cause cholestatic jaundice, although hepatotoxicity is uncommon (2% of reported cases).	• 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.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
	• 333 mg • 500 mg DR Capsule • 250 mg Erythromycin Ethyl Succinate *Suspension* • 200 mg/5 mL • 400 mg/5 mL *Oral Drops* • 100 mg/2.5 mL *Chewable Tablet* • 200 mg *Tablet* • 400 mg Erythromycin Estolate *Suspension* • 125 mg/5 mL • 200 mg/5 mL	Rare • QT prolongation • Hypersensitivity reactions (rash, exfoliative skin disorders including SJS/TEN)		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. IV formulations contain benzyl alcohol derivatives and are not recommended in neonates.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
	Erythromycin Stearate *Tablet* • 250 mg • 500 mg Erythromycin Gluceptate *IV* • 200 mg Erythromycin Lactobionate *IV* • 500 mg • 1,000 mg			
Ethambutol	Tablets • 100 mg • 400 mg	Less Frequent • Acute gouty arthritis (secondary to hyperuricemia) Rare • Hypersensitivity (rash, fever, joint pain) • Peripheral neuropathy	• GI disturbances (abdominal pain, anorexia, nausea, vomiting) • Confusion • Disorientation • Headache	Requires dose adjustment in children with impaired renal function. Take with food (e.g., gelatin, chocolate pudding) to minimize gastric irritation. Tablets may be crushed.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
		• Retrobulbar optic neuritis, decreased visual acuity, loss of red-green color discrimination • Bone marrow suppression • Abnormal LFTs, hepatotoxicity		Monitor visual acuity and red-green color discrimination. Document normal vision at baseline. Monitor renal function, LFTs, and CBC. Avoid concomitant use of neurotoxic drugs. Evaluate pregnancy status prior to treatment.
Ethionamide	Tablet • 250 mg	Less Frequent • Hepatitis, jaundice • Peripheral neuritis • Psychiatric disturbances Rare • Goiter or hypothyroidism • Hypoglycemia • Optic neuritis • 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. Avoid alcohol. Take with food to minimize gastric irritation. Monitor LFTs, glucose, and thyroid function. Perform periodic ophthalmologic exams. Monitor for signs and symptoms of SCARs.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Fluconazole	Oral Suspension • 10 mg/mL • 40 mg/mL Tablets • 50 mg • 100 mg • 150 mg • 200 mg IV • 200 mg • 400 mg	Less Frequent • Hypersensitivity (fever, chills, 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 children with impaired renal function. IV administration should be administered over 1–2 hours at a rate of ≤200 mg/hour. Daily dose is the same for oral and IV administration. Multiple potential drug interactions exist. See Table 5. Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections and Drug-Drug Interactions section of the Adult and Adolescent Antiretroviral Guidelines for more information. Monitor periodic LFTs, renal function, and CBC.
Flucytosine	Capsules • 250 mg	More Frequent	• GI disturbances (abdominal pain, constipation, diarrhea, anorexia, nausea, vomiting)	Monitor serum concentrations and adjust dose to maintain therapeutic

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
	• 500 mg Oral Liquid • Extemporaneous preparation	• 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	• Elevated ALTs and ASTs • Rash Rare • CNS symptoms (headache, drowsiness, confusion, vertigo)	levels and minimize risk of bone marrow suppression. Requires dose adjustment in children with impaired renal function; use with extreme caution. Fatal aplastic anemia and agranulocytosis rarely have been reported. Consider determination of dihydropyridine dehydrogenase (DPD) enzyme deficiency in children who develop drug toxicity. Oral preparations should be administered with food over a 15-minute period to minimize GI side effects. QT prolongation may occur. Monitor CBC, LFTs, renal function, and electrolytes.
Foscarnet	IV • 6,000 mg	More Frequent • Nephrotoxicity • Serum electrolyte abnormalities (hypocalcemia, hypophosphatemia, hypomagnesemia, hypokalemia)	Frequent • GI disturbances (abdominal pain, anorexia, nausea, vomiting) • Anxiety, confusion, dizziness, headache	Requires dose adjustment in children with impaired renal function. Use adequate hydration to decrease nephrotoxicity.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
		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 in mouth or throat	• Fever	Avoid concomitant use of other drugs with nephrotoxicity. Monitor serum electrolytes, ECG, renal function, and CBC. IV solution of 24 mg/mL can be administered via central line; must be diluted to a final concentration ≤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).
Ganciclovir	Capsules • 250 mg • 500 mg IV • 500 mg	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)	• GI disturbances (abdominal pain, anorexia, nausea, vomiting) • Rash	Requires dose adjustment in children with renal impairment. Avoid other nephrotoxic drugs. IV infusion over at least 1 hour; in-line filter required. Flush line well with NS before and after administration. Maintain good hydration. Undiluted IV solution is alkaline (pH 11); use caution when handling and preparing solutions,

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
		Rare • Retinal detachment • Seizures • Psychosis • Cardiovascular effects (hypertension, chest pain)		and avoid contact with skin and mucus membranes. Administer oral doses with a high-fat meal to increase absorption. Do not open or crush capsules. Perform ophthalmologic examinations and monitor CBC, LFTs, and renal function.
Imipenem/Cilastatin	IV • 250 mg • 500 mg	More Frequent • Hematologic toxicity (decreased hematocrit, decreased hemoglobin) • Hepatotoxicity (increased ALT and AST) Less Frequent • Hematologic toxicity (eosinophilia, thrombocythemia) • Renal toxicity (proteinuria) Rare • Seizures • Cardiovascular toxicity • Neutropenia • Phlebitis near injection site	Rare • Rash • GI disturbances (nausea and vomiting) • Oral candidiasis	Administer by IV intermittent infusion. Doses ≤500 mg may be infused over 20 to 30 minutes. Doses >500 mg should be infused over 40 to 60 minutes. If nausea and vomiting occur during infusion, decrease rate of IV infusion.

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Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Isavuconazole	Oral Capsules • 74.5 mg • 186 mg IV • 372 mg	More Frequent • Peripheral edema • Hypokalemia Less Frequent • Increase in liver enzymes Rare • Atrial fibrillation • Cholelithiasis • Acute respiratory failure	More Frequent • Back pain • GI disturbances (abdominal pain and constipation) Less Frequent • Anxiety Rare • Dermatologic (alopecia, urticaria) • Tinnitus	Administer IV over a minimum of 1 hour via infusion, set with in-line filter. Give capsules with or without food. Swallow capsules whole. Do not chew, crush, dissolve, or open capsules. Some dosage forms contain propylene glycol. Large amounts administered have been associated with potentially fatal toxicities in neonates, including metabolic acidosis, seizures, renal failure, and CNS depression.
Isoniazid	Oral Syrup • 10 mg/mL Tablets • 100 mg • 300 mg IV/IM • 100 mg	More Frequent • Hepatitis prodromal syndrome (anorexia, weakness, vomiting) • Hepatitis • Peripheral neuritis Rare • Blood dyscrasias • Hypersensitivity (fever, rash, joint pain) • Neurotoxicity (including seizure)	• 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. Avoid taking isoniazid with histamine and tyramine-containing foods. Increase dietary intake of folate, niacin, and magnesium. Use with caution in children with hepatic function impairment,

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
		• Optic neuritis		severe renal failure, or history of seizures. Pyridoxine supplementation should be provided for all children with HIV. Monitor LFTs and perform periodic ophthalmologic examinations.
Itraconazole	Oral Solution • 10 mg/mL Capsule • 100 mg IV • 250 mg	Less Frequent • Hypersensitivity (fever, chills, 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. Capsule • Administer after a full meal to increase absorption. • Grapefruit juice may alter itraconazole levels. Itraconazole oral solution has 60% greater bioavailability compared with capsules, and the oral solution and capsules should not be used interchangeably. Administer IV infusion over at least 1 hour.

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Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
				Multiple potential drug interactions. See Table 5. Significant Drug Interactions for Drugs Used to Treat or Prevent Opportunistic Infections and Drug-Drug Interactions section of the Adult and Adolescent Antiretroviral Guidelines for more information. Monitor LFTs and potassium levels. Monitor serum concentrations (TDM) in severe infections after 2 weeks of therapy. Levels may be drawn any time during the dosing interval. Box warning: May cause or exacerbate HF. Discontinue to reassess risk-benefit if signs or symptoms of HF occur.
Kanamycin	IV/IM • 75 mg • 500 mg • 1,000 mg	More Frequent • Nephrotoxicity • Neurotoxicity (including muscle twitching, seizures) • Ototoxicity (both auditory and vestibular)	N/A	Must be infused over 30 to 60 minutes to avoid neuromuscular blockade. Requires dose adjustment in children with impaired renal function.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
		Less Frequent • Hypersensitivity (rash, redness, or swelling) Rare • Neuromuscular blockade		Monitor renal function and auditory function periodically (e.g., monthly) in children on prolonged therapy. Monitor serum concentrations (TDM).
Ketoconazole	Tablet • 200 mg Topical • Shampoo • Cream • Gel • Foam Oral Suspension • Extemporaneous preparation	Less Frequent • Hypersensitivity (fever, chills, rash) Rare • Hepatotoxicity (including hepatic failure)	More 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. Administer with acidic liquid (non-diet cola or orange juice) in children with achlorhydria. Disulfiram-like reactions have occurred in pediatric patients accidentally 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 have been reported in children.

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Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
				High-dose ketoconazole suppresses corticosteroid secretion and lowers serum testosterone concentration (reversible). Multiple potential drug interactions exist. Monitor LFTs.
Mefloquine	Tablet • 250 mg	More Frequent • CNS effects (psychosis, depression, hallucinations, paranoia, seizures) Rare • Blood dyscrasias • Cholestasis, elevated bilirubin	• Rash • GI disturbances (abdominal pain, constipation, diarrhea, anorexia, nausea, vomiting) • Minor CNS effects (dizziness, vivid dreams, insomnia) • Tinnitus, blurred vision	Side effects are less prominent in children. Administer with food and plenty of water. Tablets can be crushed and added to food; administer with foods such as chocolate syrup or gelatin to mask the bitter taste of crushed tablets. Monitor LFTs.
Nitazoxanide	Oral Suspension • 20 mg/mL Tablet • 500 mg	N/A	More Frequent • GI disturbances (abdominal pain, nausea, vomiting) • Headache Rare • Scleral icterus	Should be given with food. Shake suspension well prior to dosing. Use with caution in neonates. Nitazoxanide products may contain benzyl alcohol derivatives that can

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
			• Rash	be associated with gasping syndrome.
p-Aminosalicylic Acid	DR Granules • 4,000 mg per packet	Rare • Hypersensitivity o Fever o Rash o Exfoliative dermatitis o GI symptoms o Jaundice o Hepatitis o Pericarditis o Vasculitis o Hematologic abnormalities including hemolytic anemia o Hypoglycemia o Optic neuritis o Encephalopathy o Reduction in Prothrombin • Crystalluria • Hemolytic anemia	• GI disturbances (abdominal pain, nausea, vomiting, diarrhea)	Should not be administered to children 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 children receiving for >1 month. Administer granules by sprinkling on acidic foods (e.g., applesauce, yogurt) or a fruit drink (e.g., tomato juice, orange juice). Maintain urine at neutral or alkaline pH to avoid crystalluria. The granule's soft “skeleton” may be seen in the stool. Monitor CBC and LFTs.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Pentamidine	IV/IM/Aerosol • 300 mg	For IV Administration *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) For Aerosol Administration *More Frequent* • Sneezing • Cough	For IV Administration *More Frequent* • GI disturbances (anorexia, nausea, vomiting, diarrhea) *Less Frequent* • Unpleasant metallic taste For Aerosol Administration *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 retreatment within 3 months of prior treatment. Hyperglycemia and diabetes mellitus can occur up to several months after drug is discontinued. Monitor LFTs, renal function, glucose, electrolytes, and BP. Inhalation • A special nebulizer is required for aerosol administration. Medical personnel should be trained in the proper administration of aerosolized pentamidine.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
				• An inhaled bronchodilator may be administered prior to each dose in children who experience bronchospasm or cough.
Posaconazole	IR Oral Suspension • 40 mg/mL Oral Powder Packet • 300 mg DR Tablet • 100 mg DR Oral Suspension • Extemporaneous preparation IV • 300 mg	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 effects (headache, dizziness, fatigue) • Elevated serum ALTs and ASTs	Must be given with meals to ensure adequate absorption. Monitor LFTs, renal function, and electrolytes. Monitor serum drug concentrations (TDM). Shake suspension prior to dosing. Various oral formulations are not interchangeable. Administer reconstituted DR suspension within 1 hour of prep and administer with food. Administer IR suspension during or within 20 minutes following a full meal. Infuse IV over 90 minutes via central line only.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Primaquine	Tablet • 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. Combat bitter taste with chocolate syrup, applesauce, or jelly. Monitor CBC. Recommend G6PD testing.
Pyrazinamide	Tablet • 500 mg Oral Suspension • Extemporaneous 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 children with severe hepatic impairment. Reduce dose in children with renal or hepatic impairment. Monitor LFTs and uric acid.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Pyrimethamine	Tablet • 25 mg Oral Suspension • Extemporaneous preparation	Less Frequent • Neutropenia • Thrombocytopenia • Megaloblastic anemia Rare • SJS • Seizure	• Skin rash • Photosensitivity • Dry mouth • GI disturbances (nausea, vomiting) • CNS effects (depression, insomnia)	To prevent hematologic toxicity, administer with leucovorin. Monitor CBC. Administer with meals to avoid GI side effects. Recommend G6PD testing.
Quinidine	Tablet (XR) • 324 mg Tablet • 200 mg • 300 mg	Serious • Cardiac arrhythmias • QT interval prolongation • Hypoglycemia • Hemolytic anemia (with G6PD deficiency) • Hepatotoxicity	Very Frequent • Cinchonism (dose-dependent)—syndrome of tinnitus, reversible high-frequency hearing loss, deafness, vertigo, blurred vision, diplopia, photophobia, headache, confusion, and delirium.	Monitor CBC and LFTs. Hemolysis may occur in children with G6PD.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Ribavirin	Powder for Solution for Nebulization • Reconstituted product contains 20 mg/mL. Oral Solution • 40 mg/mL Capsule • 200 mg Tablets • 200 mg • 400 mg • 600 mg	More Frequent • 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 children with severe renal impairment. Should not be used as monotherapy for treatment of hepatitis C but rather, 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 due to increased risk of pancreatitis/ mitochondrial toxicity. Oral solution contains propylene glycol. This drug is teratogenic/embryocidal and contraindicated in pregnant women and their partners. Avoid pregnancy for an additional 6 months after treatment.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
				In combination therapy with IFN-α, ribavirin may cause a reduction in growth velocity in children and adolescents 5–17 years of age. Monitor CBC, renal function, LFTs, and thyroid function. Perform pregnancy tests regularly while on therapy. High-fat meals increase AUC and C_{max}. Be consistent with fat content of meals.
Rifabutin	Capsule • 150 mg Oral Suspension • Extemporaneous 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 an empty stomach, but may be administered with food in children with GI intolerance. The contents of capsules may be mixed with applesauce for children who are unable to swallow capsules. May cause reddish to brown-orange color urine, feces, saliva, sweat, skin, or tears (can discolor soft contact lenses).

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
				Uveitis seen with high-dose rifabutin (i.e., >300 mg/day in adults), especially when combined with clarithromycin. Multiple potential drug interactions exist. Use with caution in children with renal or hepatic impairment. Monitor CBC and LFTs; conduct ophthalmologic examinations. Reduce dose in children with renal impairment.
Rifampin	Oral Suspension • Extemporaneous preparation Capsules • 150 mg • 300 mg IV • 600 mg	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 taken on an empty stomach, but can be administered with food in children with GI intolerance; take with full glass of water. Suspension formulation stable for 30 days. Shake well prior to dosing. May mix contents of capsule with applesauce or jelly. May cause reddish to brown-orange color urine, feces, saliva, sweat, skin, or tears (can discolor soft contact lenses).

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
				Multiple potential drug interactions Use with caution in children with hepatic impairment. Administer IV by slow infusion. Extravasation may cause local irritation and inflammation. Monitor CBC and LFTs.
Streptomycin	IV/IM • 1,000 mg	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 children who cannot tolerate IM injections, dilute to 12–15 mg in 100 mL of 0.9% sodium chloride; must be infused over 30–60 minutes to avoid neuromuscular blockade. Requires dose adjustment in children with impaired renal function. Monitor renal function and hearing periodically (e.g., monthly) in children on prolonged therapy. Monitor serum concentrations (TDM).

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Sulfadiazine	Tablet • 500 mg Oral Suspension • Extemporaneous 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. May potentially lead to hyperbilirubinemia and kernicterus in neonates and young infants. Avoid use in infants <2 months unless other options are not available.
Trimethoprim-Sulfamethoxazole (TMP-SMX)	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	More Frequent • Skin rash Less Frequent • Hypersensitivity reactions (skin rash, fever) • Hematologic toxicity (leukopenia, neutropenia, thrombocytopenia, anemia) Rare • Exfoliative skin disorders (including SJS)	• GI disturbances (anorexia, nausea, vomiting, diarrhea) • Photosensitivity • Rash	Requires dose adjustment in children 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. May displace bilirubin from protein binding sites which may lead to hyperbilirubinemia in neonates and young infants.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
	IV • TMP 16 mg/ mL and SMX 80 mg/mL	• Hemolytic anemia (with G6PD deficiency) • Methemoglobinemia • Renal toxicity (crystalluria, nephritis, tubular necrosis) • CNS toxicity (aseptic meningitis) • Pseudomembranous colitis • Cholestatic hepatitis • Thyroid function disturbance		Oral suspension may contain propylene glycol that can lead to fatal toxicities, such as metabolic acidosis, renal failure, or respiratory depression in neonates. Administer IV infusion over 60–90 minutes. Monitor CBC and renal function.
Valacyclovir	Tablets • 500 mg • 1,000 mg Note: An oral suspension formulation of 50 mg/mL can be prepared in Ora-Sweet or SyrPalta syrups)	Rare • Renal failure • Bone marrow suppression • Thrombotic microangiopathy/ hemolytic uremic syndrome • CNS effects (psychosis, seizures, delirium)	More Frequent • Headache, nausea Less Frequent • Arthralgia • Dizziness, fatigue • GI disturbances (diarrhea or constipation, anorexia, abdominal pain, vomiting) • Dysmenorrhea	Thrombotic thrombocytopenic purpura/hemolytic uremic syndrome has been reported in adults with HIV with advanced disease receiving high (i.e., 8 g/day) but not low doses. Monitor CBC and renal function. Avoid other nephrotoxic drugs. Maintain adequate hydration.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
Valganciclovir	Tablet • 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 or BUN • Retinal detachment	• GI disturbances (abdominal pain, anorexia, nausea, vomiting) • CNS effects (headache, insomnia)	Requires dose adjustment in children with renal impairment. Avoid other nephrotoxic drugs. Tablets should not be broken or crushed. Monitor CBC and renal function. Potentially teratogenic and carcinogenic.
Voriconazole	Tablets • 50 mg • 200 mg Oral Suspension • 40 mg/mL IV • 200 mg	Less Frequent • Hypersensitivity (fever, chills, skin rash) • Anaphylactoid reaction with IV infusion Rare • Hepatotoxicity (including hepatic failure) • Exfoliative skin disorders (including SJS) • Renal dysfunction	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	Oral tablets should be taken 1 hour before or after a meal. Shake oral suspension well prior to dosing. Maximum IV infusion rate should be 3 mg/kg/hour over 1–2 hours. Use oral administration for children with impaired renal function, if possible, because of accumulation of IV vehicle in children with renal insufficiency.

Table 4. Common Drugs Used for Treatment of Opportunistic Infections in Children With HIV: Preparations and Major Toxicities

Drug	Preparations	Major Toxicities[a]		Special Instructions
		Indicating Need for Medical Attention	Indicating Need for Medical Attention If Persistent or Bothersome	
		• Cardiac arrhythmias • Pancreatitis • QT prolongation • Electrolyte abnormalities • Optic neuritis, papilledema	• Elevated serum transaminases	Dose adjustment is needed if hepatic insufficiency exists. Visual disturbances are common (>30%) but are transient and reversible when drug is discontinued. Multiple potential drug interactions exist. 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.

[b] Source: Atovacquone/Proguanil. ScienceDirect. https://www.sciencedirect.com/topics/medicine-and-dentistry/atovaquone-proguanil.

Key: ALT = alanine transaminase; AST= aspartate transaminase; AUC = area under the curve; BP = blood pressure; BUN = blood urea nitrogen; CBC = complete blood count; C_{max} = maximum plasma concentration; CNS = central nervous system; Cr = creatinine; CrCl = creatinine clearance; D5W = dextrose 5% in water; DR = delayed-release; ECMO = extracorporeal membrane oxygenation; EKG = electrocardiogram; G6PD = glucose-6-phosphate dehydrogenase; GI = gastrointestinal; Hb = hemoglobin; HF = heart failure; IFN-α = interferon alfa; IM = intramuscular; IR = immediate-release; IV = intravenous; LFT = liver function test; NS = normal saline; PK = pharmacokinetics; QT = interval between Q and T waves; QTc = QT interval corrected for heart rate; SCAR = severe cutaneous adverse reactions; SJS = Stevens-Johnson Syndrome; SMX = sulfamethoxazole; TDM = therapeutic drug monitoring; TMP = trimethoprim; XR = extended-release.

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

Updated: June 05, 2025
Reviewed: June 05, 2025

The potential exists for significant drug interactions and overlapping toxicities in children receiving medications for treatment or prevention of opportunistic infections (OIs). These children often receive other medications, including antiretrovirals, that interfere with the metabolism or elimination of OI medications. In particular, protease inhibitors and non-nucleoside reverse transcriptase inhibitors affect the cytochrome P450 or other transporter systems and may be associated with clinically significant drug interactions. The integrase strand transfer inhibitors cabotegravir and raltegravir are primarily metabolized by uridine diphosphate glucuronosyltransferase 1A1 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 the 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 data are available from studies involving adults with HIV, whereas data in children are extremely limited. New information continues to become available, and carefully reviewing each child's current medications, including prescription and over-the-counter medications, is important. Predicting the interaction potential is difficult when three or more drugs with similar metabolic pathways are coadministered, and significant interpatient variability amplifies these challenges. When possible, alternative agents with less drug interaction potential or use of therapeutic drug monitoring should be considered.

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

Drug Name	Toxicities	Recommendation
* The drug interactions included in this table were selected based on their potential clinical significance and are not inclusive of all potential drug interactions (see FDA Online Label Repository for complete information on drug interactions).		
Acyclovir	Overlapping Toxicities • Nephrotoxic drugs	Avoid other nephrotoxic drugs.
	Increased Concentrations (Both Drugs) and Overlapping Toxicities • *Antivirals*: valacyclovir, valganciclovir, ganciclovir, cidofovir • *ARVs:* tenofovir • *Immunosuppressive agents*: mycophenolate	Monitor for toxicities of these drugs.
Albendazole	Increased Albendazole Concentrations • *Anthelmintics*: praziquantel Decreased Albendazole Concentrations • *Anticonvulsants*: carbamazepine, phenobarbital, phenytoin • *Antivirals*: nirmatrelvir and ritonavir	Caution advised.
Amikacin	Overlapping Toxicities • *Antituberculars* (injectable): kanamycin, streptomycin • *Nephrotoxic or ototoxic drugs* • *Antimycobacterials*: capreomycin • ARVs: tenofovir • *Antivirals*: cidofovir	Caution advised. Avoid combining with cidofovir.
Amphotericin B Amphotericin B Lipid Complex Amphotericin B Liposome	Overlapping Toxicities • *Bone marrow suppressants*: corticosteroids • *Nephrotoxic drugs* • *Neuromuscular blockers*	Caution advised.

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

Drug Name	Toxicities	Recommendation
Artemether-Lumefantrine	Increased Drug Concentrations • *ARVs*: nevirapine	Monitor therapy when combined.
	Overlapping Toxicities • *ARVs*: PIs • *Antibacterials*: fluoroquinolones, macrolides • *Antifungals*: fluconazole, voriconazole • *Antimalarials*: quinidine, quinine • *Psychotropics*: quetiapine, tricyclic antidepressants	Coadministration with fluconazole or voriconazole should be avoided. For all other drugs, coadministration should be avoided, if possible; monitor for toxicities (QT prolongation).
Atovaquone	Decreased Atovaquone Concentrations • *Antimycobacterials*: rifampin, rifabutin • *ARVs*: lopinavir/ritonavir, atazanavir/ritonavir • *Antibiotics*: doxycycline	Coadministration of atovaquone and rifampin or atovaquone and rifabutin should be avoided.
Azithromycin	Overlapping Toxicities • *Antimalarials*: artemether/lumefantrine, chloroquine, quinine	Caution advised. Increased risk of QT prolongation.
Bedaquiline	Overlapping Toxicities • QT-prolonging agents	Bedaquiline may enhance the QTc-prolonging effects. Avoid concomitant use.
	• *Fecal microbiota (live)* (oral and rectal)	Avoid concomitant use.
Caspofungin	Decreased Caspofungin Concentrations • *Anticonvulsants*: phenytoin • *Antimycobacterials*: rifampin • A*RVs*: efavirenz, nevirapine	Increase in dose of caspofungin is recommended when coadministered with CYP450 inducers.
Cidofovir	Overlapping Toxicities • *Antibacterials*: aminoglycosides • *Antivirals*: foscarnet • *ARVs*: tenofovir • *Nephrotoxic drugs*	Monitor for toxicities of these drugs. Prehydrate with IV normal saline and probenecid to avoid nephrotoxicity.

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

Drug Name	Toxicities	Recommendation
Ciprofloxacin	Decreased Ciprofloxacin Absorption • *ARVs*: 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 • *Antimalarials*: artemether/lumefantrine, quinine • *Antibacterials:* clarithromycin	Caution advised.
	• *Fecal microbiota (live)* (oral and rectal)	Avoid concomitant use.
Clarithromycin	Increased Clarithromycin Concentrations • *ARVs:* 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.
	Increased Concomitant Drug Concentrations • *ARVs*: etravirine	Consider alternative ARV.
	Decreased Clarithromycin Concentrations • *ARVs*: efavirenz, etravirine, nevirapine • *Antimycobacterials*: 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.
	Overlapping Toxicities • *Fecal microbiota (live)* (oral/rectal)	Clarithromycin may reduce fecal microbiota (live) (rectal) effectiveness.
Clindamycin	Decreased Clindamycin Antibacterial Efficacy • *Antibacterials*: chloramphenicol, erythromycin Overlapping Toxicities • *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.

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

Drug Name	Toxicities	Recommendation
Cycloserine	Overlapping Toxicities • *Antimycobacterials*: ethionamide, isoniazid	Caution advised.
	• *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.
Dapsone	Decreased Dapsone Concentrations • *Antimycobacterials*: rifampin	Coadministration should be avoided if possible. Consider alternatives for dapsone or use rifabutin.
	Decreased Dapsone Absorption • *ARVs*: atazanavir, didanosine suspension • *Gastrointestinal drugs*: antacids	For coadministration with antacids or didanosine suspension, give dapsone 1 hour before or 4 hours after the other medication.
	Overlapping Toxicities • *Bone marrow suppressants* or drugs associated with hemolysis	Caution advised.
	• *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.
Doxycycline	Decreased Doxycycline Concentrations • *Anticonvulsants*: carbamazepine, phenytoin • *Antimycobacterials*: rifampin	Potential for decreased doxycycline efficacy. Monitor for therapeutic failure.
	Overlapping Toxicities • *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.
Erythromycin	Increased Concentrations of Erythromycin • *Antifungals*: itraconazole (itraconazole concentrations also increased) Increased Concomitant Drug Concentrations • *ARVs*: tenofovir	Monitor for toxicities of both drugs, potential for QT prolongation.
	Overlapping Toxicities • *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.

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

Drug Name	Toxicities	Recommendation
Ethambutol	Overlapping Toxicities • *Neurotoxic drugs*	Caution advised.
	• *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.
Ethionamide	Potential for Increased Toxicity Due to Overlapping Toxicity • *Neurotoxic drugs* • *Antimycobacterials*: cycloserine, isoniazid	Caution advised.
	• *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.
Fluconazole	Decreased Fluconazole Levels • *Anticonvulsants*: phenytoin • *Antimycobacterials:* rifampin • *ARVs*: rilpivirine	Monitor for efficacy. May need to increase fluconazole dose.
	Increases Concomitant Drug Concentrations • *ARVs*: etravirine, nevirapine, saquinavir, tipranavir	May need to decrease dose of saquinavir. Avoid tipranavir with high doses of fluconazole (maximum fluconazole dose in adults: 200 mg). Caution advised with etravirine.
	• *Antineoplastics*: venetoclax	Decrease venetoclax dose by at least 50% in children requiring concomitant treatment.
	• *Antimycobacterials*: rifabutin	May need to decrease dose of rifabutin.
	• *Statins*: atorvastatin, lovastatin, simvastatin	Do not coadminister with simvastatin or lovastatin. Avoid use of atorvastatin if possible. Alternative statins, such as fluvastatin, rosuvastatin, and pravastatin, are preferred, or discontinue statin during antifungal therapy.
Flucytosine	Increased Flucytosine Concentrations • *Nephrotoxic drugs* Overlapping Toxicities • *QT-prolonging drugs*	Caution advised. Dose adjustments with therapeutic drug monitoring recommended with impaired renal function.

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

Drug Name	Toxicities	Recommendation
Foscarnet	Overlapping Toxicities • *Antivirals*: cidofovir • *Anti-pneumocystis drugs*: pentamidine • *Nephrotoxic drugs*	Monitor for toxicities of these drugs.
Ganciclovir	Increased Ganciclovir Concentrations • *ARVs*: tenofovir (concentrations also increased)	Monitor for toxicities of these drugs.
	Increased Concomitant Drug Concentrations • *ARVs*: didanosine	Caution advised.
	Overlapping Toxicities • *Antibacterials*: imipenem-cilastatin • *ARVs*: zidovudine • *Bone marrow suppressants* • *Nephrotoxic drugs*	Caution advised. Increased risk of seizures with imipenem-cilastatin.
Isavuconazole	Increased Concomitant Drug Concentrations • *Antineoplastics*: venetoclax	Reduce venetoclax dose by at least 50% in children requiring concomitant treatment. Resume previous venetoclax dose two to three days after discontinuation of isavuconazole.
Isoniazid	Decreased Isoniazid Concentrations • *Corticosteroids*: glucocorticoids (e.g., prednisolone)	Use with caution.
	Decreased Isoniazid Absorption • *Gastrointestinal drugs*: antacids	Caution advised. Take ≥1 hour before aluminum-containing antacids.
	Increased Concomitant Drug Concentrations • *Sedatives/hypnotics*: diazepam	Caution advised.
	Decreased Concomitant Drug Concentrations • *Antifungals*: itraconazole, ketoconazole	Coadministration should be avoided, if possible.

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

Drug Name	Toxicities	Recommendation
	Overlapping Toxicities • *Antimycobacterials*: cycloserine, ethionamide, itraconazole • *Hepatotoxic drugs* • *Neurotoxic drugs*	Caution advised.
Itraconazole and Ketoconazole	Increased Azole Concentrations • *Antibacterials*: clarithromycin, ciprofloxacin, erythromycin • *ARVs*: PIs	Monitor for toxicities and monitor concentrations. Consider azithromycin instead of other macrolides. High doses of itraconazole are not recommended with PIs.
	Increased Concomitant Drug Concentrations • *ARVs*: etravirine, maraviroc, PIs	Caution advised. Monitor for toxicities. Decrease adult maraviroc dose to 150 mg twice daily.
	• *Statins*: atorvastatin, lovastatin, simvastatin	Do not coadminister with simvastatin or lovastatin. Avoid use of atorvastatin if possible. Alternative statins such as fluvastatin, rosuvastatin, and pravastatin are preferred; alternatively, discontinue statin during antifungal therapy.
	• *Antibacterials:* clarithromycin, erythromycin	Consider switching to azithromycin, which has less potential for drug interaction.
	• *Sedatives/hypnotics*: alprazolam, diazepam, midazolam	Coadministration of midazolam and alprazolam should be avoided. Coadministration of diazepam should be avoided, if possible.
	• *Antimalarial:* quinidine	Coadministration of quinidine should be avoided. QT prolongation may occur.
	Decreased Azole Concentrations • *ARVs*: efavirenz, etravirine, nevirapine, rilpivirine	Monitor concentrations. Coadministration of efavirenz should be avoided if possible.
	• *Anticonvulsants*: carbamazepine, fosphenytoin	Monitor concentrations.
	• *Antimycobacterials*: isoniazid, rifabutin, rifampin, rifapentine	Coadministration with rifampin should be avoided. Coadministration with rifabutin should be avoided, if possible. Monitor for toxicities and monitor concentrations.

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

Drug Name	Toxicities	Recommendation
	Decreased Azole Absorption • *ARVs*: didanosine • *Gastrointestinal drugs*: antacids, anticholinergics/antispasmodics, histamine H2-receptor antagonists, omeprazole, sucralfate	Monitor concentrations.
Mefloquine	Decreased Mefloquine Concentrations • *Antimalarials*: quinine • *Antimycobacterials:* rifampin	Monitor for decreased mefloquine efficacy. Coadministration of rifampin should be avoided, if possible; use rifabutin instead.
	Decreased Concomitant Drug Concentrations • *ARVs*: ritonavir, possibly other PIs	Monitor for virologic failure of PI-containing ART regimen.
	Overlapping Toxicities • *Antimalarials*: quinine • *QT-prolonging drugs*	Avoid coadministration, if possible. Monitor for toxicities (EKG changes, cardiac arrest, and seizures with quinine). If coadministered with quinine, give mefloquine at least 12 hours after last dose of quinine.
Nitazoxanide	Increased Concomitant Drug Concentrations • *Anticonvulsants*: phenytoin	Potential for interaction with other medications that are highly protein-bound. Use with caution as interaction will increase concentrations of concomitant medication.
Pentamidine	Overlapping Toxicities • *Antivirals*: foscarnet	Coadministration should be avoided, if possible. Monitor for toxicities (hypocalcemia, QT prolongation).
	• *ARVs*: didanosine, PIs	Coadministration should be avoided, if possible. Monitor for toxicities (QT prolongation with PIs; pancreatitis for didanosine).
	• *Bone marrow suppressants*	Monitor for toxicities.
	• *Nephrotoxic drugs*	Monitor for toxicities.
	• *QT-prolonging drugs*	Monitor for toxicities. Avoid coadministration, if possible.
	• *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.

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

Drug Name	Toxicities	Recommendation
Posaconazole	Decreased Posaconazole Drug Concentrations • *ARVs*: efavirenz, fosamprenavir, rilpivirine	Coadministration of fosamprenavir should be avoided. Coadministration of efavirenz should be avoided, if possible. If coadministered, monitor posaconazole concentrations and adjust dose accordingly.
	• *Anticonvulsants*: phenytoin	Coadministration should be avoided, if possible. If coadministered, monitor posaconazole concentrations and adjust dose accordingly.
	• *Antimycobacterials*: rifabutin, rifampin	Coadministration should be avoided, if possible. If coadministered, monitor posaconazole concentrations and adjust dose accordingly.
	Increased Concomitant Drug Concentrations • *ARVs*: atazanavir, etravirine, lopinavir, ritonavir, saquinavir	Coadministration should be avoided, if possible. Monitor for toxicities. Consider monitoring concentrations and adjust dose as necessary.
	• *Antibacterials*: clarithromycin, erythromycin	Coadministration should be avoided.
	• *Anticonvulsants*: phenytoin	Coadministration should be avoided.
	• *Sedatives/hypnotics*: alprazolam, diazepam, midazolam	Coadministration should be avoided, if possible. Monitor for toxicities.
	• *Antimycobacterials*: rifabutin	Coadministration should be avoided.
	• *Statins*: atorvastatin, lovastatin, simvastatin • *Antineoplastics*: venetoclax • *Immunosuppressives*: sirolimus, tacrolimus	Do not coadminister with simvastatin or lovastatin. Avoid use of atorvastatin if possible. Alternative statins such as fluvastatin, rosuvastatin, and pravastatin are preferred; alternatively, discontinue statin during antifungal therapy.
	• *Antimalarials*: halofantrine, lumefantrine, mefloquine, quinidine, quinine	Coadministration should be avoided.
	Decreased Concomitant Drug Concentrations • *ARVs*: fosamprenavir	Coadministration should be avoided.
	• *QT-prolonging drugs*	Use with caution. Monitor for toxicities.

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

Drug Name	Toxicities	Recommendation
Proguanil	Decreased Proguanil Concentrations • *ARVs*: Atazanavir/ritonavir, efavirenz, lopinavir/ritonavir	Use with caution.
Pyrazinamide	Overlapping Toxicities • *Antimycobacterials*: ethionamide, rifampin • *Hepatotoxic drugs*	Use with caution. Monitor for hepatotoxicity.
	• *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.
Quinidine	Increased Quinidine Concentrations • *ARVs*: PIs	Coadministration of PIs should be avoided. Increased risk of arrhythmia. Coadministration may be necessary in the presence of life-threatening, severe malaria and in the absence of other therapy, while artesunate is obtained from the CDC.
	• *Antifungals*: itraconazole, posaconazole, voriconazole	Coadministration should be avoided. Increased risk of arrhythmia.
	Decreased Quinidine Concentrations • *ARVs*: etravirine	Use with caution. Monitor quinidine levels.
	Increased Concomitant Drug Concentrations • *Tricyclic antidepressants*	Coadministration should be avoided, if possible. Monitor for toxicities.
	Overlapping Toxicities • *QT-prolonging drugs*	Coadministration should be avoided, if possible. Monitor for toxicities (QT prolongation).
Ribavirin	Increased Concomitant Drug Concentrations • *ARVs*: didanosine	Coadministration should be avoided. Potential for increased risk of pancreatitis and mitochondrial toxicity.
	Decreased Concomitant Drug Concentrations • *ARVs*: stavudine, zidovudine	Coadministration should be avoided, if possible.
	Overlapping Toxicities • *ARVs*: zidovudine, all NRTIs	Coadministration should be avoided, if possible. Monitor for toxicities (anemia for zidovudine, lactic acidosis for all NRTIs).

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

Drug Name	Toxicities	Recommendation
Rifabutin	Increased Rifabutin Concentrations • *ARVs*: cobicistat, PIs	Use with caution. Monitor for rifabutin toxicity. Reduce rifabutin dose if coadministered with PIs.
	• Fluconazole	Use with caution. Monitor for rifabutin toxicity. Consider rifabutin dose reduction.
	• Voriconazole, itraconazole, posaconazole	Coadministration should be avoided, if possible. If coadministered, consider TDM and monitor for rifabutin toxicities (and azole clinical efficacy).
	• *Antibacterials*: clarithromycin	Coadministration should be avoided, if possible. Monitor for rifabutin toxicity. Consider rifabutin dose reduction or using azithromycin instead.
	Increased Concomitant Drug Concentrations • *ARVs*: didanosine	Use with caution. Monitor for didanosine toxicity.
	Decreased Rifabutin Concentrations • *ARVs*: efavirenz, etravirine	Use with caution. Higher rifabutin dose required with efavirenz. Consider TDM.
	Decreased Concomitant Drug Concentrations • *ARVs*: rilpivirine, bictegravir, cabotegravir, dolutegravir, raltegravir, lenacapavir	Coadministration should be avoided.
	• *ARVs*: etravirine, maraviroc, saquinavir	Coadministration should be avoided, if possible.
	• *Antibacterials*: atovaquone, dapsone	Use with caution. Monitor for dapsone treatment failure.
	• *Antifungals*: azoles (except for fluconazole)	Coadministration should be avoided, if possible. If coadministered, consider TDM and monitor for rifabutin toxicities (and azole clinical efficacy).
	• *Contraceptives*: oral	Oral contraceptives less effective. Additional non-hormonal contraceptive or alternative recommended.

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

Drug Name	Toxicities	Recommendation
Rifampin	Decreased Concomitant Drug Concentrations • *Contraceptives*: oral	Oral contraceptives less effective. Additional non-hormonal contraceptive or alternative recommended.
	• *ARVs*: PIs ± ritonavir, nevirapine, bictegravir, cabotegravir, dolutegravir, raltegravir, rilpivirine, maraviroc, cobicistat, zidovudine, lenacapavir	Significantly decreases exposure of ARVs; coadministration should be avoided if possible. Nevirapine: use only if other options are not available and close virologic and immunologic monitoring can be done; consider efavirenz instead. Raltegravir and dolutegravir dose increases may be required.
	• *Antimicrobials*: atovaquone, clarithromycin, dapsone, doxycycline	Coadministration 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.
	• *Antifungals*: azoles, caspofungin	Increase in dose of caspofungin is recommended when coadministered with CYP450 inducers. Monitor azoles for efficacy. May need to increase azole dose.
	• *Other*: corticosteroids, methadone	Caution advised with corticosteroids (decreased efficacy). Monitor for efficacy and/or opiate withdrawal symptoms with methadone.
	Overlapping Toxicities • *Bone marrow suppressants* • *Hepatotoxic drugs*	Monitor for toxicities of these drugs.
Streptomycin	Overlapping Toxicities • *Nephrotoxic drugs* • *Neuromuscular blockers*	Monitor for toxicities of these drugs.
	• *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.

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

Drug Name	Toxicities	Recommendation
Trimethoprim-Sulfamethoxazole (TMP-SMX)	Overlapping Toxicities • *Folate antagonists* • *Bone marrow suppressants*	Monitor for toxicities of these drugs.
	• *Fecal microbiota (live)* (oral/rectal)	Avoid concomitant use.
Valacyclovir	Potential for Increased Concentrations (of Both Drugs) and Overlapping Toxicities • *Antivirals*: acyclovir, cidofovir, ganciclovir, valganciclovir • *ARVs*: tenofovir, zidovudine	Monitor for toxicities of these drugs. Avoid other nephrotoxic drugs.
Valganciclovir	Potential for Increased Concentrations (of Both Drugs) and Overlapping Toxicities • *Antivirals*: acyclovir, cidofovir, ganciclovir, valacyclovir • *ARVs*: tenofovir, zidovudine	Monitor for toxicities of these drugs. Avoid other nephrotoxic drugs.
Voriconazole	Decreased Voriconazole Concentrations • *Anticonvulsants*: carbamazepine, long-acting barbiturates	Caution advised.
	• *Antimycobacterials*: rifabutin, rifampin	Rifabutin and rifampin coadministration should be avoided.
	• *ARVs*: efavirenz, nevirapine, ritonavir-boosted PIs	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.
	Increased Voriconazole Concentrations • *ARVs*: etravirine (etravirine concentrations also increased)	Monitor voriconazole concentrations to reduce toxicity.

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

Drug Name	Toxicities	Recommendation
	Increased Concomitant Drug Concentrations • *Antimycobacterials*: rifabutin	Caution advised.
	• *ARVs*: ritonavir-boosted PIs, efavirenz	Caution advised.
	• *Statins*: atorvastatin, lovastatin, simvastatin	Do not coadminister with simvastatin or lovastatin. Avoid use of atorvastatin if possible. Alternative statins such as fluvastatin, rosuvastatin, and pravastatin are preferred; alternatively, discontinue statin during antifungal therapy.
	• *Sedatives/hypnotics*: alprazolam, midazolam, triazolam	Coadministration should be avoided if possible. Monitor for toxicities.

Key: ART = antiretroviral therapy; ARV = antiretroviral; CDC = Centers for Disease Control and Prevention; CYP450 = cytochrome P450; EKG = electrocardiogram; FDA = U.S. Food and Drug Administration; IV = intravenous; NRTI = nucleoside reverse transcriptase inhibitors; PI = protease inhibitors; QT = interval between Q and T waves; QTc = QT interval corrected for heart rate; TDM = therapeutic drug monitoring