

What's New in the Guidelines

Updated: Apr. 11, 2022
Reviewed: Apr. 11, 2022

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

April 11, 2022

The U.S. Food and Drug Administration (FDA) recently approved long-acting injectable cabotegravir and rilpivirine (Cabenuva) for use in children and adolescents aged ≥ 12 years and weighing ≥ 35 kg. This change has been incorporated in the [Cabotegravir](#) and [Rilpivirine](#) drug sections; other sections have not been updated yet. The Panel has not made revisions to address the recent FDA approval of the dispersible tablet formulation of the fixed-dose combination (FDC) of abacavir/dolutegravir/lamivudine (Triumeq PD) for use in children weighing 10 kg to 25 kg; this will be addressed in a future update.

[Clinical and Laboratory Monitoring of Pediatric HIV Infection](#)

- Some updates were made for clarification and to align content in bulleted recommendations, text, and Table 5. Sample Schedule for Clinical and Laboratory Monitoring of Children Before and After Initiation of Antiretroviral Therapy.
- Some experts would consider monitoring HgbA1C in children at risk for prediabetes/diabetes, rather than routine blood glucose.
- The Panel added a statement to point out that periodic measurements of body weight—important for dose modification in the rapidly growing infant and to monitor for excessive weight gain as a possible adverse effect of some antiretroviral (ARV) drugs—are not possible with telemedicine visits.
- The Panel also noted that children with HIV who are relocating from outside the United States may benefit from thyroid function studies and additional evaluations, such as screening for tuberculosis, gastrointestinal parasites, hepatitis infection, and lead level.

[What to Start: Regimens Recommended for Initial Therapy of Antiretroviral-Naive Children](#)

- The Panel has updated its recommendations for several drugs following recent FDA approvals of new pediatric dosing strength formulations for bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF, Biktarvy) and emtricitabine/tenofovir alafenamide (FTC/TAF, Descovy) and the approval of doravirine (DOR) and doravirine/emtricitabine/tenofovir disoproxil fumarate (DOR/FTC/TDF, Delstrigo) for pediatric use.
 - The Panel now recommends BIC/FTC/TAF as a *Preferred* integrase strand transfer inhibitor (INSTI)-based regimen for children aged ≥ 2 years and weighing ≥ 14 kg (**AI***). Previously, this regimen was limited to use in children aged ≥ 6 years and weighing ≥ 25 kg.

- DOR plus a two-nucleoside reverse transcriptase inhibitor (NRTI) backbone is now recommended as an *Alternative* non-nucleoside reverse transcriptase inhibitor (NNRTI)–based regimen for children and adolescents weighing ≥ 35 kg (**BI***). The Panel’s recommendation is supported by data from studies that evaluated the efficacy and tolerability of this drug in adults, as well as early findings from pediatric pharmacokinetic (PK) studies. DOR is also available in a FDC tablet as DOR/FTC/TDF (Delstrigo).
- FTC/TAF (Descovy) is recommended as a *Preferred* dual-NRTI combination in children and adolescents weighing ≥ 14 kg when used with an INSTI or NNRTI. Use of Descovy with an INSTI or NNRTI was previously limited to children weighing ≥ 25 kg.
- The Panel recommends abacavir (ABC) plus lamivudine (3TC) or FTC as a *Preferred* dual-NRTI combination in children aged ≥ 3 months (**AI**) and now recommends it from birth in full-term infants aged < 3 months (**BIII**). A negative test for the HLA-B5701 allele should be obtained before starting ABC, regardless of age. Previously, the Panel recommended ABC for infants aged ≥ 1 month. The Panel changed its recommendation based on PK modeling of neonatal ABC dosing to target adult plasma ABC exposures and on observational data supporting safety of ABC in full-term neonates aged < 1 month. An ABC dosing recommendation based on PK simulation models has been endorsed by the World Health Organization using weight-band dosing for full-term infants from birth to 1 month of age. The FDA has approved ABC for use in children aged ≥ 3 months.

What Not to Start: Regimens Not Recommended for Use in Antiretroviral-Naive Children

- The section text and Table 9. Antiretroviral Regimens or Components That Are Not Recommended for Initial Treatment of HIV Infection in Children and Adolescents have been updated to include two-drug ARV regimens, as well as three drugs that are not FDA approved for use in ARV-naive children or adults: cabotegravir, fostemsavir, and ibalizumab.
- Any ARV regimen containing both TDF and TAF has been added to Table 10. Antiretroviral Regimens or Components That Are Never Recommended for Treating HIV in Children and Adolescents.

Special Considerations for Antiretroviral Therapy Use in Adolescents with HIV

- This section has been updated to include additional content about substance use concerns in adolescents.

Adherence to Antiretroviral Therapy in Children and Adolescents with HIV

- This section has been revised to provide recent data about the following adherence interventions: smartphone-based reminders, peer support interventions, modified directly administered ARV therapy, and a multicomponent intervention—including remote coaching, electronic dose monitoring, and tailored outreach.

Management of Medication Toxicity or Intolerance

- The Tables for Antiretroviral Therapy–Associated Adverse Effects and Management have been updated. Recommendations have been reviewed with updates regarding associated ARVs, onset

and clinical manifestations, estimated frequency, risk factors, prevention and monitoring, and management where indicated.

- [Table 15a. Central Nervous System Toxicity](#)
- [Table 15b. Dyslipidemia](#)
- [Table 15c. Gastrointestinal Effects](#)
- [Table 15d. Hematologic Effects](#)
- [Table 15e. Hepatic Events](#)
- [Table 15f. Insulin Resistance, Asymptomatic Hyperglycemia, Diabetes Mellitus](#)
- [Table 15g. Lactic Acidosis](#)
- [Table 15h. Lipodystrophies and Weight Gain](#)
- [Table 15i. Nephrotoxic Effects](#)
- [Table 15j. Osteopenia and Osteoporosis](#)
- [Table 15k. Rash and Hypersensitivity Reactions](#)

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 ARV options based on recent FDA approvals of drugs for pediatric use and changes to Panel recommendations for the use of ARV drugs. This information is summarized under the headings for [What to Start: Regimens Recommended for Initial Therapy of Antiretroviral-Naive Children](#) and [Appendix A: Pediatric Antiretroviral Drug Information](#).

Appendix A: Pediatric Antiretroviral Drug Information

Drug sections and FDC [Table 1](#) and [Table 2](#) in this appendix were reviewed and updated to include recent pediatric data and dosing and safety information, plus FDA approvals of new formulations and FDCs. Significant changes are summarized below:

- Although ABC is not approved by the FDA for use in infants aged <3 months, the [Abacavir](#) section has been updated to include a dosing recommendation for full-term infants aged <1 month. The Panel's recommendation is based on data from PK modeling of neonatal ABC dosing to target adult plasma ABC exposures and on observational data supporting safety of ABC in full-term neonates aged <1 month. The Panel has also revised its previous dosing recommendation for full-term infants aged ≥1 month to <3 months based on modeling data provided by the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) P1106 study and two observational cohorts.
- The [Bictegravir](#), [Emtricitabine](#), and [Tenofovir Alafenamide](#) sections have been updated to incorporate FDA approval of a new pediatric dosing strength for Biktarvy (BIC 30 mg/FTC 120 mg/TAF 15 mg) for use in children aged ≥2 years and weighing ≥14 kg to <25 kg.

- The [Emtricitabine](#) and [Tenofovir Alafenamide](#) sections have been updated to incorporate FDA approval of a new pediatric dosing strength for Descovy (FTC 120 mg/TAF 15 mg) for use in children weighing ≥ 14 kg to < 25 kg.
- The [Doravirine](#), [Lamivudine](#), and [Tenofovir Disoproxil Fumarate](#) sections have been updated following the FDA approval of DOR and the FDC tablet DOR/3TC/TDF (Delstrigo) for use in children and adolescents weighing ≥ 35 kg who are ARV-naive or have been virologically suppressed (HIV RNA < 50 copies/mL) on a stable ARV regimen with no history of treatment failure and no known mutations associated with resistance to DOR or to the individual components of Delstrigo.
- The [Cabotegravir](#) and [Ralpivirine](#) sections have been revised to incorporate the FDA approval of the long-acting injectable regimen, Cabenuva (co-packaged cabotegravir [CAB] and rilpivirine [RPV] suspensions), for treatment of HIV in children and adolescents aged ≥ 12 years and weighing ≥ 35 kg with HIV RNA levels < 50 copies/mL on a stable ARV regimen, no history of treatment failure, and no known or suspected resistance to CAB or RPV. The FDA has also approved the oral formulation of CAB (Vocabria) for this group of children and adolescents. Oral lead-in dosing of CAB and RPV is now an option, rather than a requirement, when starting Cabenuva; patients may proceed to Cabenuva directly from their current ARV regimen.
- In the [Efavirenz](#) (EFV) section, the Panel has added a recommendation to measure vitamin D in children receiving EFV and to prescribe vitamin D supplementation for those with vitamin D deficiency (see [Table 15j. Osteopenia and Osteoporosis](#) for additional information). This recommendation is based on studies in adults showing that use of EFV is associated with low vitamin D levels, as well as studies that have found an association between EFV use and low bone mineral density.
- Some text was removed from the [Lopinavir/Ritonavir](#) (LPV/r) section to clarify that the Panel does not endorse use of LPV/r in neonates before a postmenstrual age of 42 weeks and a postnatal age of at least 14 days due to the risk of metabolic and cardiac toxicity.
- The Panel has revised the [Nevirapine](#) (NVP) section to include dosing recommendations for preterm infants at a gestational age of 32 weeks to < 34 weeks based on review of PK modeling and simulation data. This dosing strategy has not been evaluated in clinical trials and is not approved by the FDA. Previously, the Panel's dosing recommendations for preterm infants were limited to a gestational age of 34 weeks to < 37 weeks.

December 30, 2021

[Maternal HIV Testing and Identification of Perinatal HIV Exposure](#)

- Section content has been updated to include a list of states with statutes or regulations that require repeat HIV testing in the third trimester and to recommend that this testing be offered to pregnant people who perceive themselves at increased risk for HIV infection.

Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection

- The Panel has clarified when viral load tests should be done to inform decisions about ARV prophylaxis or presumptive HIV therapy for infants with perinatal HIV exposure, changing from “near delivery” to “within 4 weeks of delivery.”
- Table 11. Antiretroviral Drug Dosing Recommendations for Newborns has been updated to include ABC dosing recommendations for infants and NVP dosing for infants ≥ 32 to < 34 weeks’ gestation at birth. The Panel does not recommend ABC for presumptive HIV therapy. However, in situations where Zidovudine (ZDV) is not available or the infant has ZDV-associated toxicity, ABC could be considered an alternative to ZDV. Because of ABC-associated hypersensitivity, negative testing for HLA-B5701 allele should be confirmed prior to administration of ABC.