What’s New in the Pediatric Guidelines  (Last updated May 22, 2018; last reviewed May 22, 2018)

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 making timely changes to this document because so many health care providers, patients, and policy experts rely on it for vital clinical information.

Major revisions made to the Pediatric Guidelines within the last 12 months are as follows:

May 22, 2018

The Panel updated the text and references of the April 2017 Pediatric Guidelines to include new data and publications. Key updates are summarized below.

Introduction
• The Panel has described the process of coordinating with the authors of the Perinatal Guidelines to jointly develop three sections of the Pediatric Guidelines that are shared with the Perinatal Guidelines.
• Contact information for the Clinician Consultation Center has been added to facilitate access to expert consultation by phone when needed. The Clinical Consultation Center can be contacted at (800) 933-3413, 9 a.m. to 8 p.m. EST, Monday through Friday.

Clinical and Laboratory Monitoring of Pediatric HIV Infection
• The list of bulleted recommendations has been updated to recommend the use of viral load measurements every 3 to 4 months to monitor antiretroviral therapy (ART) adherence and disease progression (AIII).

When to Initiate Therapy in Antiretroviral-Naive Children
• The Panel has increased the strength of its recommendations for initiating ART in children aged ≥1 year who are asymptomatic or who have mild symptoms and who have CD4 T lymphocyte (CD4) cell counts ≥1,000 cells/mm³ (for those aged 1–6 years) or CD4 cell counts ≥500 cells/mm³ (for those aged ≥6 years); ratings were changed from Moderate (BI*) to Strong (AI*). Thus, the Panel now recommends that all children receive ART, regardless of symptoms or CD4 count.

What to Start: Regimens Recommended for Initial Therapy of Antiretroviral-Naive Children
• The Panel’s bulleted recommendation about individualizing initial antiretroviral (ARV) regimens was revised to include the following additional factors for clinicians to consider when choosing an ARV regimen: drug efficacy, potential adverse effects, and patient and family preferences.
• Table 7. Antiretroviral Regimens Recommended for Initial Therapy for HIV Infection in Children and the associated text were revised to reflect updated Panel recommendations. An additional column and footnotes indicating whether drugs are available in fixed-dose combination (FDC) formulations were added to the Table. Additional information is available about drug formulations in Appendix A: Pediatric Antiretroviral Drug Information. Updated recommendations are summarized below.
  • The Panel now recommends raltegravir as a Preferred INSTI regimen from birth to age 6 years. This change adds a Preferred regimen to the limited options available for children aged <2 years. However, the Panel acknowledges that data in this age group are limited and that neonatal dosing and administration of raltegravir granules for oral suspension can be challenging.
• Genvoya, an FDC tablet that contains elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (TAF), is now an Alternative regimen for children aged ≥6 years to <12 years and weighing ≥25 kg. Genvoya continues to be a Preferred regimen for patients aged ≥12 years and weighing ≥35 kg who are not sexually mature (i.e., those who have a sexual maturity rating [SMR] 1–3).

• TAF used in combination with emtricitabine is now a Preferred nucleoside reverse transcriptase inhibitor (NRTI) backbone option for children and adolescents aged ≥6 years who are not sexually mature (SMR 1–3). TAF was previously a Preferred option only for those aged ≥12 years.

• Tenofovir disoproxil fumarate (TDF) used in combination with lamivudine or emtricitabine is now recommended as an Alternative NRTI backbone option for children aged ≥2 years to 12 years; the potential risks of decreased bone mineral density should be weighed against the benefits of therapy. These options were previously recommended for use in Special Circumstances in children aged ≥2 years with SMR of 1 or 2.

• Zidovudine used in combination with lamivudine or emtricitabine was changed from a Preferred to an Alternative NRTI backbone for children and adolescents aged ≥6 to years who are not sexually mature (SMR 1–3).

What Not to Start: Regimens Not Recommended for Initial Therapy of Antiretroviral-Naive Children

• The Panel has updated its recommendations to indicate that didanosine or stavudine should never be used as part of an ARV regimen, due to the significant toxicities of these drugs and the availability of safer agents.

• Table 9. Antiretroviral Regimens or Components Not Recommended for Initial Treatment of HIV Infection in Children and Table 10. ART Regimens or Components that Should Never Be Recommended for Treatment of HIV Infection in Children have been updated accordingly.

Management of Children Receiving Antiretroviral Therapy

• In Modifying Antiretroviral Regimens in Children with Sustained Virologic Suppression on Antiretroviral Therapy, the Panel has updated Table 16. Examples of Changes in Antiretroviral Regimen Components that Are Made for Reasons of Simplification, Convenience, and Safety Profile in Children Who Have Sustained Virologic Suppression on Their Current Regimens.

• Considerations about Intermittent Use in Antiretroviral Therapy now includes issues that may contribute to interrupted ART in children from limited resource settings, including the need to plan for potential interruptions (e.g., extended travel).

Role of Therapeutic Drug Monitoring in Management of Pediatric HIV Infection

• The section on therapeutic drug monitoring has been removed, but it is available in the archive of previous versions of the Pediatric Guidelines.

Appendix A: Pediatric Antiretroviral Drug Information

Drug sections in this appendix were reviewed and updated to include new pediatric data and dosing and safety information, plus new formulations and FDCs. Significant changes are summarized below:

• The Emtricitabine and Tenofovir Alafenamide sections have been updated with new pediatric dosing for Descovy, the FDC of emtricitabine/TAF (FTC/TAF). FTC/TAF is approved for use in children weighing ≥25 kg. There are insufficient data to recommend the use of FTC/TAF in combination with a boosted protease inhibitor (PI) in children weighing <35 kg. For children and adolescents weighing ≥35 kg, FTC/TAF can be used in combination with a non-nucleoside reverse transcriptase inhibitor, an integrase strand transfer inhibitor (INSTI), or a boosted PI.
• The Lamivudine section was updated with new Food and Drug Administration (FDA) pediatric dosing recommendations for children aged ≥3 months to address the pharmacokinetic fluctuations that occur when sorbitol is given. However, because of the lack of clinical experience with starting once-daily lamivudine at the higher dose, the Panel continues to recommend a change from twice-daily to once-daily dosing of lamivudine (solution or tablets) only in children who are aged ≥3 years and who have been stable on a twice-daily regimen for ≥36 weeks.

• The Efavirenz section now includes information about using opened capsules as a sprinkle preparation for children who are unable to swallow capsules. Information was also added about Symfî Lo, a new FDC that contains efavirenz/lamivudine/TDF and that has been FDA-approved for children weighing ≥35 kg and adults. However, the Panel has not yet discussed or made recommendations about this formulation, which contains a lower dose of efavirenz (400 mg). Use of Symfî Lo will be addressed in a later update.

• The Atazanavir section now includes once-daily dosing of atazanavir capsules for children aged ≥6 years and weighing ≥15 kg, in accordance with new FDA recommendations.

• The Ritonavir section has been updated with information about a new pediatric oral powder formulation that can be administered in 100-mg increments.

• Bictegravir, a new INSTI, was added to the drug appendix. Bictegravir (BIC) is available only as Biktarty, an FDC that contains BIC/FTC/TAF and is FDA-approved for use in adults. Although not yet approved for pediatric use, the adult dose of bictegravir is being studied in children and adolescents aged 12 years to 18 years and weighing ≥35 kg.

• Elvitegravir tablets have been discontinued by the manufacturer; the drug is only available in FDC formulations.

• The Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir Alafenamide sections were updated to reflect the recent FDA approval of Genvoya, an FDC that contains these drugs, for use in children and adolescents weighing ≥25 kg with any SMR. This FDC was previously approved only for use in adolescents weighing ≥35 kg. Genvoya can be used in ART-naïve patients or to replace the current ARV regimen in patients who are viremically suppressed (HIV-1 RNA <50 copies/mL) and who have been on a stable ARV regimen for at least 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Genvoya.

• The Raltegravir section was updated with new information about the neonatal dosing of raltegravir granules for oral suspension and the new film-coated poloxamer HD tablet.

  • Raltegravir granules for oral suspension are now FDA-approved and recommended by the Panel for use in neonates aged ≥37 weeks of gestation and weighing ≥2 kg. The updated instructions for preparing the suspension result in a final concentration of 10 mg/mL, rather than 20 mg/mL. This change is reflected in the new neonatal dosing table and updates to the dosing table for children aged ≥4 weeks and weighing ≥3 kg to <20 kg.

  • The Panel recommends once-daily raltegravir HD for use in children and adolescents weighing ≥50 kg who are ART-naïve or viremically suppressed on an initial regimen of twice-daily raltegravir tablets. The FDA approval of raltegravir HD for use in children and adolescents weighing ≥40 kg is based on modeling; this formulation has not been studied in children or adolescents.

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.