Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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What's New in the Pediatric Guidelines (Last updated November 15, 2017; last reviewed November 15, 2017)

The Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection (Pediatric Guidelines) are published in an electronic format that can be updated as relevant changes in prevention and treatment recommendations occur. The Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV (the Panel) is committed to timely changes in this document because so many health care providers, patients, and policy experts rely on this source for vital clinical information.

Major revisions within the last 12 months are as follows:

November 15, 2017

To facilitate access to relevant content, the guidelines now include three sections that will also appear in the Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States: Maternal HIV Testing and Identification of Perinatal HIV Exposure, Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV Infection, and Diagnosis of HIV Infection in Infants and Children.

Maternal HIV Testing and Identification of Perinatal HIV Exposure

- The section has been renamed with revisions to align content in the Pediatric and Perinatal Guidelines regarding maternal HIV testing for prevention on perinatal HIV transmission and identification of perinatal HIV exposure in infants and children.

Diagnosis of HIV Infection in Infants and Children

- This section was updated and reorganized to present content about the timing of diagnostic testing for infants and children prior to detailed information about the specific virologic assays used for diagnosis.

Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV Infection

- The Panel has added a new section, shared with the Perinatal Guidelines, that details recommendations on ARV management of infants born to women with HIV. This section, formerly titled Infant Antiretroviral Prophylaxis in the Perinatal Guidelines, has been updated to reflect emerging issues in the antiretroviral management of infants born to women with HIV and also incorporates content from Specific Issues in Antiretroviral Therapy for Neonates in previous versions of the Pediatric Guidelines.
- The Panel recommends that the selection of a newborn ARV regimen should be determined based on maternal and infant factors that influence risk of HIV transmission. The uses of ARV regimens in newborns include:
  - ARV prophylaxis – the administration of one or more ARVs to a newborn without confirmed HIV infection to reduce the risk of HIV acquisition
  - Empiric HIV therapy – the administration of a three-drug combination ARV regimen to newborns at highest risk of HIV acquisition. Empiric HIV therapy is intended to be early treatment for a newborn who is later confirmed to be HIV-infected but also serves as prophylaxis against HIV acquisition for those newborns who are exposed to HIV in utero, during the birthing process or during breastfeeding and who do not become infected with HIV
  - HIV therapy – the administration of three-drug combination ARVs at treatment dosages (ART) to newborns with confirmed HIV infection (see Diagnosis of HIV Infection).
- The Panel recommends combination ARV prophylaxis or empiric HIV therapy for newborns at higher risk of HIV acquisition and HIV therapy for newborns with confirmed HIV infection.

- Table 11. Newborn Antiretroviral Management According to Risk of HIV Infection in the Newborn has been added to provide an overview and guidance about antiretroviral management for different clinical categories.
- Table 12. Newborn ARV Dosing Recommendations has been revised in accordance with updated Panel recommendations for newborn antiretroviral management.

April 27, 2017

Revisions to the March 1, 2016, *Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection* include key updates to several sections. Text and references throughout the document were updated to include relevant new data and publications. In response to community input, edits were made to continue to incorporate People First Language, which focuses on the person rather than the disease and recognizes the importance of language in empowering individuals and reducing stigma. Examples of language edits include changes from use of "HIV-infected children" to "children living with HIV", "children with HIV", or "children with HIV infection." Consequently, there was also a change in the Panel's name to the Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Key section updates are summarized below:

Diagnosis of HIV Infection

- The section has been updated to clarify recommendations for diagnostic testing of infants at higher risk of perinatal HIV transmission and those who have received multidrug antiretroviral prophylaxis. The infant testing algorithm is illustrated in a new figure, Figure 1. Recommended virologic testing schedules for infants exposed to HIV by perinatal HIV transmission risk.

What Drugs to Start: Initial Combination Therapy for Antiretroviral Treatment-Naive Children

- The section has been updated to include the use of age and weight limitations in the Panel's recommendations. Although age can be used as a rough guide, body weight is the preferred determinant of the recommendation for selecting a specific drug, when available, except for infants less than 14 days of age.
- Drug-specific sections about efficacy in clinical trials, adverse events and other factors and considerations were moved to Appendix A: Pediatric Antiretroviral Drug Information.
- The Panel has updated Preferred regimens based on recent Food and Drug Administration (FDA) approvals, efficacy, ease of administration and acceptable toxicity, see Table 7. Antiretroviral Regimens Recommended for Initial Therapy for HIV Infection in Children and Figure 2. Preferred and Alternative Regimens by Age and Drug Class. Significant updates include the following:
    - The Panel has added a recommended initial regimen of nevirapine plus 2 nucleoside reverse transcriptase inhibitors (NRTIs) for infants aged birth to <14 days, but notes that there are currently no clinical trial data suggesting that initiating treatment within the first 14 days of life improves outcome compared to starting after 14 days of age. The Panel recommends that a change from nevirapine to lopinavir/ritonavir should be considered after 14 days of life and 42 weeks post-gestational age based on infant genotype and the better outcomes of lopinavir/ritonavir in children aged <3 years.
    - Dolutegravir plus 2 NRTIs has been added as a Preferred initial regimen for children aged ≥6 to <12 years (weighing ≥30 kg).
    - Tenofovir alafenamide has been added as a Preferred NRTI for adolescents aged >12 years.
    - Efavirenz or lopinavir plus 2 NRTIs are now classified as Alternative rather than Preferred regimens for children ≥3 years to <12 years of age. Twice daily boosted darunavir or raltegravir plus 2 NRTIs

were changed from Preferred to Alternative regimens for children ≥6 years to <12 years of age.

- Didanosine plus (lamivudine or emtricitabine) has been added to 2-NRTI regimens for use in Special Circumstances in Combination with Additional Drugs.

Adherence to Antiretroviral Therapy in Children and Adolescents Living with HIV

- The section now presents information about adherence monitoring in Table 13. Evidence-based Approaches for Monitoring Medication Adherence.

Management of Children Receiving Antiretroviral Therapy

- The section on Modifying Antiretroviral Regimens in Children with Sustained Virologic Suppression on Antiretroviral Therapy has been updated to include examples of new options for regimen modification.
- The section on Recognizing and Managing Antiretroviral Treatment Failure has been streamlined and updated with information about new regimen options, see Table 18. Options for Regimens with at Least Two Fully Active Agents with Goal of Virologic Suppression in Patients with Failed Antiretroviral Therapy and Evidence of Viral Resistance.

Role of Therapeutic Drug Monitoring in Management of Pediatric HIV Infection

- Use of patient pharmacogenetic profile for the selection of the dose of certain ARV drugs (e.g., efavirenz) was added to the scenarios where targeted therapeutic drug monitoring can be considered.
- Table 19. Target Trough Concentrations of Antiretroviral Drugs Relevant to Pediatric Populations was updated to include additional drugs and the format has been changed to present data as shown in the original source.

Pediatric Antiretroviral Drug Information

Drug sections in Appendix A: Pediatric Antiretroviral Drug Information were reviewed and updated to include new pediatric data, dosing, and safety information as well as some drug-specific information that was previously located in What Drugs to Start: Initial Combination Therapy for Antiretroviral Treatment-Naive Children. Interim updates were made in April 2016 and September 2016 to include information about newly released drugs (Odefsey and Descovy) and updated formulations (low-strength Truvada) and new tablet strengths of dolutegravir (10 and 25 mg). Other significant changes are summarized below:

- Zidovudine now includes a table with simplified weight band dosing (for use aged birth to 4 weeks) for infants who are ≥35 weeks gestational age.
- Maraviroc has been updated to include new dosage forms and pediatric dosing information following FDA approval for use in children aged ≥2 years and weighing ≥10 kg.
- Raltegravir now includes the investigational dose for neonates ≥37 weeks of gestation and weighing ≥2 kg under study in IMPAACT P1110.