



Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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What's New in the Pediatric Guidelines (Last updated December 14, 2018; last reviewed December 14, 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:

December 14, 2018

Updates to the guidelines include the addition of two new tables about fixed-dose combinations (FDCs) of antiretroviral (ARV) drugs in Appendix A: Pediatric Antiretroviral Drug Information and revisions to the three sections that are shared with *Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission*.

Maternal HIV Testing and Identification of Perinatal HIV Exposure

- A new bulleted recommendation was added to emphasize that partners of pregnant women should be encouraged to undergo HIV testing if their HIV status is unknown.
- Risk of HIV exposure should be assessed in all women who are considering becoming pregnant, as well as in all pregnant women who previously tested HIV negative. Women with risk factors for HIV acquisition should receive prevention counseling and appropriate interventions, including pre-exposure prophylaxis, if indicated.
- The indications for third-trimester HIV retesting have been updated to include women who are incarcerated or who reside in states that require third-trimester testing. Data about gaps in perinatal HIV testing suggest that providers should be proactive in assessing a woman's HIV acquisition risk and implementing third-trimester HIV retesting in areas where it is not routine, when indicated.

Diagnosis of HIV Infection in Infants and Children

- The use of an assay that detects HIV non-B subtype viruses or Group O is now recommended for known or suspected maternal non-B subtype virus or Group O infections (RNA nucleic acid tests (NATs) and dual-target total DNA/RNA tests).
- The case definition for indeterminate HIV infection in children aged <18 months has been added.

Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV

- Zidovudine plus lamivudine plus raltegravir is now a recommended empiric HIV therapy option for neonates who are at a higher risk of perinatal HIV transmission. Information has been added to this section about the use and safety of raltegravir in infants.
- Some Panel members opt to discontinue nevirapine, raltegravir, and/or lamivudine when the birth HIV NAT returns negative, while others choose to continue empiric HIV therapy for 6 weeks. In all cases where the newborn is at a higher risk of HIV acquisition, zidovudine should be continued for 6 weeks. The Panel recommends consulting with an expert in pediatric HIV when making a decision about the duration of empiric HIV therapy.
- Table 11. Newborn Antiretroviral Management According to Risk of HIV Infection in the Newborn and Table 12. Newborn Antiretroviral Dosing Recommendations have been revised according to updated

recommendations for the treatment of newborns with HIV infection and newborns who are at low risk or high risk of perinatal HIV transmission.

[Appendix A: Pediatric Antiretroviral Drug Information](#)

- Two new tables in Appendix A provide information about FDC formulations of ARV drugs and their use in children.
- [Appendix A, Table 1](#). Antiretrovirals Available in Fixed-Dose Combination Tablets organizes information as grid, with ARV drugs listed alphabetically by class across the top and available FDCs listed on the left.
- [Appendix A, Table 2](#). Antiretroviral Fixed-Dose Combination Tablets: Minimum Body Weights and Considerations for Use in Children and Adolescents columns include dosages of FDC component drugs, the minimum body weight requirements for these drugs, pill size (when available), and food requirements.

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 $\geq 1,000$ 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 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 Interruptions 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 Symfi 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 Symfi 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 Biktarvy, 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-naive patients or to replace the current ARV regimen in patients who are virologically 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-naive or virologically 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.