

## **What's New in the Pediatric Guidelines?**

The updated *Guidelines for the Use of Antiretroviral Agents in Pediatric Infection* include the following changes made to the February 23, 2009, version of the guidelines. Key updates are also highlighted throughout the guidelines.

### **Ratings for Primary Recommendations**

The key change prominent in the current guidelines is development of a ratings system to indicate strength and quality of evidence for each major recommendation. The strength of each recommendation is indicated by a letter (A = Strong, B = Moderate, C = Optional); the quality of the evidence supporting each recommendation is represented by a Roman numeral (I, II, III). In addition, because many pediatric recommendations will be based on data from clinical trials or observational studies in adults, with only safety and pharmacokinetic data in children, evidence ratings that are based on adult data will be indicated with an asterisk (\*).

### **Format Changes/New Sections**

#### ***Previous Appendix B: Characteristics of Available Antiretroviral Drugs and Supplement I: Pediatric Antiretroviral Drug Information***

- Information in the previous Appendix B: Characteristics of Available Antiretroviral Drugs and previous Supplement I: Pediatric Antiretroviral Drug Information of the February 23, 2009, guidelines has been combined into a new format with a table for each drug summarizing drug formulation, dosing recommendations, important adverse effects, and special instructions. Each table is followed by a short text section that includes important pediatric experience and references for that particular drug. Updated information on drugs is provided.

#### ***Previous Supplement III: Adverse Drug Effects***

- This supplement to the previous version of the guidelines describes specific adverse drug effects observed in children, including lactic acidosis, hepatic toxicity, fat maldistribution and body habitus changes, hyperlipidemia, hyperglycemia, osteopenia, hematological complications, and hypersensitivity reactions and skin rashes. The supplement has been modified into a table format and included in the body of the current guidelines, with information on common causative drugs, estimated frequency of occurrence, timing of symptoms, risk factors, potential preventive measures, and suggested clinical management strategies and provides selected references regarding these toxicities in pediatric patients.

#### ***Previous Supplement II: Managing Complications of HIV Infection in HIV-Infected Children on Antiretroviral Therapy***

- This supplement on pain management and nutrition included in the previous version of the guidelines has been retired. (See *Supplement II: Managing Complications of HIV Infection in HIV-Infected Children on Antiretroviral Therapy* in the archived February 23, 2009 *Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection* at <http://www.aidsinfo.nih.gov>.)

### **Key Updates**

Updates to the various sections of the guidelines include the following new information/key changes:

#### ***Diagnosis of HIV Infection in Infants***

- Viral diagnostic testing at birth is recommended for infants at high risk of HIV infection, such as infants born to HIV-infected mothers who did not receive prenatal care or prenatal antiretroviral therapy or who had HIV viral loads  $\geq 1,000$  copies/mL close to time of delivery (BIII). Viral diagnostic testing continues to be recommended for all HIV-exposed infants at age 14–21 days, 1–2 months, and 4–6 months (AII).

- An HIV qualitative RNA assay (APTIMA HIV-1 RNA Qualitative Assay) is an alternative diagnostic test that can be used for infant virologic diagnostic testing (AII).

### **When to Start**

- Antiretroviral therapy continues to be recommended for all children younger than 12 months of age regardless of clinical, immunologic, or virologic symptoms (AI).
- However, whereas prior guidelines said antiretroviral therapy could be *considered* for asymptomatic or mildly symptomatic children with CD4  $\geq 25\%$  (or  $\geq 350$  cells/uL if age  $\geq 5$  years) and HIV RNA  $\geq 100,000$  copies/mL, the current guidelines now *recommend* therapy in this situation (BII). Additionally, whereas prior guidelines recommended *deferral* of therapy for asymptomatic or mildly symptomatic children with CD4  $\geq 25\%$  (or  $\geq 350$  cells/uL if age  $\geq 5$  years) and HIV RNA  $< 100,000$  copies/mL, the current guidelines say therapy can be *considered or deferred* (CIII) Specific recommendations are:
  - Initiation of antiretroviral therapy is *recommended* for children age  $\geq 1$  year with AIDS or significant symptoms (Clinical Category C or most Clinical Category B conditions), regardless of CD4 percentage/count or plasma HIV RNA level (AI\*).
  - Initiation of antiretroviral therapy is also *recommended* for children age  $\geq 1$  year who have met the age-related CD4 threshold for initiating treatment (CD4  $< 25\%$  for children 1 to  $< 5$  years of age (AII) and  $< 350$  cells/mm<sup>3</sup> for children  $\geq 5$  years of age (AI\*), regardless of symptoms or plasma HIV RNA level).
  - Initiation of antiretroviral therapy is also *recommended* for children age  $\geq 1$  year who are asymptomatic or have mild symptoms (Clinical Categories N and A or the following Clinical Category B conditions: single episode of serious bacterial infection or lymphoid interstitial pneumonitis) *and* have CD4  $\geq 25\%$  for children 1 to  $< 5$  years of age or  $\geq 350$  cells/mm<sup>3</sup> for children  $\geq 5$  years of age *and* have plasma HIV RNA  $\geq 100,000$  copies/mL (BII).
  - Initiation of antiretroviral therapy may be *considered or deferred* for children age  $\geq 1$  year who are asymptomatic or have mild symptoms and who have CD4  $\geq 25\%$  for children 1 to  $< 5$  years of age and  $\geq 350$  cell/mm<sup>3</sup> for children  $\geq 5$  years of age *and* have plasma HIV RNA  $< 100,000$  copies/mL (CIII).

### **What Drugs to Start: Initial Combination Therapy for Antiretroviral-Naïve Children**

- Recent data from clinical trials of nevirapine versus lopinavir/ritonavir-based therapy in children with single-dose nevirapine exposure for prevention of mother-to-child transmission of HIV are discussed.
- NNRTI-based therapy is not recommended for infants or children age  $< 3$  years with single-dose nevirapine exposure (AI).
- Darunavir in combination with low-dose ritonavir is now recommended as an alternative protease inhibitor for initial therapy in children age  $\geq 6$  years (AI\*).
- Nelfinavir has been moved from an alternative protease inhibitor for initial therapy to a protease inhibitor for use in special circumstances in children age  $\geq 2$  years (AII).

### **Adherence to Antiretroviral Therapy in HIV-Infected Children and Adolescents**

- Results of several new studies regarding interventions to improve adherence in children and/or adolescents are described.

### **Additional Updates**

- References have been updated in many sections.