Management of Children Receiving Antiretroviral Therapy

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In the United States, most children 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 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 evaluated regularly for opportunities to change to a new regimen that facilitates adherence, simplifies administration, increases ARV potency or barrier to drug resistance, and decreases the risk of drug-associated toxicity (AII). • Before changing a patient's ARV regimen, clinicians must carefully consider the patient's previous regimens, past episodes of ARV therapy failure, prior drug-resistance test results, drug cost, and insurance coverage, as well as 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 monitored carefully after a change in treatment. Viral load measurement is recommended 2 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 postpubertal adolescents*

Clinicians choose initial ARV regimens for children with HIV by evaluating the pharmacokinetic, safety, and efficacy data for the drugs that are available in formulations suitable for the child's age and weight at the start of treatment. New ARV drug 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 wherein patients have achieved sustained virologic suppression (i.e., suppression for 6–12 months) on their current regimen, clinicians should consider switching patients to new ARV regimens 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] These changes often enhance adherence and improve quality of life.[2]

Treatment Simplification

Many infants and children with HIV initiated treatment with twice-daily dosing (especially prior to the approval of integrase strand transfer inhibitor [INSTI] medications for pediatric use), and regimens included a variety of drug formulations, depending on which formulations were 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 18 below). Clinicians also should consider a child's ART history, drug-resistance test results, and ability to swallow tablets. Small studies have shown that children who achieve virologic suppression using twice-daily dosing for certain ARV drugs (e.g., abacavir [ABC]) maintain virologic suppression when they are switched from twice-daily dosing to once-daily dosing of the same drugs (see the Abacavir and Nevirapine sections and fixed-dose combinations [FDCs] in Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets and Appendix A, Table 2. Antiretroviral Fixed-Dose Combination Tablets: Minimum Body Weights and Consideration for Use in Children and Adolescents). 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.**[3-6]

Long-acting injectable ARV medications may be considered a treatment simplification approach for some virologically suppressed adolescents. The co-packaged, two-drug injectable ARV regimen of cabotegravir and rilpivirine (CAB and RPV; Cabenuva) is approved by the U.S. Food and Drug Administration (FDA) for use in children weighing ≥35 kilograms and ≥12 years of age, with viral suppression (defined as <50 copies/mL), on a stable ARV regimen, without a history of treatment failure, and without known or suspected drug resistance to either drug. Studies in adults—such as the First Long-Acting Injectable Regimen (FLAIR) and Antiretroviral Therapy as Long-Acting Suppression (ATLAS) trials—have demonstrated non-inferiority in those receiving monthly CAB and RPV injections compared to adults who stayed on a daily three-drug oral regimen.[7,8] Similarly, in the ATLAS-2M trial, injections of CAB and RPV every 2 months were found to be non-inferior to monthly injections.[9] The International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Study 2017 is currently evaluating CAB and RPV in children 12 to 18 years of age. Participants received one injection of either CAB or RPV, and early findings showed acceptable pharmacokinetics, lack of new safety concerns,[7,8] and high acceptability from youth and their caregivers. This ongoing study is now assessing the full two-drug injectable regimen. The Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV (the Panel) notes that significant questions remain, including whether an oral lead-in is beneficial and acceptable in the adolescent population, if there are additional adverse effects specific to the pediatric population, if a two-drug nucleoside-sparing regimen for children with significant ARV treatment history[10] will be effective, and what potential implementation challenges will emerge. However, given the FDA approval for those as young as 12 years of age, some providers may consider injectable CAB and RPV in adolescents who meet the approved indications and may benefit from a long-acting injectable regimen. See Cabotegravir and Rilpivirine for additional information about these drugs and the

dosing and administration of CAB and RPV, and see Management of the Treatment-Experienced Patient: Optimizing Antiretroviral Therapy in the Setting of Viral Suppression in the Adult and Adolescent ARV Guidelines for practical considerations.

Oral two-drug regimens, specifically nucleoside-sparing regimens, have some data supporting efficacy in pediatric and adult populations. A two-drug FDC tablet containing dolutegravir (DTG)/RPV—a nucleoside-sparing, dual-therapy regimen that is marketed as Juluca—is approved by the FDA as a complete regimen to replace the current ARV regimen in adult patients who have been virologically suppressed (HIV RNA <50 copies/mL) on a stable ARV regimen for at least 6 months and who have 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- or four-drug regimens were randomized either to switch to DTG/RPV (early-switch group) or stay on their original regimens through 48 weeks and then switch to DTG/RPV (late-switch group). Results from these trials showed similar rates of virologic suppression in both groups (non-inferiority) through 3 years of follow-up.[11-13] No equivalent data exist for this drug combination in pediatric patients, although a clinical trial to evaluate it is planned. The Panel usually endorses the use of adult formulations in adolescents, and this product may be appropriate for certain adolescents. DTG/RPV regimens could be useful in patients in whom there is concern for toxicity from nucleoside reverse transcriptase inhibitors (NRTIs). Additionally, early findings from the PENTA-17 SMILE study evaluating darunavir/ritonavir (DRV/r) combined with an INSTI, including 318 children aged 6 to 18 years in 11 countries, found that DRV/r plus an INSTI was non-inferior in maintaining virologic suppression at 48 weeks in participants without INSTI or protease inhibitor (PI) resistance.[14] Although the Panel does not recommend this combination for initial treatment, it might be considered in situations in which simplification or avoidance of NRTIs is desired. However, the Panel notes that adolescents may have difficulties adhering to therapy and recommends close monitoring with viral load testing.

Treatment Optimization

The aims of treatment optimization may include improving the potency of the regimen, improving a child's growth or other health outcomes through reduced drug side effects and/or better treated HIV, or maximizing palatability. More studies are directly evaluating treatment optimization in children, and early results support the safety and efficacy of regimen switches for those with viral suppression. Older studies have demonstrated sustained viral suppression and improved growth outcomes in young children who have demonstrated good adherence and no baseline resistance and who were switched from LPV/r-based regimens an efavirenz (EFV)-based regimen (NEVEREST 3).[15-17] Replacing LPV/r with EFV may provide some benefits (e.g., once-daily dosing and a different side-effect profile), but most pediatric HIV experts would prefer replacing LPV/r with an equally potent PI (e.g., darunavir [DRV] or atazanavir [ATV]) or an INSTI (e.g., elvitegravir [EVG], raltegravir, DTG, or bictegravir [BIC]), based on studies in adults and emerging evidence of non-inferiority or superiority in children.[18,19] Although not a switch trial, findings from the randomized controlled Once-daily DTG-based ART in Young People vs. Standard Therapy (ODYSSEY) study of more than 700 children aged <18 years in eight countries initiating DTG as first- or second-line therapy showed superior virologic and clinical outcomes in children randomized to optimization with DTG-based ART compared with those in the standard of care (PI- or non-nucleoside reverse transcriptase inhibitor [NNRTI]-based regimens), contributing to evidence supporting optimization with DTG-based regimens.[20] Results from the younger ODYSSEY cohort of children weighing between 3 and 14 kilograms also showed superiority of DTG-based ART compared to other regimens, more than 70% of which were PI-based regimens.[21] Additionally, several observational studies in sub-Saharan

Africa that are evaluating efforts to optimize pediatric ARV regimens have shown improved viral suppression rates in children that were switched to DTG-based regimens.[22-25] Similarly, a retrospective study from six African countries reporting on 2,655 children aged 0 to ≤19 years demonstrated sustained high levels of viral suppression in children optimized from NNRTI- and PI-based regimens to DTG-based regimens.[26] The INSTI-based FDC regimen BIC/emtricitabine (FTC)/tenofovir alafenamide (TAF) has also shown efficacy and high rates of long-term viral suppression in adolescents and children ≥2 years weighing 14 to <25 kilograms.[27,28] Similarly, EVG/cobicistat/FTC/TAF has shown efficacy in adolescents. Early results from small, randomized studies also show potential for switches to newer-generation NNRTI medications—such as rilpivirine (RPV)[29] and doravirine (DOR)[30]—in children and adolescents weighing ≥35 kg who have been virologically suppressed on a stable ARV regimen.

Toxicity Management

Several studies of 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, TAF, zidovudine, or ABC; replacing PIs with NNRTIs), including improved lipid profiles.[31-35] Similarly, adolescents who were switched from EFV to RPV, a newer generation of NNRTIs, showed similar rates of viral suppression with improved metabolic profiles and cognitive outcomes.[29] Additionally, studies in adults have shown improved tolerability, lipid profiles, and insulin sensitivity in patients who were switched from PIs to INSTIs,[36-40] and adults who were switched from EFV to an INSTI have shown improvement in neuropsychiatric symptoms. However, the use of INSTIs, as well as TAF, has been associated with weight gain in adults and adolescents, with emerging data showing an association in children.[41-45] Finally, NRTI-sparing regimens, including the dual-drug oral regimens (DRV and an INSTI or DTG/RPV) and the approved long-acting injectable regimen (CAB with RPV) described above, may be considered in patients with NRTI toxicity who otherwise are eligible for these complete ARV regimens. In a small subgroup analysis of the SWORD study, participants switched to DTG/RPV experienced small but statistically significant improvement in bone mineral density and bone turnover markers compared to those who continued on tenofovir disoproxil fumarate (TDF).[46] Of note, however, is that, although small in number, more participant adverse events that led to discontinuation were reported in the DTG/RPV arm (3%) than in the arm in which participants stayed on their current regimen (<1%).[11]

Treatment Failure

Treatment failure is another common reason providers change ARV regimens in children with HIV. This topic is covered in Recognizing and Managing Antiretroviral Treatment Failure.

Regimens That Are Not Recommended for Use in Children

Monotherapy PI regimens (DRV/r, LPV/r, ATV/r)[47,48] and monotherapy regimens of DTG[49,50] have been used to simplify or reduce the toxicity of regimens in adult patients who have sustained virologic suppression, but with varying success. These strategies are still being explored, but they are not currently recommended as management strategies in children because of the lack of data.[48,51-54]

Potential Antiretroviral Drug Switches in Children With Virologic Suppression

Table 18 below contains examples of potential ARV drug changes in children with sustained virologic suppression on their current regimen for the purpose 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 (assessed by self and parental report, pharmacy refill, prior viral loads, etc.). Among treatment-naive youth in the United States aged 13 to 24 years, some evidence exists that single-tablet regimens (STRs) improve the odds of viral suppression[55]; emerging evidence also supports the safety, efficacy, and tolerability of STRs in younger children.[56-58] Although these data have not been replicated in treatment-experienced adolescents, clinicians should consider using STRs in children and youth with sustained viral suppression because these regimens reduce pill burden and dosing frequency. Clinicians also must consider ART history, tolerability, ability to swallow tablets, and all prior drug-resistance test results to avoid choosing new ARV drugs for which archived drug resistance would reemerge and limit the activity of the regimen.[59-63] The evidence that supports many of these ARV changes is indirect, that is, 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 2–4 weeks after making the switch to the new regimen) is important to ensure that virologic suppression is maintained.

Table 18. Examples of Changes in Antiretroviral Regimen Components for Children With Sustained Virologic Suppression

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 includes information only about switching between ARV drugs; **it does not include all the information that clinicians should consider before prescribing these drugs, such as drug cost and the patient's insurance coverage.** Refer to the individual drug sections, Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets or as a Co-Packaged Formulation, by Drug Class, and Appendix A, Table 2. Antiretroviral Fixed-Dose Combination Tablets and Co-packaged Formulations: Minimum Body Weights and Considerations for Use in Children and Adolescents in Appendix A: Pediatric Antiretroviral Drug Information for further information about the use and administration of specific ARV drugs and FDC formulations.

For images of most of the ARV drugs listed in this table, see the Antiretroviral Medications section of the National HIV Curriculum. In addition, a resource from the United Kingdom illustrates the relative sizes of individual ARV drugs FDC tablets (see the ARV Chart in HIV i-Base). Although most of the drugs listed in that chart are the same as those in the United States, not all formulations available in the United States are included, and there are differences in a few of the brand names.

Current ARV Drug(s)	Age, Weight, and Sexual Maturity Rating Requirements	Potential ARV Drug Switch[a]	Comment
NRTIs			
ABC Twice Daily	Aged ≥3 months[b]	ABC once daily	See the Abacavir[b] section.

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Current ARV Drug(s)	Age, Weight, and Sexual Maturity Rating Requirements	Potential ARV Drug Switch[a]	Comment
3TC Twice Daily	Aged ≥3 years	3TC once daily	See the Lamivudine section.
	Any age (starting at full-term birth) Any weight	FTC once daily	See the Emtricitabine section.
ZDV	Aged ≥1 months[b]	ABC	Less long-term mitochondrial toxicity Children aged ≥3 months can take ABC once daily.
	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 and in whom ZDV is not tolerated. TDF is available as an oral powder and as low-strength tablets alone or in combination with FTC.
	Weighing ≥14 kg	TAF[c]	Less long-term mitochondrial toxicity. Once-daily dosing. Only available in 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, but it may be associated with weight gain and lipid abnormalities.
	Weighing ≥14 kg	FTC/TAF[c] (Descovy)	Once-daily dosing. This combination NRTI medication may be more desirable because of smaller pill size and reduced pill burden. Benefits as described for TAF.
Any NRTI	Aged ≥12 years Weighing ≥35 kg	CAB and RPV co-packaged regimen as Cabenuva	NRTI-sparing regimen. Long-acting injectable, complete ARV regimen requiring two IM injections every 1 to 2 months that together are an alternative to daily oral ARV regimens. Must consider prior history of treatment failure and known or suspected drug resistance to individual drugs. Injection site reactions are common but do not often result in discontinuation of the regimen. See Cabotegravir.
	Aged ≥12 years Weighing ≥35 kg	DTG/RPV (Juluca)	NRTI-sparing FDC that is a complete regimen. In addition to age and weight criteria (based on RPV component since DTG approved to younger age/lower weight), must be virologically suppressed (HIV RNA <50 copies/mL) on a stable ARV regimen for at least 6 months and without history of treatment failure. Should be taken with food. No pediatric data.
NNRTIs			
NVP or EFV	Any age (starting at full-term birth) Weighing ≥2 kg	RAL[d]	RAL is preferred over NVP in infants from birth to age 4 weeks who weigh ≥2 kg. Both are dosed twice daily in children. Note that DTG and BIC have a higher barrier to resistance than RAL. In a child >1 month of age, DTG is preferred. See DTG below.

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Current ARV Drug(s)	Age, Weight, and Sexual Maturity Rating Requirements	Potential ARV Drug Switch[a]	Comment
	Age ≥4 weeks Weighing ≥3 kg	DTG	DTG is available as a single drug in dispersible and film-coated tablet formulations, or as part of an FDC tablet, all of which can be dosed once daily if no documented resistance or history of failure with INSTI agents exists. DTG plus FTC/TAF (Descovy) in patients weighing at least 14 kg or the weight-appropriate dose of FTC/TDF (Truvada) can be used in children weighing 20 kg to <25 kg. DTG is available as a component of the FDC ABC/DTG/3TC, which is a complete ARV regimen that can be given to children weighing ≥10 to <25 kg in dispersible tablets (Triumeq PD) and to children and adolescents weighing ≥25 kg in a single tablet to be swallowed (Triumeq). Higher barrier to resistance, which makes it a good choice for patients who have poor adherence. May improve lipid levels. See the Dolutegravir section for more information.
	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 any DRV resistance mutations. Note that the palatability of the RTV oral solution is poor when considering administering to children not able to swallow tablets.
	Weighing ≥14 kg	BIC as Biktarvy	Once-daily dosing. BIC is available as a component of the FDC tablet BIC/FTC/TAF (Biktarvy) in two weight-based dose formulations—one formulation for those ≥14 to <25 kg and another for those ≥25 kg. This 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 tablet EVG/c/FTC/TAF (Genvoya), which is a complete ARV regimen that must be taken with food.
	Weighing ≥35 kg	DOR	DOR is available in a once-daily FDC tablet DOR/3TC/TDF (Delstrigo). Fewer side effects than reported with EFV. It has continued activity in the setting of some NNRTI mutations.

Table 18. Examples of Changes in Antiretroviral Regimen Components for Children With Sustained Virologic Suppression

Current ARV Drug(s)	Age, Weight, and Sexual Maturity Rating Requirements	Potential ARV Drug Switch[a]	Comment
	Aged ≥12 years Weighing ≥35 kg	CAB and RPV co-packaged regimen as Cabenuva	Long-acting injectable, complete ARV regimen requiring two IM injections every 1 to 2 months that together are an alternative to daily oral ARV regimens. Must consider prior history of treatment failure and known or suspected drug resistance to individual drugs. Injection site reactions are common but do not often result in discontinuation of the regimen. See Cabotegravir.
	Aged ≥12 years Weighing ≥35 kg	RPV	Lower incidence of adverse lipid effects. May have fewer sleep disturbances and neuropsychiatric symptoms compared to EFV. RPV has continued activity in the setting of some NNRTI mutations.
PIs			
LPV/r Twice Daily	Any age (starting at full-term birth) Weighing ≥2 kg	RAL[d]	Better palatability. RAL HD can only be given once daily in those weighing ≥40 kg. Unlike LPV/r, the use of RAL is not restricted to infants with a corrected gestational age of ≥42 weeks and a postnatal age of ≥14 days. RAL granules may be difficult to dose for some caregivers.
	Age ≥4 weeks Weighing ≥3 kg	DTG	Once-daily dosing if no documented resistance or history of failure with INSTI agents exists. May be better tolerated, and it can be given as a dispersible tablet in young children. DTG is available as a component of the FDC ABC/DTG/3TC, which is a complete ARV regimen that can be given to children weighing ≥10 kg to <25 kg in dispersible tablets (Triumeq PD) and to children and adolescents weighing ≥25 kg in a single tablet to be swallowed (Triumeq). DTG plus FTC/TAF (Descovy) in those weighing at least 14 kg or the weight-appropriate dose of FTC/TDF (Truvada) can be used in children weighing 20 kg to <25 kg. May improve lipid levels. See the Dolutegravir section for more information.
	Aged ≥3 years Weighing ≥10 kg	EFV	Once-daily dosing. Better palatability. Lower incidence of adverse lipid effects. Review NNRTI mutations before use. See the Efavirenz section for concerns about EFV dosing for children aged <3 years.
	Aged ≥3 months Weighing ≥5 kg	ATV/r	Once-daily dosing. ATV/r may have a lower incidence of adverse lipid effects; 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 have a lower incidence of adverse lipid effects. DRV/r is administered twice daily to patients aged <12 years, but it may be administered once daily in children aged ≥12 years who do not have DRV resistance mutations. Note that palatability of the RTV oral solution is poor when

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Current ARV Drug(s)	Age, Weight, and Sexual Maturity Rating Requirements	Potential ARV Drug Switch[a]	Comment
			considering administering to children not able to swallow tablets.
	Weighing ≥14 kg	BIC as Biktarvy	Once-daily dosing. BIC is available as a component of the FDC tablet BIC/FTC/TAF (Biktarvy) in two weight-based dose formulations—one for those ≥14 to <25 kg and another for those ≥25 kg. This 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 tablet EVG/c/FTC/TAF (Genvoya), which is a complete ARV regimen that must be taken with food.
	Weighing ≥35 kg	DOR	DOR is available in a once-daily FDC tablet DOR/3TC/TDF (Delstrigo). Fewer side effects than reported with EFV. It has continued activity in the setting of some NNRTI mutations.
	Aged ≥12 years Weighing ≥35 kg	CAB and RPV co-packaged regimen as Cabenuva	Long-acting injectable, complete ARV regimen requiring two IM injections every 1 to 2 months that together are an alternative to daily oral ARV regimens. Must consider prior history of treatment failure and known or suspected drug resistance to individual drugs. Injection site reactions are common but do not often result in discontinuation of the regimen. See Cabotegravir.
	Aged ≥12 years Weighing ≥35 kg	RPV	May be better tolerated. Lower incidence of adverse lipid effects. It has continued activity in the setting of some NNRTI mutations.
INSTIs			
RAL	Age >1 month and weighing <14 kg Weighing ≥14 kg	DTG DTG or BIC	Once-daily dosing. Higher barrier to resistance. DTG is available as a single drug in a dispersible tablet for infants and children weighing ≥3 kg; in a single-drug film-coated tablet for children weighing ≥14 kg; or as an FDC. All of these can be dosed once daily if no documented resistance or history of failure with INSTI agents exists. DTG plus FTC/TAF (Descovy) in those weighing at least 14 kg or the weight-appropriate dose of FTC/TDF (Truvada) can be used in children weighing 20 kg to <25 kg. DTG is available as a component of the FDC ABC/DTG/3TC, which is a complete ARV regimen that can be given to children weighing ≥10 to <25 kg in dispersible tablets (Triumeq PD) and to children and adolescents weighing ≥25 kg in a single tablet to be swallowed (Triumeq). See the Dolutegravir section for more information. BIC has once-daily dosing and a higher barrier to resistance. BIC is available as a component of the FDC tablet BIC/FTC/TAF (Biktarvy) in two weight-based dose

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Current ARV Drug(s)	Age, Weight, and Sexual Maturity Rating Requirements	Potential ARV Drug Switch[a]	Comment
			formulations—one for those ≥14 to <25 kg and another for those ≥25 kg. This is a complete ARV regimen that can be taken with or without food.
	Aged ≥12 years Weighing ≥35 kg	CAB and RPV co-packaged regimen as Cabenuva	Long-acting injectable, complete ARV regimen requiring two IM injections every 1 to 2 months that together are an alternative to daily oral ARV regimens. Must consider prior history of treatment failure and known or suspected drug resistance to individual drugs. Injection site reactions are common but do not often result in discontinuation of the regimen. See Cabotegravir.
EVG/c	Weighing ≥14 kg	DTG or BIC	Once-daily dosing. Higher barrier to resistance. DTG is available as a single drug in a dispersible tablet for infants and children weighing ≥3 kg; in a single-drug film-coated tablet for children weighing 14 kg; or as an FDC. All of these can be dosed once daily if no documented resistance or history of failure with INSTI agents exists. DTG plus FTC/TAF (Descovy) in those weighing at least 14 kg or the weight-appropriate dose of FTC/TDF (Truvada) can be used in children weighing 20 kg to <25 kg. DTG is available as a component of the FDC ABC/DTG/3TC), which is a complete ARV regimen that can be given to children weighing ≥10 to <25 kg in dispersible tablets (Triumeq PD) and to children and adolescents weighing ≥25 kg in a single tablet to be swallowed (Triumeq), See the Dolutegravir section for more information. BIC has once-daily dosing and a higher barrier to resistance. BIC is available as a component of the FDC tablet BIC/FTC/TAF (Biktarvy) in two weight-based dose formulations—one for those ≥14 to <25 kg and another for those ≥25 kg. This is a complete ARV regimen that can be taken with or without food.
	Aged ≥12 years Weighing ≥35 kg	CAB and RPV co-packaged regimen as Cabenuva	Long-acting injectable, complete ARV regimen requiring two IM injections every 1 to 2 months that together are an alternative to daily oral ARV regimens. Must consider prior history of treatment failure and known or suspected drug resistance to individual drugs. Injection site reactions are common but do not often result in discontinuation of the regimen. See Cabotegravir.

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Current ARV Drug(s)	Age, Weight, and Sexual Maturity Rating Requirements	Potential ARV Drug Switch[a]	Comment
Other			
Any Multi-Pill and/or Twice-Daily Regimen	Weighing ≥14 kg to <25 kg	ABC/DTG/3TC (Triumeq PD)	Once-daily dosing. Dispersible tablets with dosage for use in children based on weight. Aligns a child's regimen with an efficacious regimen that is used in adults. See the Dolutegravir section for more information.
	Weighing ≥14 kg	FTC/TAF[c] (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 more information.
	Weighing ≥14 kg	BIC/FTC/TAF (Biktarvy)	Once-daily dosing. Single pill that can be taken with or without food. Available in two weight-based dose formulations—one for those ≥14 to <25 kg and another for those ≥25 kg.
	Weighing ≥25 kg	ABC/DTG/3TC (Triumeq)	Once-daily dosing. Single pill to be swallowed. 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 more information.
	Weighing ≥25 kg	EVG/c/FTC/TAF (Genvoya)	Once-daily dosing. Single pill. Alignment with adult ARV regimens. Must be taken with food.
	Weighing ≥35 kg	DOR/3TC/TDF (Delstrigo)	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. Renal and bone toxicity of TDF limit its use. Review NNRTI mutations and check for drug–drug interactions before use.
	Weighing ≥35 kg SMR 4 or 5	EVG/c/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 of TDF limit its use.
	Aged ≥12 years Weighing ≥35 kg	CAB and RPV co-packaged regimen as Cabenuva	Long-acting injectable, complete ARV regimen requiring two IM injections every 1 to 2 months that together are an alternative to daily oral ARV regimens. Must consider prior history of treatment failure and known or suspected drug resistance to individual drugs. Injection site reactions are common but do not often result in discontinuation of the regimen. See Cabotegravir.
	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. Review NNRTI mutations and check for drug–drug interactions before use. Must be taken with food at a consistent time daily.

Table 18. Examples of Changes in Antiretroviral Regimen Components for Children With Sustained Virologic Suppression

Current ARV Drug(s)	Age, Weight, and Sexual Maturity Rating Requirements	Potential ARV Drug Switch[a]	Comment
	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. Review NNRTI mutations and check for drug–drug interactions before use. Must be taken with food at a consistent time daily. Renal and bone toxicity of TDF limit its use.
	Aged ≥12 years Weighing ≥35 kg	DTG/RPV (Juluca)	NRTI-sparing FDC that is a complete regimen. In addition to age and weight criteria (based on RPV component since DTG approved to younger age/lower weight), must be virologically suppressed (HIV RNA <50 copies/mL) on a stable ARV regimen for at least 6 months and without history of treatment failure. Should be taken with food. No pediatric data.

[a] The possibility of planned and unplanned pregnancy should be considered when selecting an ART regimen for an adolescent. When discussing ART options with adolescents of childbearing potential and their caregivers, it is important to consider the benefits and risks of all ARV drugs and to provide the information and counseling needed to support informed decision-making; refer to the Perinatal Guidelines (see Recommendations for Use of Antiretroviral Drugs During Pregnancy, Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant People and Nonpregnant People Who Are Trying to Conceive, and Appendix C: Antiretroviral Counseling Guide for Health Care Providers).

[b] 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 on twice-daily ABC, the dose can be changed from twice daily to once daily. ABC is not approved by the U.S. Food and Drug Administration for use in neonates and infants aged <3 months. Recent data from the IMPAACT P1106 trial and two observational cohorts provide reassuring evidence of the safety of ABC in infants aged <3 months. Based on these data, clinicians may consider the use of ABC in infants aged ≥1 month to <3 months, in consultation with a pediatric HIV specialist (see Abacavir).

[c] For children and adolescents weighing ≥14 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, an NNRTI, or a boosted PI.

[d] RAL is recommended for twice-daily use in children. Chewable tablets can be used as dispersible tablets starting at 4 weeks of age. RAL HD once daily is only recommended for virologically suppressed children weighing ≥40 kg.

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAB = cabotegravir; DOR = doravirine; DRV = darunavir; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FTC = emtricitabine; HD = high dose; HLA = human leukocyte antigen; IM = intramuscular; 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; ZDV = zidovudine

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