

**APPENDIX A: RECOMMENDATIONS FOR TREATMENT OF OIs IN HIV-EXPOSED AND -INFECTED CARIBBEAN INFANTS AND CHILDREN\***

PATHOGEN	PREFERRED THERAPIES AND DURATION	ALTERNATIVE THERAPIES	OTHER OPTIONS/ISSUES
<p><i>Pneumocystis jiroveci</i> (formerly <i>Pneumocystis carinii</i>) pneumonia (PCP)</p>	<p>TMP-SMX: TMP, 15-20mg/kg body weight <i>plus</i> SMX, 75-100mg/kg body weight, IV or po, divided in 3 or 4 doses per day (after acute pneumonitis resolved in mild-moderate disease, IV TMP-SMX may be changed to po) <b>Treatment Duration (followed by chronic suppressive therapy):</b> 21 days</p>	<p><b>Alternative Therapeutic Regimens (if TMP-SMX intolerant or clinical treatment failure after 5-7 days of TMP-SMX therapy):</b></p> <ul style="list-style-type: none"> <li>• Pentamidine, 4mg/kg body weight IV q.d is first-choice alternative regimen (pentamidine may be changed to atovaquone after 7-10 days IV therapy); or</li> <li>• Atovaquone, 15-20mg/kg body weight (max, 750mg/dose) po b.i.d with food; infants age 3-24 months may require a higher dose of 45mg/kg/day</li> </ul>	<ul style="list-style-type: none"> <li>• Dapsone, 2mg/kg body weight po q.d (max, 100mg/day) <i>plus</i> TMP, 15mg/kg body weight po t.i.d has been used in adults, but data in children are limited</li> <li>• Primaquine base, 0.3mg/kg body weight po q.d (max, 30mg/day) <i>plus</i> clindamycin, 10mg/kg body weight IV or po (max, 600mg IV and 300-450mg po) q6h has been used in adults, but data in children are not available</li> <li>• Indications for corticosteroids: <ul style="list-style-type: none"> <li>→ pO<sub>2</sub> &lt;70mmHg at room air or (A-a)DO<sub>2</sub> &gt;35mmHg</li> <li>→ <i>Prednisone dose:</i> 1mg/kg body weight po b.i.d for 5 days, then 1mg/kg body weight po q.d for 5 days, then 0.5mg/kg body weight po q.d for days 11-21</li> </ul> </li> <li>• Lifelong suppressive therapy (secondary prophylaxis) is recommended in children and adults following initial therapy. Safety of stopping secondary prophylaxis in children with immune reconstitution on HAART has not been studied extensively</li> </ul>
<p><i>Toxoplasma gondii</i></p>	<p><b><u>Congenital Toxoplasmosis:</u></b> Pyrimethamine loading dose: 2mg/kg body weight po q.d for 2 days, then 1mg/kg body weight po q.d for 2-6 months, then 1mg/kg body weight po t.i.w; <i>plus</i> leucovorin (folinic acid), 10mg po or IM with each dose of pyrimethamine; <i>plus</i> sulfadiazine,</p>	<p><b>For Sulfonamide-Intolerant Patients:</b> Clindamycin, 5.0-7.5mg/kg body weight (max, 600mg/dose) po or IV divided into 4 doses per day can be substituted for sulfadiazine <i>plus</i> pyrimethamine and leucovorin</p>	<ul style="list-style-type: none"> <li>• For infants born to mothers with symptomatic <i>Toxoplasma</i> infection during pregnancy, empiric therapy of the newborn should be strongly considered irrespective of the mothers' treatment during pregnancy</li> <li>• Pyrimethamine use requires complete blood count monitoring weekly to monthly</li> <li>• TMP-SMX (TMP, 5mg/kg <i>plus</i> SMX, 25mg/kg IV or po b.i.d) has been used as an alternative to</li> </ul>

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	<p>50mg/kg body weight po b.i.d  <b>Treatment Duration:</b> 12 months</p> <p><b>Acquired Toxoplasmosis:</b>  <b>Acute Induction Therapy (followed by chronic suppressive therapy):</b>  Pyrimethamine: loading dose, 2mg/kg body weight (max, 50mg) po q.d for 3 days, then 1mg/kg body weight (max, 25mg) po q.d; <i>plus</i> sulfadiazine, 25-50mg/kg body weight (max, 1-1.5gm/dose) po 4x q.d; <i>plus</i> leucovorin, 10-25mg po q.d, followed by chronic suppressive therapy  <b>Treatment Duration (followed by chronic suppressive therapy):</b> at least 6 weeks</p>		<p>pyrimethamine-sulfadiazine in adults, but has not been studied in children</p> <ul style="list-style-type: none"> <li>• Atovaquone (1.5gm po b.i.d) in regimens with pyrimethamine/leucovorin, with sulfadiazine alone, or as a single agent in patients intolerant to both pyrimethamine and sulfadiazine, has been used in adults, but these regimens have not been studied in children</li> <li>• Azithromycin (900-1,200mg/day) has also been used in adults combined with pyrimethamine-sulfadiazine, but has not been studied in children</li> <li>• Corticosteroids (e.g. prednisone or dexamethasone) have been used in children with CNS disease when CSF protein is very elevated (&gt;1,000mg/dL) or if there are focal lesions with significant mass effects, with discontinuation as soon as clinically feasible</li> <li>• Lifelong suppressive therapy (secondary prophylaxis) is recommended in children following initial induction therapy. Safety of stopping secondary prophylaxis in children with immune reconstitution on HAART has not been studied extensively</li> </ul>
Cryptosporidiosis	<p><b>Effective HAART:</b> Immune reconstitution may lead to microbiologic and clinical response</p>	<p>There is no consistently effective therapy for cryptosporidiosis in HIV-infected individuals; several agents have demonstrated some efficacy in decreasing the severity of symptoms in children:</p> <ul style="list-style-type: none"> <li>• Nitazoxanide (data from immunocompetent children, treatment period, 3 days)  <i>Age 1-3 years:</i> 100mg po b.i.d</li> </ul>	<p><b>Supportive Care:</b> Hydration, correct electrolyte abnormalities, nutritional support</p>

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		<p><u>Age 4-11 years:</u> 200mg po b.i.d; or</p> <ul style="list-style-type: none"> <li>• Paromomycin, 25-35mg/kg body weight in 2 to 4 divided doses po daily (max, 2gm q.d); or</li> <li>• Azithromycin, 10mg/kg body weight po on day 1, then 5mg/kg body weight po q.d (max, 600mg q.d)</li> </ul> <p><b>Treatment Duration:</b> Unknown</p>	
Microsporidiosis	<p><b>Effective HAART:</b> Immune reconstitution may lead to microbiologic and clinical response</p> <ul style="list-style-type: none"> <li>• Albendazole, 7.5mg/kg body weight (max, 400mg/dose) po b.i.d for intestinal or disseminated infection by <i>Microsporidia</i> other than <i>E. bienuesi</i></li> </ul> <p><b>Treatment Duration:</b> Unknown</p>		<ul style="list-style-type: none"> <li>• <b>Supportive Care:</b> Hydration, correct electrolyte abnormalities, nutritional support</li> <li>• Fumagillin recommended for treatment of diarrhoeal and ocular infections due to <i>E. bienuesi</i> in HIV-infected adults</li> </ul>
<i>Mycobacterium tuberculosis</i> (TB)	<p><b>Induction Phase (8 weeks):</b> Isoniazid (INH), 10-15mg/kg body weight (max, 300mg/day) po q.d; <i>plus</i> Rifampin (RIF), 10-20mg/kg body weight (max, 600mg/day) po q.d; <i>plus</i> Pyrazinamide (PZA), 20-40mg/kg (max, 2gm/day) body weight po q.d; <i>plus</i> Ethambutol (EMB), 15-25mg/kg body weight (max, 2.5gm/day) po q.d</p>	<ul style="list-style-type: none"> <li>• Alternative drug for RIF is rifabutin, 10-20mg/kg body weight (max, 300mg/day) po q.d (same dose is given for intermittent two or three times weekly regimen)</li> <li>• Alternative drug for EMB is streptomycin, 20-40mg/kg body weight (max, 1gm/day) IM q.d (or 20mg/kg given as intermittent b.i.w. or t.i.w. regimen)</li> <li>• Ethionamide, 15-20mg/kg body weight po (max, 1gm/day) divided into 2 or 3 doses/day should be used</li> </ul>	<ul style="list-style-type: none"> <li>• DOT should be standard of care for children with TB</li> <li>• Potential drug interactions, especially with HAART medications, must be carefully reviewed (see text)</li> <li>• In ARV-naïve child, initiate therapy for TB 4-8 weeks prior to starting HAART; for children already receiving HAART who are diagnosed with TB, the child's HAART regimen should be reviewed and altered, if needed, to ensure optimal treatment for both TB and HIV and to minimise potential toxicities and drug-drug interactions</li> <li>• For children with severe immunosuppression,</li> </ul>

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	<p><b>Continuation Phase (for drug-sensitive TB):</b></p> <p><u>Daily:</u></p> <ul style="list-style-type: none"> <li>• INH, 10-15mg/kg body weight (max, 300mg/day) po q.d; <i>plus</i></li> <li>• RIF, 10-20mg/kg body weight (max, 600mg/day) po q.d</li> </ul> <p><b>OR</b></p> <p><u>Intermittent:</u></p> <ul style="list-style-type: none"> <li>• INH, 20-30mg/kg body weight (max, 900mg/day) po q.d given b.i.w or t.i.w; <i>plus</i></li> <li>• RIF, 10-20mg/kg body weight (max, 600mg/day) po q.d given b.i.w or t.i.w</li> </ul> <p><b>Treatment Duration (drug-sensitive TB):</b></p> <ul style="list-style-type: none"> <li>• <b>Pulmonary TB:</b> 9 months for HIV-infected child (6 months if not HIV-infected)</li> <li>• <b>Extrapulmonary TB:</b> 12 months</li> </ul>	<p>for TB meningitis</p> <p><b>Drug Resistant TB:</b></p> <p><u>Resistance to INH Alone:</u></p> <ul style="list-style-type: none"> <li>• Discontinue INH</li> <li>• RIF <i>plus</i> PZA <i>plus</i> EMB (ethionamide or streptomycin can be substituted for EMB if <i>M. tb</i> isolate is sensitive to these agents)</li> </ul> <p><u>Resistance to RIF Alone:</u></p> <ul style="list-style-type: none"> <li>• Discontinue RIF</li> <li>• INH <i>plus</i> PZA <i>plus</i> EMB <i>plus</i> streptomycin for first 2 months, followed by continuation phase of INH <i>plus</i> PZA <i>plus</i> EMB to complete 12-month course</li> </ul> <p><u>Multi-Drug Resistance (MDR-TB):</u></p> <ul style="list-style-type: none"> <li>• Therapy should be based on resistance pattern, and children should be managed in consultation with an expert consultant</li> </ul> <p><b>Treatment Duration (Drug Resistant TB):</b></p> <ul style="list-style-type: none"> <li>• <u>Single-drug INH or RIF resistant TB:</u> 12 months</li> <li>• <u>MDR-TB:</u> 12-24 months</li> </ul>	<p>continuation phase for drug-sensitive TB disease should include either q.d or t.i.w treatment; b.i.w regimens should <i>not</i> be used because they may lead to rifamycin resistance in immunosuppressed patients</p> <ul style="list-style-type: none"> <li>• Pyridoxine should be given if INH is administered</li> <li>• Adjunctive treatment with corticosteroids is indicated for children with CNS disease and may be considered for children with pleural or pericardial effusions, severe miliary disease, significant endobronchial disease, or severe IRS (see text)</li> <li>• Children receiving EMB who are old enough to undergo routine eye testing should have monthly monitoring of visual acuity and colour discrimination if available</li> <li>• Thiacetazone can cause severe or fatal reactions in HIV-infected children including rash and aplastic anaemia and should not be used</li> <li>• For drug resistant strains, at least 2 drugs to which the isolate is susceptible should be given (minimum of 3 drugs should be given through the continuation phase of therapy)</li> </ul> <p><b>For MDR-TB, Second-Line Drugs Include:</b></p> <ul style="list-style-type: none"> <li>• Amikacin, 15-30mg/kg body weight (max, 1gm/day) IM q.d</li> <li>• Ciprofloxacin, 10-15mg/kg body weight po b.i.d (max, 1.5gm/day); levofloxacin, 500-1,000mg po q.d; or moxifloxacin, 400mg po q.d (fluoroquinolones are not labelled for use in children &lt;age 18 years due to concerns regarding potential effects on cartilage; use in younger persons requires an assessment of potential risks and benefits)</li> </ul>

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<p><i>Mycobacterium avium</i> Complex (MAC)</p>	<p><b>Initial Treatment (at least 2 drugs):</b></p> <ul style="list-style-type: none"> <li>• Clarithromycin, 7.5-15mg/kg body weight (max, 500mg/dose) po b.i.d; <i>plus</i></li> <li>• EMB, 15-25mg/kg body weight (max, 2.5gm/day) po q.d;</li> <li>• followed by chronic suppressive therapy</li> </ul> <p><b><u>For Severe Disease, Add:</u></b></p> <ul style="list-style-type: none"> <li>• Rifabutin, 10-20mg/kg body weight (max, 300mg/day) po q.d</li> </ul>	<p>Azithromycin, 10-12mg/kg body weight (max, 500mg/day) po q.d if intolerant to clarithromycin</p> <p><b><i>If Rifabutin Cannot Be Administered (or if a fourth drug is needed for patients with more severe symptoms or disseminated disease):</i></b></p> <ul style="list-style-type: none"> <li>• Ciprofloxacin, 20-30mg/kg body weight (max, 1.5gm/day) IV or po q.d); <b>OR</b></li> <li>• levofloxacin, 500mg po q.d; <b>OR</b></li> <li>• amikacin, 15-30mg/kg body weight IV in 1 or 2 divided doses per day (max, 1.5gm/day)</li> </ul>	<ul style="list-style-type: none"> <li>• Combination therapy with a minimum of 2 drugs is recommended</li> <li>• Children receiving EMB who are old enough to undergo routine eye testing should have monthly monitoring of visual acuity and colour discrimination if available</li> <li>• Fluoroquinolones (e.g. ciprofloxacin, levofloxacin) are not labelled for use in children &lt;age 18 years due to concerns regarding potential effects on cartilage; use in younger persons requires an assessment of potential risks and benefits</li> <li>• Lifelong suppressive therapy (secondary prophylaxis) is recommended in children and adults following initial therapy. Safety of stopping secondary prophylaxis in children with immune reconstitution on HAART has not been studied extensively</li> <li>• If rifabutin is used, potential drug interactions, especially with HAART medications, must be carefully reviewed (see text)</li> </ul>
<p>Syphilis</p>	<p><b><u>Congenital:</u></b> <b><i>Proven or Highly Probable Disease:</i></b></p> <ul style="list-style-type: none"> <li>• Aqueous crystalline penicillin G, 100,000-150,000U/kg body weight per day, administered as 50,000U/kg body weight IV q12h for the first 7 days of life then q8h for a total of 10 days</li> <li>• If diagnosed after age 1 month, aqueous penicillin G, 200,000-</li> </ul>	<p><b><u>Congenital:</u></b> <b><i>Alternative for Proven or Highly Probable Disease (less desirable if CNS involvement):</i></b></p> <p>Procaine penicillin G, 50,000U/kg body weight IM q.d for 10 days</p> <p><b><i>Infants with Possible Congenital Syphilis (maternal treatment and response adequate, normal physical examination, normal CSF studies, but serum quantitative nontreponemal serologic titre that is the same or 4-fold</i></b></p>	<ul style="list-style-type: none"> <li>• For treatment of congenital syphilis, repeat entire course of treatment if even 1 day of treatment is missed</li> <li>• Children with congenital syphilis should be evaluated at age 1, 2, 3, 6, and 12 months, and have nontreponemal testing at 3, 6, and 12 months after conclusion of therapy or until test becomes negative. Children with increasing titres or persistently positive titres (even if low levels) at age 6-12 months should be evaluated and considered for retreatment</li> <li>• Children and adolescents with acquired syphilis</li> </ul>

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	<p>300,000U/kg body weight IV q6h (max, 18-24MU/day) for 10 days</p> <p><b>Acquired:</b></p> <p><b>Early Stage (primary, secondary, early latent):</b></p> <p>Benzathine penicillin, 50,000U/kg body weight (max, 2.4MU) IM for 1 dose</p> <p><b>Late Latent:</b></p> <p>Benzathine penicillin, 50,000U/kg body weight (max, 2.4MU) IM q.w for 3 doses</p> <p><b>Neurosyphilis (including ocular):</b></p> <p>Aqueous penicillin G, 200,000-300,000u/kg body weight IV q6h (max, 18-24MU/day) for 10-14 days</p>	<p><b>higher than maternal titre):</b></p> <p>Benzathine penicillin G, 50,000U/kg body weight IM in a single dose (max, 2.4MU)</p>	<p>should have clinical and serologic response monitored at 3, 6, 9, 12, and 24 months after therapy</p>
<p><i>Candida</i></p>	<p><b>Oropharyngeal:</b></p> <ul style="list-style-type: none"> <li>• Fluconazole, 3-6mg/kg body weight (max, 400mg/dose) po q.d for 7-14 days; <b>OR</b></li> <li>• Itraconazole cyclodextrin oral solution, 2.5mg/kg body weight po b.i.d (max, 200mg/day) for 7-14 days; <b>OR</b></li> <li>• Clotrimazole troches: 10mg troche po 4x q.d for 14 days; <b>OR</b></li> <li>• Nystatin suspension: 4-6mL po 4x q.d <b>OR</b> 1 to 2 200,000U flavoured pastilles po q4-5d for</li> </ul>	<p><b>Oropharyngeal (fluconazole-refractory):</b></p> <ul style="list-style-type: none"> <li>• Itraconazole cyclodextrin oral solution, 2.5mg/kg body weight po b.i.d (max, 200-400mg/day) for 7-14 days; <b>OR</b></li> <li>• Amphotericin B oral suspension, 1mL (100mg/mL) po 4x q.d for 14 days</li> </ul>	<ul style="list-style-type: none"> <li>• Itraconazole cyclodextrin oral solution should not be used interchangeably with itraconazole capsules. Itraconazole capsules are generally ineffective for treatment of oesophageal disease</li> <li>• Central venous catheters should be removed when feasible in HIV-infected children with fungaemia</li> <li>• Fluconazole should not be used for the empiric treatment of fungaemia because resistance of non-<i>albicans Candida</i> species to fluconazole has been reported <ul style="list-style-type: none"> <li>→ In uncomplicated catheter-associated <i>C. albicans</i> candidaemia, an initial course of amphotericin B followed by fluconazole to complete treatment may be used</li> </ul> </li> </ul>

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	<p>7-14 days</p> <p><b><u>Oesophageal Disease:</u></b></p> <ul style="list-style-type: none"> <li>Fluconazole, 6mg/kg body weight po q.d on day 1, then 3-6mg/kg body weight (max, 400mg/dose) po q.d for minimum of 14-21 days; <b>OR</b></li> <li>Itraconazole cyclodextrin oral solution, 2.5mg/kg body weight po b.i.d or 5.0mg/kg body weight po q.d for minimum of 14-21 days</li> </ul> <p><b><u>Invasive Disease:</u></b></p> <p>Amphotericin B, 0.5-1.5mg/kg body weight IV q.d</p> <p><b><i>Treatment Duration:</i></b> Based on presence of deep tissue foci and clinical response in patients with candidaemia, treat until 2-3 weeks after last positive blood culture</p>	<p><b><u>Oesophageal Disease:</u></b></p> <p>Amphotericin B, 0.3-0.5mg/kg body weight IV q.d for a minimum of 7 days</p> <p><b><u>Invasive Disease:</u></b></p> <ul style="list-style-type: none"> <li>Fluconazole, 5-6mg/kg body weight IV or po b.i.d (max, 800mg/day) for minimum 4 weeks (if uncomplicated <i>C. albicans</i> candidaemia)</li> <li>Lipid formulations of amphotericin B: <ul style="list-style-type: none"> <li>→ <i>Lipid Complex</i> (Abelcet®), 5mg/kg body weight IV q.d for at least 2-4 weeks</li> <li>→ <i>Liposomal</i> (AmBisome®), 3-5mg/kg body weight IV q.d for at least 2-4 weeks</li> </ul> </li> <li>Amphotericin B (as per preferred therapy dose) <i>plus</i> flucytosine, 100-150mg/kg body weight po divided into 4 doses for severe invasive disease, especially involving CNS</li> </ul>	<ul style="list-style-type: none"> <li>Amphotericin B initiation doses: <ul style="list-style-type: none"> <li>→ <i>Mild to moderate disease:</i> Initiate at doses of 0.25-0.5mg/kg body weight IV q.d, then increase as tolerated to 0.5-1.5mg/kg body weight IV q.d</li> <li>→ <i>Severe disease:</i> Initiate treatment at target daily dose</li> </ul> </li> <li>Following stabilisation and resolution of fever on daily therapy in children with invasive disease, amphotericin B may be given as 1.5mg/kg body weight IV q.o.d</li> <li>Lipid formulation of amphotericin B may be used in patients with renal insufficiency or infusion-related toxicity to amphotericin B</li> <li>Caspofungin has been used to treat oesophageal and invasive candidiasis in adults but data in children are limited and a definitive paediatric dose has not been defined</li> <li>Flucytosine dose should be adjusted to keep drug levels 40-60µg/mL</li> </ul>

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<p><i>Cryptococcus neoformans</i></p>	<p><b><u>Mild, Isolated Pulmonary Disease:</u></b> Fluconazole, 3-6mg/kg body weight po q.d followed by chronic suppressive therapy</p> <p><b><u>Severe, Isolated Pulmonary Disease:</u></b> Amphotericin B, 0.7-1.5mg/kg body weight IV q.d (usually with an initial 2 weeks of flucytosine) until stable followed by chronic suppressive therapy with fluconazole or itraconazole</p> <p><b><u>Meningeal and Extrameningeal Disseminated Disease:</u></b> <i>Acute Therapy (minimum 2-week induction followed by consolidation therapy):</i> Amphotericin B, 0.7-1.5mg/kg body weight IV q.d <i>plus</i> flucytosine, 25mg/kg body weight po given 4x q.d <i>Consolidation Therapy (followed by chronic suppressive therapy):</i> Fluconazole, 5-6mg/kg body weight IV or po b.i.d (max, 800mg/day) for a minimum of 8 weeks or until CSF cultures are sterile</p>	<p><b><u>Mild, Isolated Pulmonary Disease:</u></b> Itraconazole, 2-5mg/kg body weight po q.d or b.i.d (max, 400mg/day), followed by chronic suppressive therapy</p> <p><b><u>Meningeal and Extrameningeal Disseminated Disease:</u></b> <i>Acute Therapy (minimum 2-week induction followed by consolidation therapy):</i> Amphotericin B, 0.7-1.5mg/kg body weight IV q.d alone</p> <ul style="list-style-type: none"> <li>Liposomal amphotericin B (AmBisome®), 3-5mg/kg body weight IV q.d (with or without an initial 2 weeks of flucytosine) in children with renal insufficiency or infusion-related toxicity to amphotericin B</li> </ul> <p><i>Consolidation Therapy (followed by chronic suppressive therapy):</i> Itraconazole, 2-5mg/kg body weight (max, 200mg/dose) IV or po b.i.d for a minimum of 8 weeks or until CSF cultures are sterile</p>	<ul style="list-style-type: none"> <li>Flucytosine dose should be adjusted to keep drug levels 40-60µg/mL</li> <li>An alternative for treatment of cryptococcal meningitis is fluconazole, 5-6mg/kg body weight IV or po b.i.d (max, 800mg/day) <i>plus</i> flucytosine, 25mg/kg body weight po given 4x q.d, but there is little data in children and toxicity of this regimen limits its utility</li> <li>In cases of refractory cryptococcal meningitis with failure of systemic therapy, intrathecal or intraventricular amphotericin B has been used</li> <li>Oral acetazolamide should not be used for reduction of elevated intracranial pressure in cryptococcal meningitis</li> <li>CSF cryptococcal antigen titres &gt;1:8 suggest failure or relapse</li> <li>Lifelong suppressive therapy (secondary prophylaxis) with fluconazole is recommended in children and adults following initial therapy. Safety of stopping secondary prophylaxis in children with immune reconstitution on HAART has not been studied extensively</li> </ul>

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<i>Histoplasma capsulatum</i>	<p><b><u>Mild Disseminated Disease:</u></b> Intraconazole, 4-10mg/kg body weight IV or capsules po b.i.d for 3 days (max, 600mg/day), followed by 2-5mg/kg body weight (max, 200mg/dose) po b.i.d for at least 12-16 weeks followed by chronic suppressive therapy</p> <p><b><u>Severe Disseminated Disease:</u></b> <i>Acute Therapy (minimum 2-3 weeks induction until improved, followed by consolidation therapy; meningitis should be treated with 12-16 weeks of amphotericin):</i> Amphotericin B, 1mg/kg body weight IV q.d until stable (a minimum 2-3 weeks) <i>Consolidation Therapy (followed by chronic suppressive therapy):</i> Itraconazole capsules, 2-5mg/kg body weight (max, 200mg/dose) po b.i.d given for 3-6 months</p>	<p><b><u>Mild Disseminated Disease:</u></b> Fluconazole, 5-6 mg/kg body weight IV or po b.i.d (max, 800mg/day) for at least 12-16 weeks followed by chronic suppressive therapy</p> <p><b><u>Severe Disseminated Disease:</u></b> <i>Acute Therapy (minimum 2-3 weeks induction until improved, followed by consolidation therapy; meningitis should be treated with 12-16 weeks of amphotericin):</i> Liposomal amphotericin B (AmBisome®), 3-5mg/kg body weight IV q.d in children with renal insufficiency or infusion-related toxicity to amphotericin B</p>	<p>Lifelong suppressive therapy (secondary prophylaxis) with itraconazole is recommended in children and adults following initial therapy. Safety of stopping secondary prophylaxis in children with immune reconstitution on HAART has not been studied extensively</p>
<i>Coccidioides immitis</i>	<p><b><u>Diffuse Pulmonary or Disseminated Non-Meningitic Disease:</u></b> Amphotericin B, 0.5-1.0mg/kg body weight IV q.d until clinical improvement (minimum of several weeks), followed by chronic suppressive therapy with fluconazole or itraconazole</p> <p><b><u>Meningeal Infection:</u></b></p>	<p><b><u>Diffuse Pulmonary or Disseminated Non-Meningitic Disease (in stable patient):</u></b></p> <ul style="list-style-type: none"> <li>• Fluconazole, 5-6mg/kg body weight IV or po b.i.d (max, 800mg/day), followed by chronic suppressive therapy</li> <li>• Itraconazole, 4-10mg/kg body weight IV or po b.i.d for 3 days, followed by 2-5mg/kg body weight po b.i.d (max,</li> </ul>	<ul style="list-style-type: none"> <li>• Surgical debridement of bone and lung lesions may be helpful</li> <li>• Lifelong suppressive therapy (secondary prophylaxis) with fluconazole or itraconazole is recommended in children and adults following initial induction therapy. Safety of stopping secondary prophylaxis in children with immune reconstitution on HAART has not been studied extensively</li> </ul>

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	<p>Fluconazole, 5-6mg/kg body weight IV or po b.i.d (max, 800mg/day), followed by chronic suppressive therapy</p>	<p>400mg/day), followed by chronic suppressive therapy</p> <p><b><u>Meningeal Infection (unresponsive to fluconazole):</u></b></p> <p>Amphotericin B <i>plus</i> intrathecal amphotericin B, followed by chronic suppressive therapy</p>	
<p>Cytomegalovirus (CMV)</p>	<p><b><u>Symptomatic Congenital Infection:</u></b></p> <p>Ganciclovir, 6mg/kg body weight IV q12h for 6 weeks</p> <p><b><u>Disseminated Disease and Retinitis:</u></b></p> <p><b><i>Induction Therapy (followed by chronic suppressive therapy):</i></b></p> <p>Ganciclovir, 5mg/kg body weight IV q12h for 14-21 days (may be increased to 7.5mg/kg body weight IV b.i.d), then 5mg/kg per day for 5 to 7 days per week for chronic suppression</p>	<p><b><u>Disseminated Disease and Retinitis:</u></b></p> <p><b><i>Induction Therapy (followed by chronic suppressive therapy):</i></b></p> <p>Foscarnet, 60mg/kg body weight IV q8h for 14-21 days, then 90-120mg/kg q.d for chronic suppression</p> <p><b><i>Alternative for Retinitis (followed by chronic suppressive therapy):</i></b></p> <ul style="list-style-type: none"> <li>• IV ganciclovir <i>plus</i> IV foscarnet (at above induction doses) – may be considered as initial induction therapy in children with sight-threatening disease</li> <li>• <b><i>Older Children:</i></b> Ganciclovir intraocular implant <i>plus</i> oral ganciclovir, 30mg/kg t.i.d or if old enough to receive adult dosing, oral valganciclovir, 900mg po q.d</li> </ul>	<ul style="list-style-type: none"> <li>• Valganciclovir is used in adults for treatment of CMV retinitis: induction dosing in adults is 900mg po b.i.d for 14-21 days, followed by chronic suppressive therapy; however, data on valganciclovir dosing in children is unavailable</li> <li>• Cidofovir is also used for treatment of CMV retinitis in adults: induction dosing in adults is 5mg/kg body weight IV q.w for 2 weeks, followed by chronic suppressive therapy; however, data on dosing in children is unavailable</li> <li>• Intravitreal injections not practical for most children</li> <li>• Intraocular implant should not be used in children &lt;age 3 years due to small size of eyes</li> <li>• Lifelong suppressive therapy (secondary prophylaxis) is recommended in children and adults following initial induction therapy. Safety of stopping secondary prophylaxis in children with immune reconstitution on HAART has not been studied extensively</li> </ul>

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Herpes Simplex Virus (HSV)	<p><b><u>Neonatal CNS or Disseminated Disease:</u></b> Acyclovir, 20mg/kg body weight IV t.i.d for 21 days</p> <p><b><u>Neonatal Skin, Eye, or Mouth Disease:</u></b> Acyclovir, 20mg/kg body weight IV t.i.d for 14 days</p> <p><b><u>CNS or Disseminated Disease in Children Outside the Neonatal Period:</u></b> Acyclovir, 10mg/kg body weight IV t.i.d for 21 days</p> <p><b><u>Moderate to Severe Symptomatic Gingivostomatitis:</u></b> Acyclovir, 5-10mg/kg body weight IV t.i.d for 7-14 days</p> <p><b><u>Genital Herpes (Adults and Adolescents):</u></b> Acyclovir, 20mg/kg body weight (max, 400mg/dose) po t.i.d for 7-10 days.</p>	<p><b><u>Acyclovir-Resistant HSV Infection:</u></b> Foscarnet, 40mg/kg body weight given IV t.i.d or 60mg/kg body weight given IV b.i.d</p> <p><b><u>Mild Symptomatic Gingivostomatitis:</u></b> Acyclovir, 20mg/kg body weight (max, 400mg/dose) po t.i.d for 7-14 days</p>	<ul style="list-style-type: none"> <li>• <i>For neonatal CNS disease:</i> Repeat CSF HSV DNA PCR should be performed at day 19-21 of therapy; do not stop acyclovir until repeat CSF HSV DNA PCR is negative</li> <li>• Suppressive secondary prophylaxis with oral acyclovir can be considered for children with severe and recurrent gingivostomatitis</li> </ul>
Varicella Zoster Virus (VZV)	<p><b><u>Primary Varicella (Chickenpox):</u></b> <i>Children with Moderate or Severe Immune Suppression, High Fever, or Necrotic Lesions:</i> Acyclovir, 10mg/kg body weight IV t.i.d for 7 days after no new lesions</p> <p><i>Children with Mild Immune Suppression and Mild Disease:</i></p>	<p><b><i>For Patients Not Responding to Acyclovir:</i></b> Foscarnet, 40-60mg/kg body weight IV t.i.d for 7-10 days</p>	<p>Some experts base IV acyclovir dosing in children <math>\geq</math> age 1 year on body surface area (500mg/m<sup>2</sup>/dose IV q8h) instead of body weight</p>

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	<p>Acyclovir, 20mg/kg body weight po (max, 200mg/dose) 4x q.d, continued for 7 days after no new lesions</p> <p><b><u>Zoster:</u></b></p> <p><i>Children with Severe Immune Suppression, Trigeminal Nerve Involvement, or Extensive Multi-Dermatomal Zoster:</i></p> <p>Acyclovir, 10mg/kg body weight IV t.i.d for 7-10 days</p> <p><i>Children with Mild Immune Suppression and Mild Disease:</i></p> <p>Acyclovir, 20mg/kg body weight po (max, 200mg/dose) 4x q.d for 7-10 days</p>		
Human Papillomavirus (HPV)	Individual lesions can be removed by cryotherapy or electrodesiccation; may be repeated q.w to b.i.w up to 4 times	<ul style="list-style-type: none"> <li>• Podofilox solution/gel (0.5%) applied topically b.i.d for 3 consecutive days a week for up to 4 weeks</li> <li>• Imiquimod cream (5%) applied topically at night and washed off in the morning for 3 nonconsecutive days a week for up to 16 weeks</li> <li>• Trichloroacetic acid applied topically q.w for up to 3-6 weeks</li> <li>• Podophyllin resin applied topically and washed off several hours later q.w for 3-6 weeks</li> </ul>	<ul style="list-style-type: none"> <li>• Standard topical therapy in children is often ineffective</li> <li>• Cidofovir topical gel (1%) is an experimental therapy studied in HIV-infected adults, but is not commercially available and has very limited use in children; systemic absorption can occur</li> <li>• HAART has not been consistently associated with reduced risk of HPV-related cervical abnormalities in HIV-infected women</li> <li>• Laryngeal papillomatosis generally requires referral to a paediatric otolaryngologist. Treatment is directed at maintaining the airway, rather than removal of all disease. Adjuvant therapy with interferon-alfa or intralesional cidofovir is being used investigationally for invasive disease</li> </ul>

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Hepatitis B Virus (HBV)	<p><b><i>For Children Who Require HIV Therapy:</i></b>            3TC, 4mg/kg body weight po (max, 150mg/dose) b.i.d as part of a fully suppressive HAART regimen for a minimum of 12 months or 6 months after HBeAg seroconversion</p> <p><b><i>For Children Who Do Not Require HIV Therapy:</i></b></p> <ul style="list-style-type: none"> <li>• Interferon-alfa, 5MU/m<sup>2</sup> body surface area subcoetaneously (max, 10MU/dose) t.i.w</li> <li>• If HBeAg-positive, recommended duration of interferon-alfa therapy is 6 months; if HBeAg-negative, a duration of 12 months or longer may be desirable</li> </ul>	Interferon-alfa, 10MU/m <sup>2</sup> body surface area subcoetaneously t.i.w for 6 months (sometimes used for retreatment of failed lower dose interferon therapy)	<ul style="list-style-type: none"> <li>• Indications for treatment include:               <ul style="list-style-type: none"> <li>→ Detectable serum HBV DNA, with or without +HBeAg, for at least 6 months;</li> <li>→ Persistent elevation of serum transaminases (at least 2x the upper limit of normal); and</li> <li>→ Evidence of chronic hepatitis on liver biopsy</li> </ul> </li> <li>• Interferon-alfa is contra-indicated in children with decompensated liver disease, significant cytopaenias, severe renal or cardiac disorders, and auto-immune disease</li> <li>• Prednisone co-administration not recommended</li> <li>• Interferon-beta 5MU/m<sup>2</sup> body surface area IM t.i.w for 6 months for children who have not responded to interferon-alpha</li> <li>• In children receiving 3TC and responding to therapy, clinical and laboratory exacerbations of hepatitis may occur if 3TC is discontinued; thus, once anti-HBV/HIV therapy has begun, it should be continued unless contra-indicated or until the child has been treated for &gt;6 months after HBeAg seroconversion and can be closely monitored on discontinuation</li> </ul>

*\*Note: Information contained in these guidelines might not represent U.S. Food and Drug Administration (FDA) approval or approved labelling for products or indications. Specifically, the terms ‘safe’ and ‘effective’ might not be synonymous with the FDA-defined legal standards for product approval. Letters and Roman numerals in parentheses after regimens indicate the strength of the recommendations and the quality of evidence supporting it.*