What's New in the Pediatric Guidelines

(Last updated December 30, 2020; last reviewed December 30, 2020)

The Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV (the Panel) has reviewed previous versions of the Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection and revised the text and references. Key updates are summarized below.

December 30, 2020

Maternal HIV Testing and Identification of Perinatal HIV Exposure

- Bulleted recommendations have been updated to point out that repeat HIV testing is recommended for pregnant women with a sexually transmitted infection or with signs and symptoms of acute HIV infection **(AIII)** and that expedited HIV testing during labor is recommended for those who are at increased risk of HIV infection and were not retested in the third trimester **(AIII)**.

Antiretroviral Management of Newborns with Perinatal HIV Exposure of HIV Infection

- In describing infants at high or low risk of perinatal acquisition of HIV and maternal risk factors for perinatal HIV transmission, viral suppression is defined as HIV RNA <50 copies/mL.
- Information about recommended antiretroviral drugs for infants with perinatal exposure to HIV-2 infection is available in Table 12 and HIV-2 Infection and Pregnancy.
- Table 12 has been updated to include dosing of dolutegravir dispersible tablets for oral suspension for HIV therapy, which can replace lopinavir/ritonavir, nevirapine, or raltegravir in infants at least 4 weeks of age and weighing at least 3 kg.
- Information about the two-drug regimen of nevirapine and zidovudine used in NICHD-HPTN 040/PACTG 1043 has been removed from Table 12 but is available in the text (see Two-Drug Antiretroviral Prophylaxis).
- Maraviroc (MVC) was approved recently for infants weighing ≥2 kg and may provide an additional treatment option for newborns of women carrying multidrug resistant HIV-1 that remains CCR5-trophic. However, the lack of data about MVC as prophylaxis or treatment in infants weighing <10 kg and the risk of drug interactions will limit its role for routine use in neonates.

Diagnosis of HIV Infection in Infants and Children

- Maternal HIV viral loads that categorize infants at a high risk of perinatal HIV transmission have been defined at HIV RNA ≥50 copies/mL.
- A statement has been added to clarify that HIV testing at birth might be considered when there are concerns that a newborn at low risk of perinatal HIV transmission may be lost to follow-up without testing.
- Content has been added about the potential for false-positive HIV nucleic acid tests (NATs) with chimeric antigen receptor T cell (CAR-T cell) and lentiviral-based gene therapy.

April 14, 2020

When to Initiate Therapy in Antiretroviral-Naive Children

- The Panel now recommends rapid initiation of antiretroviral therapy (ART) for **all** children, not just those aged <1 year. Rapid initiation is defined as initiating therapy immediately or within days of HIV diagnosis.
- Because the Panel no longer makes recommendations about when to initiate ART based on a child's age (either <1 year of age or ≥1 year of age), Table A has been deleted and the data that support rapid initiation have been grouped by outcome (i.e., survival and health benefits, neurodevelopmental benefits, immune benefits, and viral reservoirs and viral suppression). References have been updated to reflect recently published findings, and older references have been removed.

- The Panel acknowledges that, on a case-by-case basis, initiation of ART may be deferred based on a patient's clinical or psychosocial factors. The Panel highlights medical factors, including HIV signs and symptoms, that should be considered when clinicians, patients, and caregivers make collaborative decisions about whether to defer treatment.
- With the changes described above, the Treatment Recommendations section is no longer needed and has been deleted.

What to Start: Regimens Recommended for Initial Therapy of Antiretroviral-Naive Children

- Text and Table 7. Antiretroviral Regimens Recommended for Initial Therapy for HIV Infection in Children have been updated following Food and Drug Administration (FDA) approval of cobicistat (COBI) for pediatric use.
- The Panel now recommends atazanavir (ATV) boosted with COBI (ATV/c) or darunavir (DRV) boosted with COBI (DRV/c) plus two nucleoside reverse transcriptase inhibitors as *Alternative* protease inhibitor-based initial regimens for children and adolescents aged ≥12 years with a sexual maturity rating of 1 to 3 who weigh ≥35 kg or ≥40 kg, respectively.
- Throughout the guidelines, the Panel refers to the Adult and Adolescent Antiretroviral Guidelines and the Perinatal Guidelines for guidance about the use of dolutegravir (DTG) and other antiretroviral (ARV) drugs in people of childbearing potential and those who are pregnant or who are trying to conceive.
    - Wording has been revised in accordance with updated recommendations about the use of DTG, and a link to the new Appendix D. Dolutegravir Counseling Guide for Health Care Providers in the Perinatal Guidelines has been inserted into several sections.

Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection

- The Panel has changed the term "empiric HIV therapy" to "presumptive HIV therapy" in this section and throughout the guidelines to be consistent with the terminology used by the World Health Organization. The Panel recommends presumptive HIV therapy for infants who are at a higher risk of perinatal HIV acquisition. For clarity, the term "multidrug ARV prophylaxis" has been changed to "two-drug ARV prophylaxis."
- Table 11. Neonatal Antiretroviral Management According to Risk of HIV Infection in the Newborn and Table 12. Antiretroviral Dosing Recommendations for Newborns have been revised to clarify the ARV regimens and the duration and dosing of ARV drugs that are used for presumptive HIV therapy.
- The two-drug regimen that was used in NICHD-HPTN 040/PACTG 1043 for infants who were at a higher risk of HIV acquisition is no longer included in Tables 11 and 12; this regimen is described in the text instead, see the Two-Drug Antiretroviral Prophylaxis section.

Special Considerations for Antiretroviral Therapy Use in Adolescents with HIV

- The Panel added a new subsection entitled Special Considerations for Adolescents with HIV Who Are Sexual Minorities with links to Adolescents and Young Adults with HIV and Transgender People with HIV in the Adult and Adolescent Antiretroviral Guidelines.

Management of Medication Toxicity or Intolerance

- Table 15a. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Central Nervous System Toxicity includes updated information about neuropsychiatric symptoms and other central nervous system manifestations that are associated with the use of integrase strand transfer inhibitors. Information on bictegravir has also been added to the table.

- Information about the association between ARV drugs and weight gain has been added to Table 15h, and the table has been renamed Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Lipodystrophies and Weight Gain.

Management of Children Receiving Antiretroviral Therapy

- The sections on Modifying Antiretroviral Regimens in Children with Sustained Virologic Suppression on Antiretroviral Therapy and Recognizing and Managing Antiretroviral Treatment Failure have been updated to incorporate the most recent ART options for pediatric patients based on new pediatric ARV drug approvals and Panel recommendations.

Appendix A: Pediatric Antiretroviral Drug Information

The drug sections and Appendix A, Table 2 were updated to include new pediatric data and dosing and safety information, plus new drug formulations and fixed-dose combination (FDC) drugs. Significant changes include:

- In accordance with FDA approval, raltegravir (RAL) HD is now recommended for use in children and adolescents weighing ≥40 kg who are treatment naive or who are virologically suppressed on an initial dose of RAL 400 mg twice daily.
- Although lopinavir/ritonavir is not approved by the FDA for use in neonates before a postmenstrual age of 42 weeks and a postnatal age of at least 14 days, the Panel now provides some guidance for situations where no alternatives are available for neonates who have not met these age thresholds.
- The ATV, DRV, and COBI drug sections have been updated to reflect recent FDA approvals and updated Panel recommendations. COBI (Tybost) is now approved by the FDA for use with ATV in children and adolescents weighing ≥35 kg and for use with DRV in children and adolescents weighing ≥40 kg. The FDC tablet darunavir/cobicistat/emtricitabine/tenofovir alafenamide (DRV/c/FTC/TAF; Symtuza) is now approved by the FDA for use in children and adolescents weighing ≥40 kg. Although coformulated ATV/c (Evotaz) and DRV/c (Prezcobix) are not approved by the FDA for use in children, the Panel does recommend using these FDC tablets in pediatric patients weighing ≥35 kg or ≥40 kg, respectively, based on FDA approvals of the individual component drugs.