Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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What's New in the Pediatric Guidelines (Last updated April 27, 2017; last reviewed 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 11. 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 16. 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 17. 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.