



Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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What's New in the Pediatric Guidelines (Last updated March 1, 2016; last reviewed March 1, 2016)

Key changes made by the Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children (the Panel) to update the March 5, 2015, Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection are summarized below. Text and references have been updated throughout the document to include new data and publications where relevant. Minor changes and edits have been made to enhance clarity and facilitate use of the Guidelines. All new changes are highlighted.

Identification of Perinatal HIV Infection

- The Panel has provided additional explanation and has emphasized the new recommendations to use the fourth generation HIV testing platform as the initial test of choice for pregnant HIV-negative women.

Diagnosis of HIV Infection

- The Panel has clarified that recommended virologic testing at 1–2 months of age is preferably scheduled 2–4 weeks after cessation of antiretroviral (ARV) prophylaxis. In such situations, the test would be obtained at 6 weeks (in the case of 4 weeks of neonatal ARV prophylaxis) or at 2 months (in the case of 6 weeks of ARV prophylaxis).
- The Panel has updated information about Food and Drug Administration (FDA)-approved HIV diagnostic tests.

Clinical and Laboratory Monitoring of Pediatric HIV Infection

- Content has been reorganized according to the Panel's bulleted recommendations, followed by information about general considerations in immunologic and HIV RNA monitoring.
- The Panel's bulleted recommendations about antiretroviral drug resistance testing, as part of laboratory monitoring, have been moved into this section.
- Changes have also been made in accordance with the Panel's revised recommendations about when to initiate therapy in antiretroviral naive children.

When to Initiate Therapy in Antiretroviral-Naive Children

- Based on data from the multinational START and PENPACT1 trials, the Panel now recommends antiretroviral treatment (ART) for all HIV-infected children, regardless of clinical symptoms, viral load or CD4 T lymphocyte (CD4) count. The strength of the Panel's recommendations varies by age and pretreatment CD4 cell count due to fewer available pediatric data regarding benefits and risks of therapy in asymptomatic HIV-infected children than in adults.
- The text offers guidance on the urgency of initiation of ART based on age, clinical status and CD4 cell counts.

What Drugs to Start: Initial Combination Therapy for Antiretroviral Treatment-Naive Children

- Content has been reorganized to enhance usability, and a figure has been added to provide an overview of Preferred and Alternative regimens for initiation of ART in treatment -naive children.
- The Panel has added the tenofovir alafenamide (TAF) containing fixed dose combination tablet elvitegravir/cobicistat/emtricitabine/TAF (Genvoya) as a preferred integrase strand transfer inhibitor (INSTI) regimen in adolescents 12 years and older.

- Darunavir boosted with ritonavir is now considered a preferred protease inhibitor (PI) in children and adolescents aged 3 years and older.
- Dolutegravir is now considered a preferred INSTI in adolescents aged 12 years and older.
- Raltegravir is now considered a preferred INSTI in children aged 2 to 12 years.
- The Panel has determined that fosamprenavir, nelfinavir, stavudine, and unboosted atazanavir should not be used for initial therapy; these drugs have been moved to the “What Not to Start” section.

Specific Issues in Antiretroviral Therapy for Neonates

- The Panel has updated this section with information about a recent study of nevirapine pharmacokinetics in premature infants and the dosing regimen for infants born between 34 and 37 weeks gestation to be studied in IMPAACT P1115.

Specific Issues in Antiretroviral Therapy for HIV-Infected Adolescents

- The Panel has reviewed and updated this section to harmonize with and complement content in the [Adult and Adolescent Antiretroviral Guidelines](#).
- The Panel has changed to the use of sexual maturity rating (SMR), rather than Tanner staging, and has clarified that adolescents in early puberty (i.e., SMR I–III) should receive pediatric dosing, whereas those in late puberty (i.e., SMR IV–V) should follow adult dosing guidelines.
- Content has been added about timing and selection of ART, adherence concerns, and sexually transmitted infections in adolescents. Additional guidance has been provided about approaches to improve retention in care and minimize the risk of interruptions to ART during the transition from pediatric to adult HIV care settings.

Management of Medication Toxicity

- Toxicity table sections have been reviewed and updated throughout. Examples of notable changes include the following:
 - The Central Nervous System Toxicity Table has been updated to include dolutegravir-associated neuropsychiatric symptoms and new data on neuropsychiatric symptoms associated with rilpivirine in adolescents.
 - The Dyslipidemia Toxicity Table now includes information about TAF when given in combination with elvitegravir, cobicistat, and emtricitabine as a single tablet regimen (Genvoya) in adults and adolescents.
 - The Rash and Hypersensitivity Toxicity Table has been updated to include rash with hepatic dysfunction associated with dolutegravir and information about drug rash/reaction with eosinophilia and systemic symptoms (DRESS) associated with several different drugs.

Role of Therapeutic Drug Monitoring in the Management of Pediatric HIV Infection

- The Panel has condensed the section on the role of therapeutic drug monitoring by moving some information to relevant drug sections.

Antiretroviral Drug-Resistance Testing

- The Antiretroviral Drug-Resistance Testing section has been deleted. This content has been integrated in relevant sections throughout the guidelines with links to detailed information available in the [Adult and Adolescent Antiretroviral Guidelines](#) section on [Drug-Resistance Testing](#).

Pediatric Antiretroviral Drug Information

Drugs sections have been reviewed and updated to include new pediatric data and dosing information. Weight parameters or sexual maturity ratings for adolescent dosing have been added to drug tables where indicated. Information about Genvoya, a fixed dose combination of elvitegravir, cobicistat, emtricitabine, and TAF (approved by the FDA in November 2015), has been incorporated into each of those drug sections. A new drug section was added for TAF.

Nucleoside Analogue Reverse Transcriptase Inhibitors

- **Abacavir:** Children weighing at least 14 kg who can be treated with pill formulations can initiate therapy with once daily abacavir dosing. However, initiation of therapy with once daily abacavir liquid is not generally recommended. Refined guidance has been provided on the transition from twice daily to once daily dosing of abacavir after 6 months in clinically stable patients with undetectable viral load and stable CD4 cell counts. The section was also revised to follow FDA recommendations for use of adult doses of abacavir in children and adolescents weighing 25 kg or more.
- **Emtricitabine:** The section was updated to include information about the fixed dose combination, Genvoya, for use in persons aged ≥ 12 years and weighing at least 35 kg.
- **Lamivudine:** Based on a study demonstrating lower bioavailability of lamivudine oral solution versus tablets in pediatric patients, a statement was added to reinforce that once daily administration is not generally recommended in infants and young children being treated with lamivudine oral solution. The section was updated to follow FDA recommendations for use of adult doses of lamivudine in children weighing 25 kg or more.
- **TAF:** A new section was added for TAF based on FDA approval of the fixed dose combination Genvoya (emtricitabine, elvitegravir, cobicistat, and TAF) for use in persons aged ≥ 12 years and weighing at least 35 kg.
- **Tenofovir Disoproxil Fumarate (TDF):** The discussion about monitoring for potential renal toxicity has been updated. In clinical practice, renal tubular damage associated with TDF is perhaps easiest to identify using a renal dipstick to identify normoglycemic glycosuria and proteinuria.

Non-Nucleoside Analogue Reverse Transcriptase Inhibitors

- **Nevirapine:** The Panel has added information about the investigational dose of nevirapine (not FDA approved) for premature infants born at 34–37 weeks gestation and less than one month of age.
- **Rilpivirine:** Dosing information has been updated to follow the FDA recommendation for use of adult doses of rilpivirine in adolescents 12 years and older weighing at least 35 kg.

Protease Inhibitors

- **Atazanavir:** The section has been updated based on FDA approval of atazanavir oral powder for use in children 3 months of age and older weighing at least 5 kg and in children weighing 25 kg or more who cannot swallow pills. Atazanavir oral powder must be given with ritonavir. Information about Evotaz, a fixed dose combination of atazanavir and cobicistat approved by FDA, has also been added.
- **Darunavir:** Dosing information has been added for adolescents 12 years of age and older weighing at least 30 kg with at least one darunavir-associated mutation.

Integrase Strand Transfer Inhibitors

- **Elvitegravir:** The section was updated to include information about the fixed dose combination, Genvoya, for use in persons aged ≥ 12 years and weighing at least 35 kg.

Pharmacokinetic Enhancers

- **Cobicistat:** The section was updated to include information about the fixed dose combination, Genvoya, for use in persons aged ≥ 12 years and weighing at least 35 kg.