



Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Management of Children Receiving Antiretroviral Therapy (Last updated September 12, 2019; last reviewed September 12, 2019)

In the United States, the majority of children living with HIV are receiving antiretroviral therapy (ART), making treatment-experienced children the norm. Providers may consider antiretroviral (ARV) regimen changes for the following reasons:

- Treatment Simplification: Modifying ARV regimens in children who are currently receiving effective ART in order to simplify the regimen.
- Treatment Optimization: Increasing the treatment potency or barrier to resistance of an effective, but older or potentially fragile, regimen or improving the adverse event profile.
- Toxicity Management: Recognizing and managing ARV drug toxicity or intolerance (see [Management of Medication Toxicity or Intolerance](#)).
- Treatment Failure: Recognizing and managing treatment failure (see [Recognizing and Managing Antiretroviral Treatment Failure](#)).

Modifying Antiretroviral Regimens in Children with Sustained Virologic Suppression on Antiretroviral Therapy

Panel's Recommendations

- Children who have sustained virologic suppression on their current antiretroviral (ARV) regimen should be regularly evaluated for opportunities to change to a new regimen that facilitates adherence, simplifies administration, increases ARV potency or barrier to resistance, and decreases the risk of drug-associated toxicity (**AII**).
- Before making changes to a patient's regimen, clinicians must carefully consider the patient's previous regimens, past episodes of ARV therapy failure, prior drug resistance test results, and the patient's ability to tolerate the new drug regimen (**AIII**). Archived drug resistance can limit the antiviral activity of a new drug regimen.
- Children should be carefully monitored after a change in treatment. Viral load measurement is recommended 2 weeks to 4 weeks after a change in a child's ARV regimen (**BIII**).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials in children[†] with clinical outcomes and/or validated endpoints; I* = One or more randomized trials in adults with clinical outcomes and/or validated laboratory endpoints with accompanying data in children[†] from one or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; II = One or more well-designed, nonrandomized trials or observational cohort studies in children[†] with long-term outcomes; II* = One or more well-designed, nonrandomized trials or observational studies in adults with long-term clinical outcomes with accompanying data in children[†] from one or more similar nonrandomized trials or cohort studies with clinical outcome data; III = Expert opinion

[†] Studies that include children or children/adolescents, but not studies limited to post-pubertal adolescents

Clinicians choose initial antiretroviral (ARV) regimens for children with HIV by evaluating the pharmacokinetic, safety, and efficacy data for the drugs that are available in formulations that are suitable for the child's age and weight at the start of treatment. New ARV options may become available as children grow and learn to swallow pills, and as new drugs, drug formulations, and data become available. Even in cases where patients have achieved sustained virologic suppression (e.g., suppression for 6 months–12 months) on their current regimen, clinicians should consider switching patients to new ARV regimens in order to permit the use of pills instead of liquids, reduce pill burden, allow the use of once-daily medications, reduce the risk of adverse events, minimize drug interactions, and align a child's regimen with widely used, efficacious adult regimens.¹ Often the changes enhance adherence and improve quality of life.²

Treatment Simplification

Many children with HIV must initiate treatment with twice-daily dosing, and regimens may include a variety of drug formulations, depending on which formulations are available for a child's age and weight. Clinicians

should regularly review treatment options as children grow, because it may be possible to simplify dosing using coformulated drugs and/or once-daily regimens (see Table 16 below). Clinicians should also consider a child's antiretroviral therapy (ART) history and resistance test results. Small studies have shown that children who achieve virologic suppression using twice-daily dosing for certain ARV drugs (i.e., abacavir, nevirapine) maintain virologic suppression when they switch from twice-daily regimens to once-daily regimens (see the [abacavir](#) and [nevirapine](#) drug sections and fixed-dose combinations [FDCs] in Table 1 and Table 2). However, these studies reported mixed results when switching the dosing for lopinavir/ritonavir (LPV/r) from twice daily to once daily; therefore, once-daily dosing of LPV/r **is not recommended**.³⁻⁷

Treatment Optimization

Several studies have addressed switching ARV regimen components in children with sustained virologic suppression. Treatment optimization may include improving the potency of regimen, improving a child's growth or other health outcomes, or maximizing palatability. Despite concerns for drug class resistance, the results of the NEVEREST 2 study demonstrated that young children (i.e., those aged <2 years) with virologic suppression who switch from LPV/r to a nevirapine-based regimen can maintain virologic suppression as well as those who continue taking LPV/r, provided that they have good adherence and no baseline resistance to nevirapine.^{8,9} In the NEVEREST 3 study, children aged ≥ 3 years who had a history of exposure to nevirapine and who achieved virologic suppression on a LPV/r-based regimen maintained virologic suppression when switched from LPV/r to an efavirenz-based regimen.¹⁰⁻¹² Similarly, in the NEVEREST 2 study, children who switched to a nevirapine-based regimen showed better immune and growth responses than those who stayed on a LPV/r regimen.⁸ Replacing LPV/r with an equally potent protease inhibitor (PI) (e.g., darunavir, atazanavir) or an integrase strand transfer inhibitor (INSTI) (e.g., elvitegravir, raltegravir, dolutegravir) would likely be effective, but these substitutions have not been directly studied in children.

Toxicity Management

Several studies in small cohorts of children have demonstrated sustained virologic suppression and reassuring safety outcomes when drugs that have greater long-term toxicity risks are replaced with drugs that are thought to have lower toxicity risks (e.g., replacing stavudine with tenofovir disoproxil fumarate, tenofovir alafenamide, zidovudine, or abacavir; replacing PIs with non-nucleoside reverse transcriptase inhibitors), including improved lipid profiles.¹³⁻¹⁷

Regimens That Are Not Recommended for Use in Children

Dual-therapy and monotherapy PI regimens (darunavir/ritonavir, LPV/r, atazanavir/ritonavir)^{18,19} and monotherapy INSTI regimens (dolutegravir)^{20,21} have been used to simplify or reduce the toxicity of regimens in adult patients who have sustained virologic suppression, with varying success. These strategies are still being explored, but they are not currently recommended as management strategies in children due to the lack of data.^{19,22-25} The FDC of dolutegravir/rilpivirine (Juluca), a nucleoside-sparing, dual-therapy regimen, was recently approved by the Food and Drug Administration as a complete regimen to replace the current ARV regimen in patients who have been virologically suppressed (HIV RNA <50 copies/mL) on a stable ARV regimen for at least 6 months with no history of treatment failure. This approval was based on two Phase 3 clinical trials, SWORD-1 and SWORD-2, in which treatment-experienced adults who were virologically suppressed on three-drug or four-drug regimens were randomized to either switch to dolutegravir/rilpivirine or to stay on their original regimens. Results from these trials showed similar rates of virologic suppression in both groups (noninferiority) through 48 weeks.²⁶ There are no equivalent data for this drug combination in pediatric patients. The Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV (the Panel) usually endorses the use of adult formulations in adolescents, and this product may be appropriate for certain adolescents. However, because this treatment simplification strategy has not been evaluated in adolescents, who may have difficulties adhering to therapy, the Panel does not recommend use of the FDC dolutegravir/rilpivirine (Juluca) in adolescents and children until more data are available.

Potential Antiretroviral Drug Switches in Children with Virologic Suppression

Table 16 contains examples of potential ARV changes in children with sustained virologic suppression on their current regimen for the purposes of treatment simplification, optimization, or reduced toxicity. When considering such a change, a clinician should first ensure that a recent viral load test indicates that the child is not experiencing virologic failure and that the child has a reliable history of good adherence. It is also critical to consider ART history, tolerability, and all prior drug resistance test results in order to avoid choosing new ARV drugs for which archived drug resistance would re-emerge and limit the activity of the regimen.²⁷⁻³¹ The evidence that supports many of these ARV changes is indirect, extrapolated from data about drug performance during initial therapy or follow-up therapy after treatment failure. When such changes are made, careful monitoring (e.g., taking a viral load measurement 2 weeks–4 weeks after making the switch to the new regimen) is important to ensure that virologic suppression is maintained.

Table 16. Examples of Changes in Antiretroviral Regimen Components for Children with Sustained Virologic Suppression (page 1 of 3)

Note: This list is not exhaustive and does not necessarily contain all potential treatment options. Instead, it provides examples of changes that could be made. The table only includes information about switching between ARV drugs; **it does not include all the information that clinicians should consider before prescribing these drugs.** Please refer to individual drug sections, [Table 1](#), and [Table 2](#) in [Appendix A: Pediatric Antiretroviral Drug Information](#) for further information about the use of specific ARV drugs and FDC formulations.

Current ARV Drug(s)	Age, Weight, and SMR Requirements	Potential ARV Drug Switch	Comment
NRTIs			
ABC or 3TC Twice Daily	Aged ≥1 year	ABC once daily	See the abacavir ^a and lamivudine sections.
	Aged ≥3 years	3TC once daily	
ZDV, ddl, or d4T^b	Aged ≥3 months	ABC	Less long-term mitochondrial toxicity. Children aged ≥1 year can take ABC once daily.
	Aged ≥2 years Weighing 17 kg to <25 kg	TDF	TDF is a reasonable, once-daily option for HLA-B*5701–positive children for whom ABC is not recommended. TDF is available in low-strength tablets alone or in combination with FTC.
	Aged ≥2 years Weighing ≥25 kg	TAF ^c	Less long-term mitochondrial toxicity. Once-daily dosing. Coformulation with other ARV drugs can further reduce pill burden. TAF is preferred over TDF because of the lower risk of bone and renal toxicity.
NNRTIs			
NVP	Any age (starting at full-term birth) and weighing ≥2 kg	RAL ^d	RAL has potentially greater barrier to resistance than NVP. Both are dosed twice daily in children.
EFV	Aged ≥3 months Weighing ≥5 kg	ATV/r	ATV/r has a potentially greater barrier to resistance; however, taking ATV/r may be difficult for some patients, as ATV oral powder must be mixed with food or a beverage before administration, and the palatability of the RTV oral solution is poor.
	Aged ≥3 years Weighing ≥10 kg	DRV/r	DRV/r has a potentially greater barrier to resistance. DRV/r is administered twice daily to patients aged <12 years, but may be administered once daily in children aged ≥12 years who do not have DRV resistance mutations.
	Weighing ≥25 kg	BIC as Biktarvy	Once-daily dosing. BIC is available as a component of the FDC BIC/FTC/TAF (Biktarvy), which is a complete ARV regimen that can be taken with or without food.
	Weighing ≥25 kg	EVG as Genvoya	EVG is available as a component of the FDC EVG/COBI/FTC/TAF (Genvoya), which is a complete ARV regimen that must be taken with food.

Table 16. Examples of Changes in Antiretroviral Regimen Components for Children with Sustained Virologic Suppression (page 2 of 3)

Current ARV Drug(s)	Age, Weight, and SMR Requirements	Potential ARV Drug Switch	Comment
NNRTIs, continued			
EFV, continued	Weighing ≥ 20 kg	DTG	DTG is available as a smaller single-drug tablet or as an FDC, both of which can be dosed once daily if there are no concerns about INSTI resistance. DTG plus the weight-appropriate dose of FTC/TDF (Truvada) can be used in children weighing 20 kg to <25 kg. Higher barrier to resistance, which makes it a good choice for patients who have trouble with adherence. See the dolutegravir section for information regarding safety concerns when using DTG in adolescent females of childbearing potential and pregnant adolescents. ^e
	Aged ≥ 12 years Weighing ≥ 35 kg	RPV	RPV may improve lipid levels.
PIs			
LPV/r Twice Daily	Any age (starting at full-term birth) and weighing ≥ 2 kg	RAL ^d	Better palatability. RAL HD can only be given once daily in children weighing >50 kg. Unlike LPV/r, the use of RAL is not restricted to infants with a corrected gestational age of >42 weeks. RAL granules may be difficult to dose for some caregivers.
	Aged ≥ 3 years Weighing ≥ 10 kg	EFV	Once-daily dosing. Better palatability. Lower incidence of adverse lipid effects. See the efavirenz section in Appendix A: Pediatric Antiretroviral Drug Information regarding concerns about EFV dosing for children aged <3 years.
	Aged ≥ 3 months Weighing ≥ 5 kg	ATV/r	Once-daily dosing. ATV/r may improve lipid levels; however, taking ATV/r may be difficult for some patients, as ATV oral powder must be mixed with food or a beverage before administration, and the palatability of the RTV oral solution is poor.
	Aged ≥ 3 years Weighing ≥ 10 kg	DRV/r	DRV/r may improve lipid levels. DRV/r is administered twice daily to patients aged <12 years, but may be administered once daily in children aged ≥ 12 years who do not have DRV resistance mutations.
	Weighing ≥ 25 kg	EVG as Genvoya	EVG is available as a component of the FDC EVG/COBI/FTC/TAF (Genvoya), which is a complete ARV regimen that must be taken with food.
	Weighing ≥ 20 kg	DTG	Once-daily dosing if not concerned about INSTI resistance. May be better tolerated, and can be given as an FDC to children weighing ≥ 25 kg. DTG plus the weight-appropriate dose of FTC/TDF (Truvada) can be used in children weighing 20 kg to <25 kg. See the dolutegravir section for information regarding safety concerns when using DTG in female adolescents of childbearing potential and pregnant adolescents. ^e
	Aged ≥ 12 years Weighing ≥ 35 kg	RPV	May be better tolerated.
	Weighing ≥ 25 kg	BIC as Biktarvy	Once-daily dosing. BIC is available as a component of the FDC BIC/FTC/TAF (Biktarvy), which is a complete ARV regimen that can be taken with or without food.
Other			
Any Multi-Pill and/or Twice-Daily Regimen	Weighing ≥ 25 kg	EVG/COBI/FTC/TAF (Genvoya)	Once-daily dosing. Single pill. Alignment with adult regimens. Must be taken with food.
	Weighing ≥ 25 kg	FTC/TAF ^e (Descovy) plus DTG	Once-daily dosing. This regimen may be more desirable because of smaller pill sizes, but it has a higher pill burden (two pills instead of one). Aligns a child's regimen with an efficacious regimen that is used in adults. See the dolutegravir section for information regarding safety concerns when using DTG in female adolescents of childbearing potential and pregnant adolescents. ^e

Table 16. Examples of Changes in Antiretroviral Regimen Components for Children with Sustained Virologic Suppression (page 3 of 3)

Current ARV Drug(s)	Age, Weight, and SMR Requirements	Potential ARV Drug Switch	Comment
Other, continued			
Any Multi-Pill and/or Twice-Daily Regimen, continued	Weighing ≥35 kg SMR 4 or 5	EVG/COBI/FTC/TDF (Stribild)	Once-daily dosing. Single pill. Aligns a child's regimen with an efficacious regimen that is used in adults. Must be taken with food. Renal and bone toxicity limit its use.
	Aged ≥12 years Weighing ≥35 kg	FTC/RPV/TAF (Odefsey)	Once-daily dosing. Single pill. Aligns a child's regimen with an efficacious regimen that is used in adults. Must be taken with food at a consistent time daily.
	Weighing ≥25 kg	BIC/FTC/TAF (Biktarvy)	Once-daily dosing. Single pill that can be taken with or without food.
	Aged ≥12 years Weighing ≥35 kg SMR 4 or 5	FTC/RPV/TDF (Complera)	Once-daily dosing. Single pill. Aligns a child's regimen with an efficacious regimen that is used in adults. Must be taken with food at consistent time daily.
	Weighing ≥25 kg	ABC/DTG/3TC (Triumeq)	Once-daily dosing. Single pill. Aligns a child's regimen with an efficacious regimen that is used in adults. Large pill size may be a deterrent. See the dolutegravir section for information regarding safety concerns when using DTG in female adolescents of childbearing potential and pregnant adolescents. ^e
	Weighing ≥40 kg SMR 4 or 5	EFV/FTC/TDF (Atripla)	Once-daily dosing. Single pill. Aligns a child's regimen with an efficacious regimen that is used in adults.

^a For infants and young children who are being treated with liquid formulations of ABC, initiation with once-daily ABC is not generally recommended. In clinically stable patients with undetectable viral loads who have had stable CD4 T lymphocyte cell counts for >6 months (24 weeks) on twice-daily ABC, the dose can be changed from twice daily to once daily.

^b d4T and ddl should be replaced with a safer drug **as soon as possible** because of concerns about long-term adverse effects (see [Archived Drugs](#) in [Appendix A: Pediatric Antiretroviral Drug Information](#)).

^c For children and adolescents weighing 25 kg to <35 kg, TAF can be used in combination with an INSTI or an NNRTI, but not a boosted PI. For children and adolescents weighing ≥35 kg, TAF can be used in combination with an INSTI, NNRTI, or a boosted PI.

^d RAL is recommended for twice-daily use in children. Chewable tablets can be used in children weighing ≥11 kg. RAL HD once daily is **only** recommended for virologically suppressed children weighing ≥50 kg.

^e Because of recent concerns about the potential for neural tube defects in infants born to women who conceived while taking regimens that contained dolutegravir, this drug should be prescribed with caution in female adolescents. Specific recommendations about the initiation and use of DTG in women of childbearing potential and in pregnant women are available in the Adult and Adolescent Antiretroviral Guidelines (see [Table 6b](#) and [Adolescents and Young Adults with HIV](#)) and in the Perinatal Guidelines (see [Teratogenicity and Recommendations for the Use of Antiretroviral Drugs in Pregnancy](#)).

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; BIC = bictegravir; COBI = cobicistat; d4T = stavudine; ddl = didanosine; DRV/r = darunavir/ritonavir; DTG = dolutegravir; Efavirenz = efavirenz; EVG = elvitegravir; FDA = Food and Drug Administration; FDC = fixed-dose combination; FTC = emtricitabine; HLA = human leukocyte antigen; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SMR = sexual maturity rating; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; ZDV = zidovudine

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