

# HIV CareLink

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Primary Care Providers

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## Pediatric Guidelines for Use of Antiretroviral Agents Updated February 28, 2008

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The Department of Health and Human Services (DHHS) released an update of the Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection on February 28, 2008. This edition of HIV CareLink summarizes some of the major changes to the Guidelines. The clinician is encouraged to consult the full set of Guidelines online at <http://aidsinfo.nih.gov/contentfiles/PediatricGuidelines.pdf>.

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### ABOUT US

The Florida/Caribbean AIDS Education and Training Center provides HIV education, consultation, and resource materials to health care providers in Florida, Puerto Rico and the US Virgin Islands.

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### HIV Testing in Infants

- Infants < 18 months old require direct virologic assays (HIV DNA PCR or HIV RNA) to diagnose HIV, since antibody assays cannot be used due to the persistence of maternal HIV antibody.
- Virologic diagnostic testing in infants with known perinatal HIV exposure is recommended at age 14–21 days; 1–2 months; and 4–6 months. Some experts also perform virologic testing at birth since as many as 30–40% of infants with HIV infection can be identified by 48 hours of age.
- HIV infection can be presumptively excluded in non-breastfed infants with  $\geq 2$  negative virologic tests, with one test at  $\geq 14$  days and one at  $\geq 1$  month of age; or one negative virologic test result obtained at  $\geq 2$  months of age; or one negative HIV antibody test obtained at  $\geq 6$  months of age.
- Definitive exclusion of HIV infection in a non-breastfed infant is based on  $\geq 2$  negative virologic tests, with one at age  $\geq 1$  month and one at  $\geq 4$  months, or two negative HIV antibody tests from separate specimens at age  $\geq 6$  months.

- For both presumptive and definitive exclusion of HIV infection, the child should have no other laboratory or clinical evidence of HIV infection.

### Specific Situations

- If suspected of a non-subtype B perinatal exposure, HIV DNA PCR may be falsely negative and repeat testing using one of the newer RNA assays, shown to be more sensitive in the detection of non-subtype B HIV, is recommended.
- Consult with a pediatric HIV expert when HIV DNA PCR and RNA assays are negative in those whom non-subtype B infection is suspected, continue to closely monitor clinically, and perform definitive HIV serologic testing at age 18 months.
- An antibody test at age 12–18 months can be used to document seroreversion to HIV antibody negative status.
- In children  $\geq 18$  months of age, HIV antibody assays can be used for diagnosis.
- Diagnosis of HIV infection can be made by the use of virologic assays in most non-breastfed HIV-infected infants by age 1 month and in virtually all infected infants by age 4 months.

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- A positive virologic test (i.e., detection of HIV by culture or DNA polymerase chain reaction [PCR] or RNA assays) indicates likely HIV infection and should be confirmed by a repeat virologic test on a second specimen as soon as possible.

## Antibiotic Prophylaxis Against PCP

- Antibiotic prophylaxis against PCP is recommended for infants with indeterminate HIV infection status starting at 4–6 weeks of age until they are determined to be HIV-uninfected or presumptively uninfected with HIV.
- Initiation of PCP prophylaxis can be avoided if the infant has negative virologic tests at 2 weeks and at 1 month of age or, if prophylaxis was initiated, can be stopped if virologic testing is negative at or beyond 2 months of age.

## Monitoring HIV-Infected Children and Initiation of Therapy (See Table 1)

- In HIV-infected children < 5 years of age, CD4 percentage is preferred for monitoring immune status, absolute CD4 count can be used in older children.
- CD4 count and percentage declines as HIV infection progresses and patients with lower CD4 values have a poorer prognosis than patients with higher values.
- CD4 values should be obtained as soon as possible after a child has a positive test for HIV and every 3–4 months thereafter.
- HIV-infected children ≥ 5 years of age have an ↑ in risk of mortality when CD4 cell count fell to < 350 cells/mm<sup>3</sup>.
- Virologic suppression may take longer in young children given their higher viral load at the time of initiation of therapy.
- Plasma HIV RNA should be measured at diagnosis and every 3–4 months thereafter.
- Because the risk of disease progression slows in children age ≥ 1 year, the option of deferring treatment can be considered for certain children meeting specific CD4 and plasma HIV RNA criteria.
- Several studies have shown that older children with HIV RNA levels of ≥ 100,000 copies/mL are at higher risk of mortality.
- When therapy is deferred, the health care provider should closely monitor virologic, immunologic, and clinical status.
- Adherence must be assessed and discussed, with frequent follow-up even if this delays starting treatment.
- Zidovudine chemoprophylaxis should be discontinued in infants identified as HIV-infected and combination therapy with ≥ 3 drugs should be initiated (with drug choice based on results from antiretroviral drug resistance testing).

**Table 1**

(Adapted from Table 6: Indications for Initiation of Antiretroviral Therapy in Children infected with Human Immunodeficiency Virus (HIV), February 28, 2008)

Age	Criteria	Recommendation
< 12 months	Regardless of clinical symptoms, immune status, or viral load	Treat
Any age	AIDS or significant HIV-related symptoms	Treat
1- < 5 years	CD4 <25%, regardless of symptoms or HIV RNA	Treat
1- < 5 years	Asymptomatic or mild symptoms <i>and</i> CD4 ≥25% <i>and</i> HIV RNA ≥100,000 copies/mL	Consider treatment
1- < 5 years	Asymptomatic or mild symptoms <i>and</i> CD4 ≥ 25% <i>and</i> HIV RNA <100,000 copies/mL	Defer treatment
Age ≥ 5 years	CD4 < 350 cells/mm <sup>3</sup>	Treat
Age ≥ 5 years	Asymptomatic or mild symptoms <i>and</i> CD4 ≥ 350 cells/mm <sup>3</sup> <i>and</i> HIV RNA ≥ 100,000 copies/mL	Consider treatment
Age ≥ 5 years	Asymptomatic or mild symptoms <i>and</i> CD4 ≥ 350 cells/mm <sup>3</sup> <i>and</i> HIV RNA <100,000 copies/mL	Defer treatment

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## Recommended Antiretroviral Regimens

**Table 2**

(Adapted from Table 7: Recommended Antiretroviral Regimens for Initial Therapy for Human Immunodeficiency Virus (HIV) Infection in Children, February 28, 2008)

<b>Non-Nucleoside Reverse Transcriptase Inhibitor-Based Regimens</b>
<p><b>Preferred Regimen:</b></p> <ul style="list-style-type: none"> <li>• ≥ 3 yrs old: 2 NRTIs <i>plus</i> efavirenz</li> <li>• &lt; 3 yrs old or can't swallow caps: 2 NRTIs <i>plus</i> nevirapine</li> </ul> <p><b>Alternative:</b> 2 NRTIs <i>plus</i> nevirapine (≥ 3 yrs old)</p>
<b>Protease Inhibitor-Based Regimens</b>
<p><b>Preferred Regimen:</b> 2 NRTIs <i>plus</i> lopinavir/ritonavir</p> <p><b>Alternative:</b> 2 NRTIs <i>plus</i> fosamprenavir/ritonavir (low dose) (&gt; 6 yrs old)</p>
<b>Use in Special Circumstances</b>
<ul style="list-style-type: none"> <li>• 2 NRTIs <i>plus</i> fosamprenavir (2-6 yrs old)</li> <li>• 2 NRTIs <i>plus</i> low-dose ritonavir <i>plus</i> (atazanavir or indinavir or saquinavir) only in post-pubertal adolescents who weigh enough to receive adult doses</li> <li>• Zidovudine <i>plus</i> lamivudine <i>plus</i> abacavir</li> </ul>
<b>2-NRTIs Backbone Options (for use in combination with additional drugs) (alphabetical ordering)</b>
<p><b>Preferred:</b></p> <ul style="list-style-type: none"> <li>• Abacavir <i>plus</i> (lamivudine or emtricitabine)</li> <li>• Didanosine <i>plus</i> emtricitabine</li> <li>• Tenofovir <i>plus</i> (lamivudine or emtricitabine) (for Tanner Stage 4 or post-pubertal adolescents only)</li> <li>• Zidovudine <i>plus</i> (lamivudine or emtricitabine)</li> </ul> <p><b>Alternative:</b></p> <ul style="list-style-type: none"> <li>• Abacavir <i>plus</i> zidovudine</li> <li>• Zidovudine <i>plus</i> didanosine</li> </ul> <p><b>Use in Special Circumstances:</b> Stavudine <i>plus</i> (lamivudine or emtricitabine)</p>

## General Considerations

- As of January 2008, 25 ARVs approved for use in HIV-infected adults/adolescents; 14 have a pediatric indication; 13 available in pediatric formulation or capsule size.

## Agents Without Sufficient Pediatric Data for Use as Initial Therapy ([See Tables 12 and 13 in the Guidelines](#))

- Darunavir/ritonavir, tipranavir/ritonavir, maraviroc (CCR5 antagonist), raltegravir (integrase inhibitor), etravirine (a new NNRTI), and tenofovir (Tanner Stage 1-3). Pharmacokinetic, safety, and efficacy data are not yet available and no pediatric formulations are commercially available.
- Enfuvirtide (T-20), a fusion inhibitor, is approved for use in children ≥ 6 years with other ARVs and in treatment-experienced patients with evidence of HIV replication despite ongoing ARV therapy.

## What Not to Use: Antiretroviral Drug Regimens that Should Not be Offered at Any Time ([See Table 8 in the Guidelines](#))

- Monotherapy
- 2 NRTIs alone
- Certain 2 NRTI combinations as part of HAART regimen
- Two NRTIs + unboosted saquinavir
- Atazanavir + indinavir
- Tenofovir + didanosine + (lamivudine or emtricitabine) as triple NRTI regimen
- Tenofovir + abacavir + (lamivudine or emtricitabine) as triple NRTI regimen
- Nelfinavir-containing regimens

## Nelfinavir-Containing Regimens

- HIV-infected children just initiating therapy should limit their exposure to ethyl methane sulfonate (EMS) which is found in Viracept® (nelfinavir mesylate) as a result of a process-related impurity.
- Nelfinavir is a powder that has a poor acceptance rate when mixed with food or formula, and the pharmacokinetics of the drug is extremely variable in children.
- Pediatric patients who are currently receiving nelfinavir containing regimens and are stable, the risk benefit ratio remains favorable for the continued use of nelfinavir.

### Reference

Working Group on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. February 28, 2008, 1-134. Available at <http://aidsinfo.nih.gov/ContentFiles/PediatricGuidelines.pdf>. Accessed (March 3, 2008)

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