



Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Table 1. Outline of the Guidelines Development Process

Topic	Comment
Goal of the Guidelines	The guidelines provide guidance to HIV care practitioners on the optimal use of antiretroviral (ARV) agents in infants, children, and adolescents in early to mid-puberty (sexual maturity rating [SMR] 1-3) who are living with HIV in the United States.
Panel Members	The Panel is composed of approximately 35 voting members who have expertise in the management of HIV infection in infants, children, and adolescents. Members include representatives from the Committee on Pediatric AIDS of the American Academy of Pediatrics and community representatives with knowledge of pediatric HIV infection (e.g., parents and caregivers of children and youth living with HIV). The Panel also includes at least one representative from each of the following Department of Health and Human Services (HHS) agencies: the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the Health Resources and Services Administration (HRSA), and the National Institutes of Health (NIH). A representative from the Canadian Pediatric AIDS Research Group participates as a nonvoting, <i>ex officio</i> member of the Panel. The U.S. government representatives are appointed by their respective agencies; nongovernmental members are selected after an open announcement to call for nominations. Each member serves on the Panel for a 3-year term with an option for reappointment. A list of current members can be found in the Panel Roster .
Financial Disclosure	All members of the Panel submit an annual financial disclosure statement in writing, reporting any association with manufacturers of ARV drugs or diagnostics used to manage HIV infections. A list of the latest disclosures is available on the AIDSinfo website .
Users of the Guidelines	Providers of care to infants, children, and adolescents living with HIV in the United States
Developer	Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV—a working group of the Office of AIDS Research Advisory Council (OARAC)
Funding Source	Office of AIDS Research, NIH, and HRSA
Evidence Collection	A standardized review of recent, relevant literature related to each section of the guidelines is performed by a technical assistance consultant (through funding from HRSA) and provided to individual Panel section working groups. The recommendations are generally based on studies published in peer-reviewed journals. The Panel may occasionally use unpublished data to revise the guidelines, particularly when the new information relates to dosing or patient safety. These data come from presentations at major conferences or from the FDA and/or drug manufacturers.
Recommendation Grading	Described in Table 2
Method of Synthesizing Data	Each section of the guidelines is assigned to a small group of Panel members with expertise in the area of interest. The members synthesize the available data and propose recommendations to the Panel. The Panel discusses all proposals during monthly teleconferences. Proposals are modified based on Panel discussion and then distributed with ballots to all Panel members for concurrence and additional comments. If there are substantive comments or votes against approval, the recommended changes and areas of disagreement are brought back to the full Panel (by email or teleconference) for additional review, discussion, and further modification to reach a final version that is acceptable to all Panel members. The recommendations in these final versions represent endorsement from a consensus of members and are included in the guidelines as official Panel recommendations.
Other Guidelines	<p>These guidelines focus on infants, children, and adolescents in early-to-mid-puberty (SMR 1–3) who are living with HIV. Guidelines for the treatment of adolescents in late puberty (SMR 4–5) are provided by the Panel on Antiretroviral Guidelines for Adults and Adolescents.</p> <p>Separate guidelines outline the use of antiretroviral therapy (ART) in pregnant women with HIV infection (including maternal and infant interventions to prevent perinatal transmission), ART for nonpregnant adults and postpubertal adolescents with HIV infection, and ARV prophylaxis for those who experience occupational or nonoccupational exposure to HIV. These guidelines are also available on the AIDSinfo website.</p>
Update Plan	The full Panel meets monthly by teleconference to review data that may warrant modification of the guidelines. Smaller working groups of Panel members hold additional teleconferences to review individual drug sections or other specific topics (e.g., What to Start). Updates may be prompted by new drug approvals (or new indications, formulations, or frequency of dosing), new significant safety or efficacy data, or other information that may have a significant impact on the clinical care of patients. In the event of significant new data that may affect patient safety, the Panel may issue a warning announcement and post accompanying recommendations on the AIDSinfo website until the guidelines can be updated with appropriate changes. All sections of the guidelines will be reviewed at least once a year, with updates as appropriate.
Public Comments	A 2-week public comment period follows the release of the updated guidelines on the AIDSinfo website . The Panel reviews these comments to determine whether additional revisions to the guidelines are indicated. The public may also submit comments to the Panel at any time at contactus@aidinfo.nih.gov .

Table 2. Rating Scheme for Recommendations

Strength of Recommendation	Quality of Evidence for Recommendation
<p>A: Strong recommendation for the statement</p> <p>B: Moderate recommendation for the statement</p> <p>C: Optional recommendation for the statement</p>	<p>I: One or more randomized trials in children^a with clinical outcomes and/or validated laboratory endpoints</p> <p>I*: One or more randomized trials in adults, with clinical outcomes and/or validated laboratory endpoints plus accompanying data in children^a from one or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes</p> <p>II: One or more well-designed, nonrandomized trials or observational cohort studies in children^a with long-term clinical outcomes</p> <p>II*: One or more well-designed, nonrandomized trials or observational cohort studies in adults with long-term clinical outcomes plus accompanying data in children^a from one or more smaller nonrandomized trials or cohort studies with clinical outcome data</p> <p>III: Expert opinion</p>

^a These are studies that include children or children and adolescents, but not studies that are limited to postpubertal adolescents.

Table 3. Sample Schedule for Clinical and Laboratory Monitoring of Children Before and After Initiation of Antiretroviral Therapy

Laboratory Testing	Entry Into Care^a	Pre-Therapy^b	ART Initiation^c	Weeks 1–2 on Therapy	Weeks 2–4 on Therapy	Every 3–4 Months^d	Every 6–12 Months^e	When Switching ARV Regimens
Medical History and Physical Examination	✓	✓	✓	✓	✓	✓		✓
Adherence Evaluation		✓	✓	✓	✓	✓		✓
CD4 Count	✓	✓	✓			✓		✓
Plasma Viral Load	✓	✓	✓		✓	✓		✓
Resistance Testing	✓							✓
CBC with Differential	✓	✓	✓		✓	✓		✓
Chemistries ^f	✓	✓	✓		✓	✓		✓
Lipid Panel	✓		✓				✓	
Random Plasma Glucose ^g			✓				✓	
Urinalysis	✓		✓				✓	
Hepatitis B Screening ^h		✓						✓
Pregnancy Test for Women of Childbearing Ageⁱ		✓						✓

^a See text for details on recommended laboratory tests to perform.

^b A patient's ability to adhere to an ARV regimen is assessed prior to starting ART. If abacavir is being considered as part of the regimen, send HLA-B*5701 testing prior to initiating abacavir and choose an alternative ARV drug if the patient is HLA-B*5701 positive (see the [abacavir](#) section in [Appendix A: Pediatric Antiretroviral Drug Information](#)). Genotype resistance testing is recommended if it has not already been performed (see [Drug-Resistance Testing](#) in the [Adult and Adolescent Antiretroviral Guidelines](#)). Send tests that are appropriate for the toxicity profile that is associated with a patient's ART regimen and the patient's medical history (see text).

^c If ART is initiated within 30 days to 90 days of a pre-therapy lab result, repeat testing may not be necessary.

^d CD4 cell count, CBC, and chemistries can be monitored less frequently (every 6 months–12 months) in children and youth who are adherent to therapy, who have CD4 cell values that are well above the threshold for OI risk, and who have had sustained virologic suppression and stable clinical status for more than 2 years to 3 years. Viral load testing every 3 to 4 months is generally recommended to monitor ARV adherence.

^e If lipid levels have been abnormal in the past, more frequent monitoring might be needed. For patients treated with TDF, more frequent urinalysis should be considered.

^f Chemistries refer to a comprehensive metabolic panel.

^g Random plasma glucose is collected in a gray-top blood collection tube or other designated tube.

^h This screening is only recommended for individuals who have previously demonstrated no immunity to hepatitis B and who are initiating a regimen that contains ARV drugs with activity against hepatitis B, specifically lamivudine, emtricitabine, TAF, or TDF.

ⁱ See the [Adult and Adolescent Antiretroviral Guidelines](#), as well as [Preconception Counseling and Care for Women of Childbearing Age Living with HIV](#) in the [Perinatal Guidelines](#).

Key to Acronyms: ART = antiretroviral therapy; ARV = antiretroviral; CBC = complete blood count; CD4 = CD4 T lymphocyte; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; OI = opportunistic infection

Table 4. Primary, Food and Drug Administration-Approved Assays for Monitoring Viral Load

Assay	Abbott Real Time	NucliSens EasyQ v2.0	COBAS AmpliPrep/TaqMan v2.0	Versant v1.0
Method	Real-time RT-PCR	Real-time NASBA	Real-time RT-PCR	Real-time RT-PCR
Dynamic Range	40–10 ⁷ copies/mL	25–10 ⁷ copies/mL	20–10 ⁷ copies/mL	37–11x10 ⁷ copies/mL
Specimen Volume ^a	0.2–1 mL	0.1–1 mL	1 mL	0.5 mL
Manufacturer	Abbott	bioMerieux	Roche	Siemens

^a Smaller volumes for children can be accommodated.

Key to Acronyms: NASBA = nucleic acid sequence-based amplification; RT-PCR = reverse transcription polymerase chain reaction

Table 5. HIV Infection Stage Based on Age-Specific CD4 Cell Count or Percentage

Stage ^a	Age at the Time of the CD4 Test					
	<1 Year		1 Year to <6 Years		≥6 Years	
	Cells/μL	%	Cells/μL	%	Cells/μL	%
1	≥1,500	≥34	≥1,000	≥30	≥500	≥26
2	750–1,499	26–33	500–999	22–29	200–499	14–25
3	<750	<26	<500	<22	<200	<14

^a The stage is based primarily on the CD4 cell count; the CD4 cell count takes precedence over the CD4 percentage, and the percentage is considered only when the count is missing. If a Stage 3-defining condition has been diagnosed (see Table 6), then the stage is 3 regardless of CD4 test results.

Source: Centers for Disease Control and Prevention. Revised surveillance case definition for HIV infection—United States, 2014. *MMWR* 2014;63(No. RR-3):1-10.

Key to Acronyms: CD4 = CD4 T lymphocyte

Table 6. HIV-Related Symptoms and Conditions

Mildly Symptomatic
<p>Children with two or more of the conditions listed, but none of the conditions listed in the Moderate Symptoms category:</p> <ul style="list-style-type: none"> • Lymphadenopathy (lymph nodes are ≥ 0.5 cm at more than two sites and/or bilateral at one site) • Hepatomegaly • Splenomegaly • Dermatitis • Parotitis • Recurrent or persistent upper respiratory tract infection, sinusitis, or otitis media
Moderately Symptomatic
<ul style="list-style-type: none"> • Anemia (hemoglobin < 8 g/dL [< 80 g/L]), neutropenia (white blood cell count $< 1,000$ per μL [$< 1.0 \times 10^9$ per L]), and/or thrombocytopenia (platelet count $< 100 \times 10^3$ per μL [$< 100 \times 10^9$ per L]) persisting for ≥ 30 days • Bacterial meningitis, pneumonia, or sepsis (single episode) • Candidiasis, oropharyngeal (thrush), persisting for > 2 months in children aged > 6 months • Cardiomyopathy • Cytomegalovirus infection, with onset before age 1 month • Diarrhea, recurrent or chronic • Hepatitis • HSV stomatitis, recurrent (more than two episodes within 1 year) • HSV bronchitis, pneumonitis, or esophagitis with onset before age 1 month • Herpes zoster (shingles) involving at least two distinct episodes or more than one dermatome • Leiomyosarcoma • Lymphoid interstitial pneumonia or pulmonary lymphoid hyperplasia complex • Nephropathy • Nocardiosis • Persistent fever (lasting > 1 month) • Toxoplasmosis, onset before age 1 month • Varicella, disseminated (complicated chickenpox)
AIDS-Defining Conditions
<ul style="list-style-type: none"> • Bacterial infections, multiple or recurrent^a • Candidiasis of bronchi, trachea, or lungs • Candidiasis of esophagus

Table 6. HIV-Related Symptoms and Conditions, continued

AIDS-Defining Conditions, continued
<ul style="list-style-type: none">• Cervical cancer, invasive^b• Coccidioidomycosis, disseminated or extrapulmonary• Cryptococcosis, extrapulmonary• Cryptosporidiosis, chronic intestinal (>1 month duration)• CMV disease (other than liver, spleen, or lymph nodes), onset at age >1 month• CMV retinitis (with loss of vision)• Encephalopathy attributed to HIV^c• HSV: chronic ulcers (>1 month duration) or bronchitis, pneumonitis, or esophagitis (onset at age >1 month)• Histoplasmosis, disseminated or extrapulmonary• Isosporiasis, chronic intestinal (>1 month duration)• Kaposi sarcoma• Lymphoma, Burkitt (or equivalent term)• Lymphoma, immunoblastic (or equivalent term)• Lymphoma, primary, of brain• <i>Mycobacterium avium</i> complex or <i>Mycobacterium kansasii</i>, disseminated or extrapulmonary• <i>Mycobacterium tuberculosis</i> of any site, pulmonary, disseminated, or extrapulmonary• <i>Mycobacterium</i>, other species or unidentified species, disseminated or extrapulmonary• <i>Pneumocystis jirovecii</i> (previously known as <i>Pneumocystis carinii</i>) pneumonia• Pneumonia, recurrent^b• Progressive multifocal leukoencephalopathy• Salmonella septicemia, recurrent• Toxoplasmosis of brain, onset at age >1 month• Wasting syndrome attributed to HIV^c

^a Only among children aged <6 years.

^b Only among adults, adolescents, and children aged ≥6 years.

^c Suggested diagnostic criteria for these illnesses, which might be particularly important for HIV encephalopathy and HIV wasting syndrome, are described in the following references:

Centers for Disease Control and Prevention. 1994 Revised classification system for human immunodeficiency virus infection in children less than 13 years of age. *MMWR*. 1994;43(No. RR-12).

Centers for Disease Control and Prevention. 1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR*. 1992;41(No. RR-17).

Key to Acronyms: CDC = Centers for Disease Control and Prevention; CMV = cytomegalovirus; HSV = herpes simplex virus

Modified from:

Centers for Disease Control and Prevention. 1994 revised classification system for human immunodeficiency virus infection in children less than 13 years of age. *MMWR*. 1994;43(No. RR-12).

Centers for Disease Control and Prevention: Revised Surveillance Case Definition for HIV Infection—United States, 2014. *MMWR*. 2014;63(No. RR-3):1-10.

Table 7. Antiretroviral Regimens Recommended for Initial Therapy for HIV Infection in Children

An ART regimen for treatment-naive children is generally made up of a two-NRTI backbone and either one NNRTI **or** one INSTI **or** one PI boosted with RTV or COBI. *Preferred* regimens are designated based on efficacy, ease of administration, and acceptable toxicity. *Alternative* regimens have also demonstrated efficacy, but clinical experience with these regimens is limited or these regimens are more difficult to administer than *Preferred* regimens. Regimens should be tailored to the individual patient by weighing the advantages and disadvantages of each combination. Many agents have multiple formulations and age and weight recommendations. Please consult [Appendix A: Pediatric Antiretroviral Drug Information](#) for additional information and recommended dosages and formulations (see [Table 8](#) below).

Children who are receiving effective and tolerable ART regimens can continue using those regimens as they age, even if the combinations they are receiving are no longer *Preferred* regimens.

Preferred Regimens			
Age	Regimens	FDC Available (see Fixed-Dose Combinations)	
Infants, Birth to Age <14 Days ^{a,b}	Two NRTIs plus NVP	No	
	Weight ≥2 kg	Two NRTIs plus RAL ^c	No
Children Aged ≥14 Days to <3 Years	Two NRTIs plus LPV/r	No	
	Weight ≥2 kg	Two NRTIs plus RAL ^c	No
Children Aged ≥3 Years	Weight <25 kg	Two NRTIs plus ATV/r	No
		Two NRTIs plus twice-daily DRV/r ^d	No
		Two NRTIs plus RAL ^c	No
	Weight ≥25 kg	Two NRTIs plus DTG ^e	Yes
		Two NRTIs plus EVG/COBI ^f	Yes
Adolescents Aged ≥12 Years with SMR 1–3	Weight ≥25 kg	Two NRTIs plus BIC ^g	Yes
Adolescents Aged ≥12 Years with SMR 4 or 5	Refer to the Adult and Adolescent Antiretroviral Guidelines		Yes
Alternative Regimens			
Age	Regimens	FDC Available	
Children Aged ≥14 Days to <3 Years	Two NRTIs plus NVP ^h	No	
Children Aged ≥3 Months to <3 Years	Two NRTIs plus ATV/r	No	
Children Aged ≥3 Years	Weight ≥20 kg to <25 kg	Two NRTIs plus DTG ^e	No
Children Aged ≥3 Years	Weight ≥25 kg	Two NRTIs plus ATV/r	No
		Two NRTIs plus DRV/r ^d	No
		Two NRTIs plus RAL ^c	No
Children Aged ≥3 Years	Two NRTIs plus EFV ⁱ	No ^j	
	Two NRTIs plus LPV/r	No	
Children Aged ≥6 Years to <12 Years	Weight ≥25 kg	Two NRTIs plus BIC ^g	Yes
Adolescents Aged ≥12 Years with SMR 1–3	Weight ≥35 kg	Two NRTIs plus RPV ^k	Yes
Adolescents Aged ≥12 Years with SMR 4 or 5	Refer to the Adult and Adolescent Antiretroviral Guidelines		Yes
Preferred Dual-NRTI Backbone Options for Use in Combination with Other Drugs			
Age	Dual-NRTI Backbone Options	FDC Available	
Children, Birth to Age <3 Months	ZDV plus (3TC or FTC) ^l	No ^j	
Children Aged ≥3 Months to <6 Years	ABC plus (3TC or FTC) ^m	Yes	
	ZDV plus (3TC or FTC) ^l	Yes	
Children and Adolescents Aged ≥6 Years with SMR 1–3	ABC plus (3TC or FTC) ^m	Yes	
	Weighting ≥25 kg and receiving a regimen that contains an INSTI or an NNRTI	FTC/TAF ⁿ	Yes

Table 7. Antiretroviral Regimens Recommended for Initial Therapy for HIV Infection in Children,
continued

Preferred Dual-NRTI Backbone Options for Use in Combination with Other Drugs, continued		
Age	Dual-NRTI Backbone Options	FDC Available
Adolescents Aged ≥12 Years with SMR 4 or 5	Refer to the Adult and Adolescent Antiretroviral Guidelines	Yes
Alternative Dual-NRTI Backbone Options for Use in Combination with Other Drugs		
Age	Dual-NRTI Backbone Options	FDC Available
Children Aged ≥3 Months	ZDV plus ABC	No
Children Aged ≥2 Years to 12 Years	TDF plus (3TC or FTC) ^b	Yes
Children and Adolescents Aged ≥6 Years and SMR 1–3	ZDV plus (3TC or FTC) ⁱ	Yes

^a If treatment is scheduled to begin before a patient is aged 14 days, NVP or RAL are *Preferred* agents because they are the only options with dosing information available for this age group. While many pediatric experts favor initiating ART as soon as possible after birth in order to limit the establishment of viral reservoirs, available clinical trial data does not suggest that initiating treatment within the first 14 days of life leads to better clinical outcomes than initiating treatment after 14 days of age. Clinicians should consult an expert in pediatric HIV infection before initiating treatment in infants aged <14 days. Additional considerations regarding the use of NVP or RAL in infants aged <14 days can be found in [Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV](#). Switching from NVP to LPV/r should be considered when the infant is aged ≥14 days with a postmenstrual age of 42 weeks (the span of time between the first day of the mother's last menstrual period and birth, plus the time elapsed after birth); LPV/r has produced better clinical outcomes in studies of children aged <3 years than NVP. Data are limited on the clinical outcomes of using RAL in infants and children aged <2 years.

^b LPV/r should not be administered to neonates before a postmenstrual age of 42 weeks and postnatal age ≥14 days.

^c RAL pills or chewable tablets can be used in children aged ≥2 years. Granules can be administered in infants and children from birth to age 2 years. No dosing information is available for preterm infants or those with a weight of < 2 kg at birth.

^d DRV should only be used in children weighing ≥10 kg. Once-daily DRV should not be used in children aged <12 years or weighing <40 kg. Once-daily DRV should also not be used when any one of the following resistance-associated substitutions are present: V11I, V32I, L33F, I47V, I50V, I54L, I54M, T74P, L76V, I84V, and L89V. DRV/r is recommended as an *Alternative* drug combination for children aged ≥6 years to <12 years and weighing >25 kg, because there are other drugs that can be administered once daily and that are better tolerated. Note that DRV/r can be administered once daily in adolescents aged ≥12 years and weighing ≥40 kg who are not sexually mature (SMR 1–3).

^e DTG is recommended as a *Preferred* agent for children and adolescents aged ≥3 years and weighing ≥25 kg. It is recommended as an *Alternative* agent in children aged ≥3 years and weighing 20 kg to <25 kg. An FDC tablet containing ABC/DTG/3TC (Triumeq) is available for children weighing ≥25 kg.

^f EVG is currently recommended only as a component of FDC tablets. Tablets containing EVG/COBI/FTC/TAF are recommended as a *Preferred* regimen for children and adolescents weighing ≥35 kg, and as an *Alternative* regimen for children and adolescents weighing ≥25 kg.

^g BIC is available only as part of an FDC tablet that contains BIC/FTC/TAF and is recommended as a *Preferred* regimen for adolescents aged ≥12 years and weighing ≥25 kg. It is recommended as an *Alternative* regimen for children aged ≥6 years and weighing ≥25 kg.

^h NVP should not be used in post-pubertal girls with CD4 cell counts >250/mm³, unless the benefit clearly outweighs the risk. NVP is approved by the FDA for treatment of infants aged ≥15 days.

ⁱ EFV is approved by the FDA for use in children aged ≥3 months and weighing ≥3.5 kg, but it **is not recommended** by the Panel for initial therapy in children aged ≥3 months to 3 years. An FDC tablet containing EFV/FTC/TDF (Atripla) and EFV 600 mg/3TC/TDF (Symfi) is available. See [efavirenz](#) section for information about use of the FDC EFV 400 mg/3TC/TDF (Symfi Lo).

^j FDA-approved FDCs are not included in this table when they are not approved for use in the specific patient populations being discussed.

^k RPV should be administered to adolescents aged ≥12 years and weighing ≥35 kg who have initial viral loads ≤100,000 copies/mL. FDC tablets containing FTC/RPV/TAF (Odefsey) and FTC/RPV/TDF (Complera) are available.

^l An FDC containing 3TC/ZDV (Combivir and generic) is available.

^m An FDC containing ABC/3TC (Epzicom and generic) is available.

ⁿ FTC/TAF is recommended as a *Preferred* combination for children and adolescents weighing ≥25 kg; an FDC containing FTC/TAF is available. FTC/TAF is approved by the FDA for children weighing ≥25 kg when used in the single-tablet regimen EVG/COBI/FTC/TAF or as TAF/FTC in combination with an NNRTI or INSTI. FTC/TAF plus a boosted PI is only recommended for use in children and adolescents weighing ≥35 kg.

^o An FDC containing FTC/TDF (Truvada) is available.

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ATV/r = atazanavir/ritonavir; ART = antiretroviral therapy; **BIC = bicitegravir**; CD4 = CD4 T lymphocyte; COBI = cobicistat; DRV = darunavir; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; FDA = Food and Drug Administration; FDC = fixed-dose combination; FTC = emtricitabine; 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; SMR = sexual maturity rating; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

Table 8. Advantages and Disadvantages of Antiretroviral Components Recommended for Initial Therapy in Children (page 1 of 4)

See [Appendix A: Pediatric Antiretroviral Drug Information](#) and [Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios](#) in the [Adult and Adolescent Antiretroviral Guidelines](#) for more information.

ARV Class	ARV Agent(s)	Advantages	Disadvantages
INSTIs In Alphabetical Order	All INSTIs	<p><u>INSTI Class Advantages:</u></p> <ul style="list-style-type: none"> • Few drug-drug interactions • Well-tolerated 	<p><u>INSTI Class Disadvantages:</u></p> <ul style="list-style-type: none"> • Limited data on pediatric dosing or safety
	BIC	<p>Once-daily administration</p> <p>Can give with or without food</p> <p>Available in FDC tablets (see Fixed-Dose Combinations)</p>	<p>FDC tablet is not recommended for patients with hepatic impairment or an estimated creatinine clearance <30 mL/min</p> <p>FDC tablet should not be coadministered with rifampin or dofetilide</p>
	DTG	<p>Once-daily administration</p> <p>Can give with food</p> <p>Available in FDC tablets (see Fixed-Dose Combinations)</p> <p>Single-agent DTG pills are available in several dosages and are small in size.</p>	<p>Drug interactions with EFV, FPV/r, TPV/r, and rifampin, necessitating twice-daily dosing of DTG</p> <p>CNS side effects, particularly sleep disturbances and possible increased risk of neural tube defects in infants born to women who were receiving dolutegravir at the time of conception</p>
	EVG	<p>Once-daily administration</p> <p>Available in FDC tablets (see Fixed-Dose Combinations)</p>	<p>Among INSTIs, EVG has the lowest barrier to the development of resistance.</p> <p>If EVG is administered with COBI, there is potential for multiple drug interactions because COBI is metabolized by hepatic enzymes (e.g., CYP3A4).</p> <p>COBI inhibits tubular secretion of creatinine, and this may result in increased serum creatinine but normal glomerular clearance.</p>
	RAL	<p>Can give with food</p> <p>Available in tablet, chewable tablet, and powder formulations</p> <p>Once-daily administration (with RAL HD) can be used for treatment-naïve or virologically suppressed children weighing ≥50 kg.</p>	<p>Potential for rare systemic allergic reaction or hepatitis</p> <p>Granule formulation requires a multistep preparation before administration; caregiver must be taught how to properly prepare this formulation.</p>
NNRTIs In Alphabetical Order	All NNRTIs	<p><u>NNRTI Class Advantages:</u></p> <ul style="list-style-type: none"> • Long half-life • Lower risk of dyslipidemia and fat maldistribution than PIs • PI-sparing • Lower pill burden than PIs for children taking the solid formulation; easier to use and adhere to than PI-based regimens 	<p><u>NNRTI Class Disadvantages:</u></p> <ul style="list-style-type: none"> • A single mutation can confer resistance, with cross-resistance between EFV and NVP. • Rare but serious and potentially life-threatening cases of skin rash, including SJS, and hepatic toxicity. All NNRTIs pose this risk, but the risk is greatest with NVP. • Potential for multiple drug interactions due to metabolism via hepatic enzymes (e.g., CYP3A4)

Table 8. Advantages and Disadvantages of Antiretroviral Components Recommended for Initial Therapy in Children^a (page 2 of 4)

ARV Class	ARV Agent(s)	Advantages	Disadvantages
NNRTIs In Alphabetical Order, continued	EFV	Once-daily administration Available in the FDC tablets (see Fixed-Dose Combinations) Potent ARV activity Can give with food (but avoid high-fat meals) Capsules can be opened and added to food.	Neuropsychiatric AEs (bedtime dosing is recommended to reduce CNS effects) Rash (generally mild) No commercially available liquid formulation Limited data on dosing for children aged <3 years No data on dosing for children aged <3 months
	NVP	Liquid formulation is available. Dosing information for young infants is available. Can give with food Extended-release formulation is available that allows for once-daily dosing in older children.	Reduced virologic efficacy in young infants, regardless of exposure to NVP as part of a peripartum preventive regimen Higher incidence of rash/HSR than other NNRTIs Higher rates of serious hepatic toxicity than EFV Decreased virologic response compared with EFV Twice-daily dosing necessary in children with BSA <0.58 m ² Low barrier for resistance
	RPV	Once-daily dosing Available in FDC tablets (see Fixed-Dose Combinations)	Should not use in patients with HIV viral loads >100,000 copies/mL Must be taken with a ≥500 kcal meal at a consistent time each day; this may affect adherence. Low barrier for resistance
PIs In Alphabetical Order	All PIs	PI Class Advantages: <ul style="list-style-type: none"> • NNRTI-sparing • Clinical, virologic, and immunologic efficacy are well-documented. • Resistance to PIs requires multiple mutations. • When combined with a dual-NRTI backbone, a regimen containing a PI targets HIV at two steps of viral replication by inhibiting the activity of viral reverse transcriptase and protease enzymes. 	PI Class Disadvantages: <ul style="list-style-type: none"> • Metabolic complications, including dyslipidemia, fat maldistribution, and insulin resistance • Potential for multiple drug interactions because of metabolism via hepatic enzymes (e.g., CYP3A4) • Higher pill burden than NRTI-based or NNRTI-based regimens for patients taking solid formulations • Poor palatability of liquid preparations, which may affect adherence • Most PIs require RTV boosting, resulting in drug interactions that are associated with RTV.
	Boosted ATV	Once-daily dosing Powder formulation is available. ATV has less effect on TG and total cholesterol levels than other PIs (but RTV boosting may be associated with elevations in these parameters).	No liquid formulation Should be administered with food) Indirect hyperbilirubinemia is common, but asymptomatic. Scleral icterus may be distressing to the patient, which may affect adherence. Must be used with caution in patients with preexisting conduction system defects (can prolong PR interval of ECG). RTV is associated with a large number of drug interactions.

Table 8. Advantages and Disadvantages of Antiretroviral Components Recommended for Initial Therapy in Children^a (page 3 of 4)

ARV Class	ARV Agent(s)	Advantages	Disadvantages
PIs In Alphabetical Order, continued	Boosted DRV	Can be used once daily in children aged ≥ 12 years Liquid formulation is available. DRV requires a boosting agent. Available in FDC tablets (see Fixed-Dose Combinations)	Pediatric pill burden high with current tablet dose formulations Should be administered with food Must be boosted to achieve adequate plasma concentrations Contains sulfa moiety. The potential for cross-sensitivity between DRV and other drugs in sulfonamide class is unknown. RTV is associated with a large number of drug interactions. Can only be used once daily in the absence of certain PI-associated resistance mutations
	LPV/r	LPV is only available coformulated with RTV in liquid and tablet formulations. Tablets can be given without regard to food, but they may be better tolerated when taken with meal or snack.	Poor palatability of liquid formulation (bitter taste), although the palatability of the FDC is better than RTV alone Liquid formulation should be administered with food. RTV is associated with a large number of drug interactions. Should not be administered to neonates before a postmenstrual age (the span of time between the first day of the mother's last menstrual period and birth, plus the time elapsed after birth) of 42 weeks and a postnatal age ≥ 14 days Must be used with caution in patients with pre-existing conduction system defects (can prolong PR and QT interval of ECG)
Dual-NRTI Backbones In Alphabetical Order	ABC plus (3TC or FTC)	Palatable liquid formulations Can give with food Available in FDC tablets (see Fixed-Dose Combinations)	Risk of ABC HSR; perform HLA-B*5701 screening before initiation of ABC treatment.
	FTC/TAF for children aged ≥ 6 years	Once-daily dosing Small tablet size Lower risk of TFV-associated renal and bone toxicity with TAF than with TDF in adults Available in FDC tablets (see Fixed-Dose Combinations)	Limited data on the safety and efficacy of this combination in children Increased lipid levels
	TDF plus (3TC or FTC) for adolescents with SMR 4 or 5	Once-daily dosing for TDF Resistance is slow to develop. Lower risk of mitochondrial toxicity than other NRTIs Can give with food Available as reduced-strength tablets and oral powder for use in younger children Available in FDC tablets (see Fixed-Dose Combinations)	Limited pediatric experience Potential bone and renal toxicity Appropriate dosing is complicated by numerous drug-drug interactions with other ARV agents, including ddI, LPV/r, ATV, and TPV.

Table 8. Advantages and Disadvantages of Antiretroviral Components Recommended for Initial Therapy in Children^a (page 4 of 4)

ARV Class	ARV Agent(s)	Advantages	Disadvantages
Dual-NRTI Backbones In Alphabetical Order, continued	ZDV plus (3TC or FTC)	Extensive pediatric experience Coformulations of ZDV and 3TC are available (Combivir and generic) for children weighing ≥ 30 kg. Palatable liquid formulations Can give with food FTC is available as a palatable liquid formulation that can be administered once daily.	Bone marrow suppression with ZDV Lipoatrophy with ZDV
	ZDV plus ABC	Palatable liquid formulations Can give with food	Risk of ABC HSRs; perform HLA-B*5701 screening before initiation of ABC treatment. Bone marrow suppression and lipoatrophy with ZDV

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; AE = adverse event; ARV = antiretroviral; ATV = atazanavir; **BIC = bictegravir**; BSA = body surface area; CNS = central nervous system; COBI = cobicistat; CYP = cytochrome P450; ddi = didanosine; DRV = darunavir; DTG = dolutegravir; ECG = electrocardiogram; EFV = efavirenz; EVG = elvitegravir; FDC = fixed-dose combination; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; HSR = hypersensitivity reaction; INSTI = integrase strand transfer inhibitor; LPV = lopinavir; 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; SJS = Stevens-Johnson Syndrome; SMR = sexual maturity rating; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV= tenofovir; TG = triglycerides; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine

Table 9. Antiretroviral Therapy Regimens or Components Not Recommended for Initial Treatment of HIV Infection in Children

Regimen or ARV Component	Rationale
Unboosted ATV -containing regimens in children	Reduced exposure
Once-daily DRV -based regimens in children aged ≥ 3 years to 12 years	Insufficient data to recommend
Unboosted DRV	Use without RTV has not been studied
Dual (full-dose) PI regimens	Insufficient data to recommend Potential for added toxicities
Dual-NRTI combination of ABC plus TDF	Insufficient data to recommend
EFV -based regimens for children aged < 3 years	Appropriate dose not determined
ETR -based regimens	Insufficient data to recommend
LPV/r dosed once daily	Reduced drug exposure
MVC -based regimens	Insufficient data to recommend
Regimens containing only NRTIs	Inferior virologic efficacy
Regimens containing three drug classes	Insufficient data to recommend
Full-dose RTV or use of RTV as the sole PI	GI intolerance Metabolic toxicity
Regimens containing three NRTIs and one NNRTI	Added cost and complexity outweighs any benefit
TDF -containing regimens in children aged < 2 years	Potential bone toxicity Appropriate dose has yet to be determined

Key to Acronyms: ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; DRV = darunavir; EFV = efavirenz; ETR = etravirine; GI = gastrointestinal; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RTV = ritonavir; TDF = tenofovir disoproxil fumarate

Table 10. Antiretroviral Therapy Regimens or Components Never Recommended for Treatment of HIV Infection in Children

ART Regimens <u>Never</u> Recommended for Children		
Regimen	Rationale	Exceptions
One ARV Drug Alone (Monotherapy)	Rapid development of resistance Inferior antiviral activity compared to combinations that include ≥ 3 ARV drugs Monotherapy “holding” regimens are associated with more rapid CD4 cell count declines than nonsuppressive ART.	Infants with perinatal HIV exposure and negative virologic tests who are receiving 4 weeks to 6 weeks of ZDV prophylaxis to prevent perinatal transmission of HIV
Two NRTIs Alone	Rapid development of resistance Inferior antiviral activity compared to combinations that include ≥ 3 ARV drugs	Not recommended for initial therapy Some clinicians may opt to continue this treatment in patients who are currently on two NRTIs alone and who achieve virologic goals.
TDF plus ABC plus (3TC <u>or</u> FTC) as a Triple-NRTI Regimen	High rate of early viral failure when this triple-NRTI regimen was used as initial therapy in treatment-naive adults	No exceptions
TDF plus ddI plus (3TC <u>or</u> FTC) as a Triple-NRTI Regimen	High rate of early viral failure when this triple-NRTI regimen was used as initial therapy in treatment-naive adults	No exceptions
ARV Components <u>Never</u> Recommended as Part of an ARV Regimen for Children		
Regimen	Rationale	Exceptions
Dual-NNRTI Combinations	Enhanced toxicity	No exceptions
Dual-NRTI Combination 3TC plus FTC	Similar resistance profile and no additive benefit	No exceptions
Dual-NRTI Combination d4T plus ZDV	Antagonistic effect on HIV	No exceptions
NVP as Initial Therapy in Adolescent Girls with CD4 Counts >250 cells/mm³ or Adolescent Boys with CD4 Counts >400 cells/mm³	Increased incidence of symptomatic (including serious and potentially fatal) hepatic events in these patient groups	Only if benefit clearly outweighs risk

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; CD4 = CD4 T lymphocyte; d4T = stavudine; ddI = didanosine; DRV = darunavir; FTC = emtricitabine; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

Table 11. Neonatal Antiretroviral Management According to Risk of HIV Infection in the Newborn

Drug selection and dosing considerations are related to the age and gestational age of the newborn. Consultation is available through the [National Perinatal HIV Hotline](https://www.hiv.gov/national-perinatal-hiv-hotline) (1-888-448-8765).

Level of Perinatal HIV Transmission Risk	Description	Neonatal ARV Management
Low Risk of Perinatal HIV Transmission	Mothers who received ART during pregnancy with sustained viral suppression (defined as a confirmed HIV RNA level < 50 copies/ml) near delivery and no concerns related to adherence	ZDV for 4 weeks
Higher Risk of Perinatal HIV Transmission^{a,b}	Mothers who received neither antepartum nor intrapartum ARV drugs Mothers who received only intrapartum ARV drugs Mothers who received antepartum and intrapartum ARV drugs but who have detectable viral loads near delivery, particularly when delivery was vaginal Mothers with acute or primary HIV infection during pregnancy or breastfeeding (in which case, the mother should discontinue breastfeeding) ^c	Empiric HIV therapy using either ZDV, 3TC, and NVP (treatment dose) or ZDV, 3TC, and RAL administered from birth to age 6 weeks. ^d <i>or</i> Two-drug ARV prophylaxis (NICHD-HPTN 040/PACTG 1043 regimen) with 6 weeks ZDV and three doses of NVP (prophylactic dose, with doses given within 48 hours of birth, 48 hours after first dose, and 96 hours after second dose)
Presumed Newborn HIV Exposure	Mothers with unconfirmed HIV status who have at least one positive HIV test at delivery or postpartum <i>or</i> Whose newborns have a positive HIV antibody test	ARV management as described above for newborns with a higher risk of perinatal HIV transmission Infant ARV drugs should be discontinued immediately if supplemental testing confirms that the mother does not have HIV

^a See text for evidence that supports the use of empiric HIV therapy and a two-drug ARV prophylaxis regimen.

^b See [Intrapartum Care](#) for guidance on indications for scheduled cesarean delivery and intrapartum IV ZDV to reduce the risk of perinatal HIV transmission for mothers with an elevated viral load at delivery.

^c Most Panel members would opt to administer empiric HIV therapy to infants whose mothers had acute HIV during pregnancy because of the higher risk for *in utero* transmission. If acute HIV is diagnosed during breastfeeding, the mother should stop breastfeeding.

^d The optimal duration of empiric HIV therapy in newborns at higher risk of perinatal HIV transmission is unknown. Some Panel members opt to discontinue NVP, RAL, and/or 3TC when a NAT performed shortly after birth returns negative, while others would continue empiric HIV therapy for infants at highest risk of HIV acquisition for 2 to 6 weeks. In all cases, ZDV should be continued for 6 weeks. It is recommended that providers consult with an expert in pediatric HIV infection to determine therapy duration based on case-specific risk factors and interim HIV NAT results.

^e Most Panel members do not recommend delaying the initiation of ART pending results of the confirmatory HIV NAT, given the low likelihood of a false-positive HIV NAT.

Note: ARV drugs should be initiated as close to the time of birth as possible, preferably within 6 to 12 hours of delivery. See Table 7 for dosing specifics.

Key: 3TC = lamivudine; ART = antiretroviral therapy; ARV =antiretroviral; IV = intravenous; NAT = nucleic acid test; NVP = nevirapine; the Panel = Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission; RAL = raltegravir; ZDV = zidovudine

Table 12. Antiretroviral Dosing Recommendations for Newborns (page 1 of 3)

Newborns at Low Risk of Perinatal HIV Transmission	
Recommended Regimen	Recommended Duration
ZDV	ZDV administered for 4 weeks
Newborns at Higher Risk of Perinatal HIV Transmission	
Recommended Regimen	Recommended Duration
Empiric HIV therapy with ZDV plus 3TC plus NVP, <i>or</i>	ZDV administered for 6 weeks; 3TC and NVP administered for 2–6 weeks, up to 6 weeks of age ^a
Empiric HIV therapy with ZDV plus 3TC plus RAL, <i>or</i>	ZDV administered for 6 weeks; 3TC and RAL administered for 2–6 weeks, up to 6 weeks of age ^a
Two-drug ARV prophylaxis with ZDV and three doses of NVP (NICHD-HPTN 040/PACTG 1043 regimen)	ZDV administered for 6 weeks; three doses of NVP during the first week of life
Newborns with HIV Infection	
Recommended Regimen	Recommended Duration^b
HIV therapy with ZDV plus 3TC plus NVP, <i>or</i>	Lifelong therapy. NVP can be replaced with LPV/r when infant reaches a postmenstrual age ≥ 42 weeks and a postnatal age ≥ 14 days; NVP can be replaced with RAL at any age.

Indication																			
Drug	Low-Risk Prophylaxis	Higher-Risk Prophylaxis: Two-Drug Regimens	Higher-Risk Prophylaxis: Empiric and HIV Therapy																
ZDV Note: For newborns who are unable to tolerate oral agents, the IV dose is 75% of the oral dose while maintaining the same dosing interval.	≥ 35 Weeks Gestation at Birth: <ul style="list-style-type: none"> ZDV 4 mg/kg per dose orally twice daily Simplified Weight-Band Dosing for Newborns Aged ≥ 35 Weeks Gestation at Birth <table border="1"> <thead> <tr> <th>Weight Band</th> <th>Volume of ZDV 10 mg/mL Oral Syrup Twice Daily</th> </tr> </thead> <tbody> <tr> <td>2 to <3 kg</td> <td>1 mL</td> </tr> <tr> <td>3 to <4 kg</td> <td>1.5 mL</td> </tr> <tr> <td>4 to <5 kg</td> <td>2 mL</td> </tr> </tbody> </table>	Weight Band	Volume of ZDV 10 mg/mL Oral Syrup Twice Daily	2 to <3 kg	1 mL	3 to <4 kg	1.5 mL	4 to <5 kg	2 mL		≥ 35 Weeks Gestation at Birth <i>Birth to Age 4 Weeks:</i> <ul style="list-style-type: none"> ZDV 4 mg/kg per dose orally twice daily <i>Age >4 Weeks:</i> <ul style="list-style-type: none"> ZDV 12 mg/kg per dose orally twice daily Simplified Weight-Band Dosing for Newborns Aged ≥ 35 Weeks Gestation from Birth to 4 Weeks <table border="1"> <thead> <tr> <th>Weight Band</th> <th>Volume of ZDV 10 mg/mL Oral Syrup Twice Daily</th> </tr> </thead> <tbody> <tr> <td>2 to <3 kg</td> <td>1 mL</td> </tr> <tr> <td>3 to <4 kg</td> <td>1.5 mL</td> </tr> <tr> <td>4 to <5 kg</td> <td>2 mL</td> </tr> </tbody> </table>	Weight Band	Volume of ZDV 10 mg/mL Oral Syrup Twice Daily	2 to <3 kg	1 mL	3 to <4 kg	1.5 mL	4 to <5 kg	2 mL
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≥ 30 to <35 Weeks Gestation at Birth <i>Birth to Age 2 Weeks:</i> <ul style="list-style-type: none"> ZDV 2 mg/kg per dose orally twice daily <i>Age 2 Weeks to 4–6 Weeks:</i> <ul style="list-style-type: none"> ZDV 3 mg/kg per dose orally twice daily 		≥ 30 to <35 Weeks Gestation at Birth <i>Birth to Age 2 Weeks:</i> <ul style="list-style-type: none"> ZDV 2 mg/kg per dose orally twice daily <i>Age 2 Weeks to 6–8 Weeks:</i> <ul style="list-style-type: none"> ZDV 3 mg/kg per dose orally twice daily <i>Age >6 to 8 Weeks:</i> <ul style="list-style-type: none"> ZDV 12 mg/kg per dose orally twice daily 																	
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Table 12. Antiretroviral Dosing Recommendations for Newborns (page 2 of 3)

Indication																													
Drug	Low-Risk Prophylaxis	Higher-Risk Prophylaxis: Two-Drug Regimens	Higher-Risk Prophylaxis: Empiric and HIV Therapy																										
3TC	NRS	NRS	<p>≥32 Weeks Gestation at Birth</p> <p><i>Birth to Age 4 Weeks:</i></p> <ul style="list-style-type: none"> • 3TC 2 mg/kg per dose orally twice daily <p><i>Age >4 Weeks:</i></p> <ul style="list-style-type: none"> • 3TC 4 mg/kg per dose orally twice daily 																										
NVP	NRS	<p>≥32 Weeks Gestation at Birth:</p> <ul style="list-style-type: none"> • NVP in three doses, given within 48 hours of birth, 48 hours after the first dose, and 96 hours after the second dose <p>Birth Weight 1.5 to 2 kg:</p> <ul style="list-style-type: none"> • NVP 8 mg per dose orally. No calculation is required for this dose; this is the actual dose, not a mg/kg dose. <p>Birth Weight >2 kg:</p> <ul style="list-style-type: none"> • NVP 12 mg per dose orally. No calculation is required for this dose; this is the actual dose, not a mg/kg dose. 	<p>≥37 Weeks Gestation at Birth</p> <p><i>Birth to Age 4 Weeks:</i></p> <ul style="list-style-type: none"> • NVP 6 mg/kg per dose orally twice daily^c <p><i>Age >4 Weeks:</i></p> <ul style="list-style-type: none"> • NVP 200 mg/m² of BSA per dose orally twice daily <p>34 to <37 Weeks Gestation at Birth</p> <p><i>Birth to Age 1 Week:</i></p> <ul style="list-style-type: none"> • NVP 4 mg/kg per dose orally twice daily <p><i>Age 1–4 Weeks:</i></p> <ul style="list-style-type: none"> • NVP 6 mg/kg per dose orally twice daily <p><i>Age >4 Weeks:</i></p> <ul style="list-style-type: none"> • NVP 200 mg/m² of BSA per dose orally twice daily <p>Note: NVP dose adjustment at 4 weeks of age is optional for empiric HIV therapy.</p>																										
RAL	NRS	NRS	<p>≥37 Weeks Gestation at Birth and Weighing ≥2 kg^d</p> <p><i>Birth to Age 6 Weeks</i></p> <table border="1"> <thead> <tr> <th>Body Weight</th> <th>Volume (Dose) of RAL 10 mg/mL Suspension</th> </tr> </thead> <tbody> <tr> <td>Birth to 1 Week: Once Daily Dosing</td> <td>Approximately 1.5 mg/kg per dose</td> </tr> <tr> <td>2 to <3 kg</td> <td>0.4 mL (4 mg) once daily</td> </tr> <tr> <td>3 to <4 kg</td> <td>0.5 mL (5 mg) once daily</td> </tr> <tr> <td>4 to <5 kg</td> <td>0.7 mL (7 mg) once daily</td> </tr> <tr> <td>1 to 4 Weeks: Twice Daily Dosing</td> <td>Approximately 3 mg/kg per dose</td> </tr> <tr> <td>2 to <3 kg</td> <td>0.8 mL (8 mg) twice daily</td> </tr> <tr> <td>3 to <4 kg</td> <td>1 mL (10 mg) twice daily</td> </tr> <tr> <td>4 to <5 kg</td> <td>1.5 mL (15 mg) twice daily</td> </tr> <tr> <td>4 to 6 Weeks: Twice Daily Dosing</td> <td>Approximately 6 mg/kg per dose</td> </tr> <tr> <td>3 to <4 kg</td> <td>2.5 mL (25 mg) twice daily</td> </tr> <tr> <td>4 to <6 kg</td> <td>3 mL (30 mg) twice daily</td> </tr> <tr> <td>6 to <8 kg</td> <td>4 mL (40 mg) twice daily</td> </tr> </tbody> </table> <p>Note: If the mother has taken RAL 2–24 hours prior to delivery, the neonate's first dose of RAL should be delayed until 24–48 hours after birth; additional ARV drugs should be started as soon as possible.⁷</p>	Body Weight	Volume (Dose) of RAL 10 mg/mL Suspension	Birth to 1 Week: Once Daily Dosing	Approximately 1.5 mg/kg per dose	2 to <3 kg	0.4 mL (4 mg) once daily	3 to <4 kg	0.5 mL (5 mg) once daily	4 to <5 kg	0.7 mL (7 mg) once daily	1 to 4 Weeks: Twice Daily Dosing	Approximately 3 mg/kg per dose	2 to <3 kg	0.8 mL (8 mg) twice daily	3 to <4 kg	1 mL (10 mg) twice daily	4 to <5 kg	1.5 mL (15 mg) twice daily	4 to 6 Weeks: Twice Daily Dosing	Approximately 6 mg/kg per dose	3 to <4 kg	2.5 mL (25 mg) twice daily	4 to <6 kg	3 mL (30 mg) twice daily	6 to <8 kg	4 mL (40 mg) twice daily
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^b For ARV management after the newborn period, see the [Pediatric Antiretroviral Guidelines](#).

Table 12. Antiretroviral Dosing Recommendations for Newborns (page 3 of 3)

^c This dose is an investigational NVP treatment dose recommended by the Panel; the FDA has not approved a dose of NVP for infants aged <1 month.

^d RAL dosing is increased at 1 and 4 weeks of age because metabolism by UGT1A1 is low at birth and increases rapidly during the next 4–6 weeks of life. No dosing information is available for preterm infants or infants **weighing <2 kg at birth**.

Key: 3TC = lamivudine; ARV =antiretroviral; BSA = body surface area; FDA = Food and Drug Administration; IV = intravenous; **LPV/r = lopinavir/ritonavir**; NAT = nucleic acid test; **NRS = no recommendation specified**; NVP = nevirapine; the Panel = the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission; RAL = raltegravir; UGT = uridine diphosphate glucotransferase; ZDV = zidovudine

Table 13. Evidence-Based Approaches for Monitoring Medication Adherence

Routine Assessment of Medication Adherence in Clinical Care^a	Description
Monitor viral load.	Viral load monitoring should be done more frequently after initiating or changing medications. ^a
Assess quantitative self-report of missed doses.	Ask the patient and/or caregiver about the number of missed doses over a defined period (1, 3, or 7 days).
Elicit description of medication regimen.	Ask the patient and/or caregiver about the name, appearance, and number of medications, and how often the medications are taken.
Assess barriers to medication administration.	Engage the patient and caregiver in a dialogue about facilitators and challenges to adherence.
Monitor pharmacy refills.	Approaches include pharmacy-based or clinic-based assessment of on-time medication refills.
Conduct announced and unannounced pill counts.	Approaches include asking patients to bring medications to the clinic, home visits, or referral to community health nursing.
Targeted Approaches to Monitoring Adherence in Special Circumstances	Description
Implement DOT.	Include brief hospitalization if indicated.
Measure plasma drug concentration.	Measuring plasma drug concentrations can be considered for particular drugs.
Approaches to Monitoring Medication Adherence in Research Settings	Description
Measure drug concentrations in hair.	This is a good measure of adherence over time. ^{19,52,53}
Use electronic monitoring devices.	These include MEMS caps and Wisepill.
Use cell phone-based technologies.	These include interactive voice response, text messaging, and mobile apps.

^a See [Clinical and Laboratory Monitoring of Pediatric HIV Infection](#) regarding the frequency of adherence assessment after initiating or changing therapy.

Key to Acronyms: apps = applications; DOT = directly observed therapy; MEMS = Medication Event Monitoring System

Table 14. Strategies to Improve Adherence to Antiretroviral Medications

Initial Intervention Strategies
<ul style="list-style-type: none"> • Establish trust and identify mutually acceptable goals for care. • Obtain explicit agreement on the need for treatment and adherence. • Identify depression, low self-esteem, substance abuse, or other mental health issues in the child/adolescent and/or the caregiver that may affect adherence. Evaluate and initiate treatment for mental health issues before starting ARV drugs, if possible. • Identify family, friends, health team members, and others who can support adherence. • Educate the patient and family about the critical role of adherence in therapy outcome, including the relationship between partial adherence and resistance and the potential impact on future drug regimen choices. Develop a treatment plan that the patient and family understand and to which they feel committed. • Work with the patient and family to make specific plans for taking medications as prescribed and for supporting adherence. Assist them to arrange for administration in day care, school, and other settings, when needed. Consider home delivery of medications. • Establish a patient's readiness to take medication by staging practice sessions or by other means. • Schedule a home visit to review medications and determine how they will be administered in the home setting. • In certain circumstances, consider a brief period of hospitalization at the start of therapy for patient education and to assess the tolerability of the chosen medications.
Medication Strategies
<ul style="list-style-type: none"> • Choose the simplest regimen possible, reducing dosing frequency, pill size, and number of pills (see Appendix A, Table 1 and Appendix A, Table 2). • When choosing a regimen, consider the patient's daily and weekly routines and potential variations in patient and family activities. • Choose the most palatable medicine possible (pharmacists may be able to add syrups or flavoring agents to increase palatability). • Choose drugs with the fewest AEs; provide anticipatory guidance for management of AEs. • Simplify food requirements for medication administration. • Prescribe drugs carefully to avoid adverse drug-drug interactions. • Assess pill-swallowing capacity and offer pill-swallowing training and aids (e.g., pill-swallowing cup, pill glide). Adjust pill size as needed.
Follow-up Intervention Strategies
<ul style="list-style-type: none"> • Have more than one member of the multidisciplinary team monitor adherence at each visit and in between visits by telephone, email, text, and social media, as needed. • Provide ongoing support, encouragement, and understanding of the difficulties associated with maintaining adherence to daily medication regimens. • Use patient education aids, including pictures, calendars, and stickers. • Encourage use of pill boxes, reminders, mobile apps, alarms, and timers. • Provide follow-up clinic visits, telephone calls, and text messages to support and assess adherence. • Provide access to support groups, peer groups, or one-on-one counseling for caregivers and patients, especially for those with known depression or drug use issues that are known to decrease adherence. • Provide pharmacist-based adherence support, such as medication education and counseling, blister packs, refill reminders, automatic refills, and home delivery of medications. • Consider DOT at home, in the clinic, or in certain circumstances, such as during a brief inpatient hospitalization. • Consider gastrostomy tube use in certain circumstances. • Information on other interventions to consider can be found at the Complete Listing of Medication Adherence Evidence-Based Behavioral Interventions on the CDC's website. • Consult the CDC Every Dose Every Day toolkit.

Key to Acronyms: apps = applications; ARV = antiretroviral; AE = adverse effect; CDC = Centers for Disease Control and Prevention; DOT = directly observed therapy

Table 15a. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Central Nervous System Toxicity (Last updated April 16, 2019; last reviewed April 16, 2019) (page 1 of 3)

Adverse Effects		Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Global CNS Depression	LPV/r oral solution (contains both ethanol and propylene glycol as excipients)	<p><u>Onset:</u></p> <ul style="list-style-type: none"> • 1 day–6 days after starting LPV/r <p><u>Presentation</u></p> <p><i>Neonates/Premature Infants:</i></p> <ul style="list-style-type: none"> • Global CNS depression (e.g., abnormal EEG, altered state of consciousness, somnolence) 	Unknown; rare case reports have been published	<p>Prematurity</p> <p>Low birth weight</p> <p>Aged <14 days (whether birth was premature or term)</p>	Avoid use of LPV/r until a postmenstrual age of 42 weeks and a postnatal age of ≥14 days.	<p>Discontinue LPV/r; symptoms should resolve in 1 day–5 days.</p> <p>If needed, reintroduction of LPV/r can be considered once outside the vulnerable period (i.e., postmenstrual age of 42 weeks and a postnatal age ≥14 days).</p>
Neuropsychiatric Symptoms and Other CNS Manifestations	EFV	<p><u>Onset:</u></p> <ul style="list-style-type: none"> • For many symptoms, onset is 1 day–2 days after starting EFV. • Many symptoms subside or diminish by 2 weeks–4 weeks, but symptoms may persist in a significant proportion of patients. <p><u>Presentation (May Include One or More of the Following)</u></p> <p><i>Neuropsychiatric Symptoms:</i></p> <ul style="list-style-type: none"> • Abnormal dreams • Psychosis • Suicidal ideation or attempted/completed suicide <p><i>Other CNS Manifestations:</i></p> <ul style="list-style-type: none"> • Dizziness • Somnolence • Insomnia or poor sleep quality • Impaired concentration • Seizures (including absence seizures) • Cerebellar dysfunction (tremor, dysmetria, ataxia) <p>Note: CNS side effects such as impaired concentration, abnormal dreams, or sleep disturbances may be more difficult to assess in children.</p>	<p>Variable, depending on age, symptoms, and assessment method</p> <p><u>Children:</u></p> <ul style="list-style-type: none"> • 24% for any EFV-related CNS manifestations in one case series, with 18% of participants requiring drug discontinuation. • Five of 45 participants (11%) experienced new-onset seizures in one study in children aged <36 months. Two of these participants had alternative causes for seizures. • Cases of cerebellar dysfunction have been reported in children with very high EFV plasma levels. <p><u>Adults:</u></p> <ul style="list-style-type: none"> • 30% incidence for any CNS manifestations of any severity. • 6% incidence for EFV-related, severe CNS manifestations, including suicidality. However, evidence is conflicting about whether EFV use increases the incidence of suicidality. • One case series reported 20 women with ataxia that resolved upon EFV discontinuation, but frequency was not reported. 	<p>Insomnia is associated with elevated EFV trough concentration (≥4 mcg/mL)</p> <p>CYP2B6 polymorphisms that decrease EFV metabolism and cause increased EFV serum concentrations (CYP2B6 516 TT genotype or co-carriage of CYP2B6 516 G/T and 983 T/C variants)</p> <p>Prior history of psychiatric illness or use of psychoactive drugs</p>	<p>Administer EFV on an empty stomach, preferably at bedtime.</p> <p>Prescreen for psychiatric illness; avoid use in the presence of psychiatric illness, including depression or suicidal thoughts. Avoid concomitant use of psychoactive drugs.</p> <p>Consider using TDM in children with mild or moderate EFV-associated toxicities</p>	<p>If symptoms are excessive or persistent, obtain EFV trough concentration. If EFV trough concentration >4 mcg/mL and/or symptoms are severe, strongly consider drug substitution if a suitable alternative exists.</p> <p>Alternatively, consider dose reduction with repeat TDM and dose adjustment (with expert pharmacologist input).</p>

Table 15a. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Central Nervous System Toxicity (Last updated April 16, 2019; last reviewed April 16, 2019) (page 2 of 3)

Adverse Effects		Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Neuropsychiatric Symptoms and Other CNS Manifestations, continued	RPV	<p><u>Onset:</u></p> <ul style="list-style-type: none"> • Most symptoms occur in the first 4 weeks–8 weeks of treatment <p><u>Presentation</u></p> <p><i>Neuropsychiatric Symptoms:</i></p> <ul style="list-style-type: none"> • Depressive disorders • Suicidal ideation • Abnormal dreams/nightmares <p><i>Other CNS Manifestations:</i></p> <ul style="list-style-type: none"> • Headache • Dizziness • Insomnia • Somnolence 	<p><u>Adults:</u></p> <ul style="list-style-type: none"> • CNS/neuro-psychiatric adverse events of all severity grades were reported in 43% of patients at 96 weeks (mostly Grade 1). Depressive disorders of all severity grades were reported in 9% of patients. One percent of patients discontinued RPV due to severe depressive disorders. <p><u>Children:</u></p> <ul style="list-style-type: none"> • Depressive disorders of all severity grades were reported in 19.4% of pediatric patients aged 12 years–17 years. Severe depressive disorders were reported in 5.6% of patients, including one suicide attempt. • Somnolence was reported in five of 36 children (14%). 	Prior history of neuropsychiatric illness	Monitor carefully for depressive disorders and other CNS symptoms.	Consider drug substitution in cases of severe symptoms.
	RAL	<p><u>Onset:</u></p> <ul style="list-style-type: none"> • As early as 3 days–4 days after starting RAL <p><u>Presentation:</u></p> <ul style="list-style-type: none"> • Increased psychomotor activity • Headaches • Insomnia • Depression • Cerebellar dysfunction (e.g., tremor, dysarthria, ataxia) 	<p><u>Children:</u></p> <ul style="list-style-type: none"> • Increased psychomotor activity was reported in one child. <p><u>Adults:</u></p> <ul style="list-style-type: none"> • Headache • Insomnia (<5% in adult trials) • Rare case reports of cerebellar dysfunction in adults 	<p>Elevated RAL concentrations</p> <p>Co-treatment with TDF, a PPI, or inhibitors of UGT1A1</p> <p>Prior history of insomnia or depression</p>	<p>Prescreen for psychiatric symptoms.</p> <p>Monitor carefully for CNS symptoms.</p> <p>Use with caution in the presence of drugs that increase RAL concentration.</p>	Consider drug substitution (RAL or coadministered drug) in cases of severe insomnia or other neuropsychiatric symptoms.

Table 15a. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Central Nervous System Toxicity (Last updated April 16, 2019; last reviewed April 16, 2019) (page 3 of 3)

Adverse Effects		Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Neuropsychiatric Symptoms and Other CNS Manifestations, continued	DTG	<p><u>Onset:</u></p> <ul style="list-style-type: none"> • 7 days–30 days after starting DTG <p><u>Presentation</u></p> <p><i>Neuropsychiatric Symptoms:</i></p> <ul style="list-style-type: none"> • Depression or exacerbation of preexisting depression • Anxiety • Suicidal ideation or attempted/completed suicide <p><i>Other CNS Manifestations (Generally Mild):</i></p> <ul style="list-style-type: none"> • Insomnia • Dizziness • Headache 	<p><u>Children:</u></p> <ul style="list-style-type: none"> • CNS symptoms were uncommonly reported in early clinical experience in children and adolescents. <p><u>Adults:</u></p> <ul style="list-style-type: none"> • Exact frequency of neuropsychiatric symptoms is uncertain; there are case reports for four adult patients. Headache, insomnia, and dizziness are common and usually mild, with a rate of 6.1% reported for insomnia in adults. More severe symptoms that require drug discontinuation, including suicidality, are less common, occurring in ≤1% patients in Phase 3 trials, but these severe symptoms are reported with increasing frequency (4% to 10%) in recent post-marketing reports. • Higher frequency of neuropsychiatric symptoms reported with DTG than with other INSTIs. A class effect has been suggested. 	<p>Pre-existing depression or other psychiatric illness</p> <p>Higher frequency of neuropsychiatric symptoms reported when coadministered with ABC; however, evidence is conflicting.</p> <p>UGT1A1*6 and/or *28 polymorphism (reported in patients of Asian descent)</p>	<p>Use with caution in the presence of psychiatric illness, especially depression.</p> <p>Consider morning dosing of DTG.</p>	<p>For persistent or severe neuropsychiatric symptoms, consider discontinuation of DTG if suitable alternative exists.</p> <p>For mild symptoms, continue DTG and counsel patient that symptoms will likely resolve with time.</p>

Key to Acronyms: ABC = abacavir; ARV = antiretroviral; CNS = central nervous system; CYP = cytochrome P; DTG = dolutegravir; EEG = electroencephalogram; EFV = efavirenz; **INSTI = integrase strand transfer inhibitor**; LPV/r = lopinavir/ritonavir; PPI = proton pump inhibitor; RAL = raltegravir; RPV = rilpivirine; TDF = tenofovir disoproxil fumarate; TDM = therapeutic drug monitoring; UGT = uridine diphosphate-glucuronosyltransferase

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Table 15b. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Dyslipidemia

(Last updated April 16, 2019; last reviewed April 16, 2019) (page 1 of 2)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Dyslipidemia	<p>PIs:</p> <ul style="list-style-type: none"> All PIs, especially RTV-boosted PIs; lower incidence reported with DRV/r and ATV with or without RTV. <p>NRTIs:</p> <ul style="list-style-type: none"> Lower incidence with TDF than with TAF <p>NNRTIs:</p> <ul style="list-style-type: none"> Lower incidence reported with NVP, RPV, and ETR than with EFV 	<p>Onset:</p> <ul style="list-style-type: none"> As early as 2 weeks to months after beginning therapy <p>Presentation</p> <p>PIs:</p> <ul style="list-style-type: none"> ↑ LDL-C, TC, and TG <p>NNRTIs:</p> <ul style="list-style-type: none"> ↑ LDL-C, TC, and HDL-C <p>NRTIs:</p> <ul style="list-style-type: none"> ↑ LDL-C, TC, and TG 	<p>Reported frequency varies with specific ARV regimen, duration of ART, and the specific laboratory parameters used to diagnose lipid abnormalities.</p> <p>10% to 20% in young children receiving LPV/r.</p> <p>40% to 75% of older children and adolescents with prolonged ART history will have lipid abnormalities.</p> <p>Higher abnormal fasting serum lipids have been observed in ART-naïve adults who received EVG/COBI/FTC/TAF than in those who received EVG/COBI/FTC/TDF.</p> <p>Increase in serum lipids from baseline has also been noted in adolescents receiving EVG/COBI/FTC/TAF.</p>	<p>Advanced-stage HIV disease</p> <p>High-fat, high-cholesterol diet</p> <p>Lack of exercise</p> <p>Obesity</p> <p>Hypertension</p> <p>Smoking</p> <p>Family history of dyslipidemia or premature CVD</p> <p>Metabolic syndrome</p> <p>Fat maldistribution</p>	<p>Prevention:</p> <ul style="list-style-type: none"> Low-fat diet Exercise Smoking-prevention counseling When possible, use ARVs associated with a lower prevalence of dyslipidemia. These include INSTIs and newer PIs (e.g., ATV, DRV). <p>Monitoring^a</p> <p>Adolescents and Adults:</p> <ul style="list-style-type: none"> Obtain FLP (TC, HDL-C, non-HDL-C, LDL-C, and TG) twice (>2 weeks but ≤3 months apart, average these results) every 6 months–12 months. <p>Children (Aged ≥2 Years) without Lipid Abnormalities or Additional Risk Factors:</p> <ul style="list-style-type: none"> Obtain nonfasting screening lipid profiles at entry into care and then every 6 months–12 months, depending on the results. If TG or LDL-C is elevated or if a patient has additional risk factors, obtain FLP. <p>Children with Lipid Abnormalities and/or Additional Risk Factors:</p> <ul style="list-style-type: none"> Obtain 12-hour FLP before initiating or changing therapy and every 6 months thereafter (more often if indicated). <p>Children Receiving Lipid-Lowering Therapy with Statins or Fibrates:</p> <ul style="list-style-type: none"> Obtain 12-hour FLP, LFT, and CK at 4 and 8 weeks, and 3 months after starting lipid therapy. 	<p>Assess all patients for additional CVD risk factors. Patients living with HIV are considered to be at moderate risk of CVD.^b</p> <p>ART regimen changes should be considered, especially when the patient is receiving older PIs (e.g., LPV/r) and/or ritonavir boosting. Substituting a PI-sparing regimen, a PI-based regimen with a more favorable lipid profile, or COBI boosting causes a decline in LDL-C or TG values. However, the lipid-lowering effect for LDL-C is less pronounced than treatment results with statin therapy.</p> <p>Refer patients to a lipid specialist early if LDL-C ≥250 mg/dL or TG ≥500 mg/dL.</p> <p>If LDL-C is ≥130 mg/dL but <250 mg, or TG is ≥150 mg/dL but <500 mg/dL, a staged treatment approach is recommended by the NHLBI guidelines.^b</p> <ul style="list-style-type: none"> Implement diet, nutrition, and lifestyle management for 6 months to 9 months. Consult with a dietician if one is available. If a 6-month to 9-month trial of lifestyle modification fails and the patient is aged ≥10 years, consider implementing lipid-lowering therapy after consulting a lipid specialist.

Table 15b. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Dyslipidemia

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Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Dyslipidemia, continued					<ul style="list-style-type: none"> If there are minimal alterations in AST, ALT, and CK, monitor every 3 months–4 months during the first year and every 6 months thereafter (or as clinically indicated). Repeat FLP 4 weeks after increasing doses of antihyperlipidemic agents. 	<ul style="list-style-type: none"> Statin therapy should be considered for patients with elevated LDL-C levels. NHLBI provides recommendations for statin therapy in patients with specific LDL-C levels and risk factors.^b Drug therapy can be considered in cases of severe hypertriglyceridemia (TG ≥500 mg/dL). Fibrates (gemfibrozil and fenofibrate) and N-3 PUFAs derived from fish oils may be used. <p>The long-term risks of lipid abnormalities in children receiving ART are unclear. However, persistent dyslipidemia in children may lead to premature CVD.</p>

^a Given the burden of collecting fasting blood samples, some practitioners routinely measure cholesterol and triglycerides from nonfasting blood samples and follow up abnormal values with a test done in the fasted state.

^b Refer to the NHLBI guidelines: [Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents](#).

Key to Acronyms: ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; ATV = atazanavir; CK = creatine kinase; COBI = cobicistat; CVD = cardiovascular disease; DRV = darunavir; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; FLP = fasting lipid profile; FTC = emtricitabine; HDL-C = high-density lipoprotein cholesterol; INSTI = integrase strand transfer inhibitor; LDL-C = low-density lipoprotein cholesterol; LFT = liver function test; LPV/r = lopinavir/ritonavir; NHLBI = National Heart, Lung, and Blood Institute; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PUFA = polyunsaturated fatty acid; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglyceride

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Table 15c. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Gastrointestinal Effects (Last updated April 16, 2019; last reviewed April 16, 2019) (page 1 of 2)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Nausea/Vomiting	All ARV drugs, but most notably RTV-boosted PIs	<p>Onset:</p> <ul style="list-style-type: none"> • Early <p>Presentation:</p> <ul style="list-style-type: none"> • Nausea and emesis, both of which may be associated with anorexia and/or abdominal pain 	Varies with ARV agent; generally <15%	Unknown	<p>Instruct patient to take PIs with food.</p> <p>Monitor for weight loss and ARV adherence.</p>	<p>Reassure patient that these adverse effects generally improve over time (usually 6–8 weeks).</p> <p>Consider switching to ARV drugs with smaller tablet sizes (see Appendix A, Table 2).</p> <p>Provide supportive care.</p> <p>In extreme or persistent cases, use antiemetics or switch to another ARV regimen.</p>
Diarrhea	All ARV drugs, but most notably RTV-boosted PIs	<p>Onset:</p> <ul style="list-style-type: none"> • Early <p>Presentation:</p> <ul style="list-style-type: none"> • More frequent bowel movements and stools that are generally soft 	Varies with ARV agent; generally <15%	Unknown	Monitor for weight loss and dehydration.	<p>If prolonged or severe, exclude infectious or noninfectious (e.g., lactose intolerance) causes of diarrhea.</p> <p>Reassure patient that this adverse effect generally improves over time (usually 6–8 weeks). Consider switching to another ARV regimen in persistent and severe cases.</p> <p>Treatment data in children are lacking; however, the following strategies may be useful when the ARV regimen cannot be changed:</p> <ul style="list-style-type: none"> • Dietary modification • Using bulk-forming agents (e.g., psyllium) • Using antimotility agents (e.g., loperamide) • Using crofelemer, which is approved by the FDA to treat ART-associated diarrhea in adults aged ≥18 years; no pediatric data are available.

Table 15c. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Gastrointestinal Effects (Last updated April 16, 2019; last reviewed April 16, 2019) (page 2 of 2)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Pancreatitis	Rare, but may occur with RTV-boosted PIs or NRTIs	<p>Onset:</p> <ul style="list-style-type: none"> Any time, usually after months of therapy <p>Presentation:</p> <ul style="list-style-type: none"> Emesis, abdominal pain, elevated amylase and lipase levels (asymptomatic hyperamylasemia or elevated lipase do not in and of themselves indicate pancreatitis) 	<2% in a recent case series	<p>Use of concomitant medications associated with pancreatitis (e.g., TMP-SMX, pentamidine, ribavirin)</p> <p>Hypertriglyceridemia</p> <p>Advanced HIV infection</p> <p>Previous episode of pancreatitis</p> <p>Alcohol use</p>	Measure serum amylase and lipase concentrations if persistent abdominal pain develops.	<p>Discontinue offending agent and avoid reintroduction.</p> <p>Manage symptoms of acute episodes.</p> <p>If pancreatitis is associated with hypertriglyceridemia, consider using interventions to lower TG levels.</p>

Key to Acronyms: ART = antiretroviral therapy; ARV = antiretroviral; FDA = Food and Drug Administration; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RTV = ritonavir; TG = triglyceride; TMP-SMX = trimethoprim sulfamethoxazole; ZDV = zidovudine

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Table 15d. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Hematologic Effects (Last updated April 16, 2019; last reviewed April 16, 2019) (page 1 of 2)

Adverse Effects		Onset/ Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Anemia ^a	ZDV	<p><u>Onset:</u></p> <ul style="list-style-type: none"> • Variable, weeks to months <p><u>Presentation</u></p> <p><i>Most Commonly:</i></p> <ul style="list-style-type: none"> • Asymptomatic • Mild fatigue • Pallor • Tachypnea <p><i>Rarely:</i></p> <ul style="list-style-type: none"> • Congestive heart failure 	<p><u>Newborns Exposed to HIV:</u></p> <ul style="list-style-type: none"> • Severe anemia is uncommon but may be seen coincident with physiologic Hgb nadir. <p><u>Children with HIV Who Are Taking ARV Drugs:</u></p> <ul style="list-style-type: none"> • Anemia is two to three times more common with ZDV-containing regimens compared to all other regimens. 	<p><u>Newborns Exposed to HIV:</u></p> <ul style="list-style-type: none"> • Premature birth • <i>In utero</i> exposure to ZDV-containing regimens • Advanced maternal HIV • Neonatal blood loss • Combination ARV prophylaxis or empiric HIV therapy, particularly with ZDV plus 3TC <p><u>Children with HIV Who Are Taking ARV Drugs:</u></p> <ul style="list-style-type: none"> • Underlying hemoglobinopathy (e.g., sickle cell disease, G6PD deficiency) • Myelosuppressive drugs (e.g., TMP-SMX, rifabutin) • Iron deficiency • Advanced or poorly controlled HIV disease • OIs of the bone marrow • Malnutrition 	<p><u>Newborns Exposed to HIV:</u></p> <ul style="list-style-type: none"> • Obtain CBC at birth. • Consider repeating CBC at 4 weeks for neonates who are at higher risk (e.g., those born prematurely or who are known to have low birth Hgb) and for neonates who receive ZDV beyond 4 weeks. <p><u>Children with HIV Who Are Taking ARV Drugs:</u></p> <ul style="list-style-type: none"> • Avoid ZDV in children with severe anemia when alternative agents are available. • Obtain CBC as part of routine care (see Clinical and Laboratory Monitoring of Pediatric HIV Infection). 	<p><u>Newborns Exposed to HIV:</u></p> <ul style="list-style-type: none"> • Anemia rarely requires intervention unless Hgb is <7.0 g/dL or is associated with symptoms. • ZDV administration can be limited to 4 weeks in low-risk neonates (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV). <p><u>Children with HIV Who Are Taking ARV Drugs:</u></p> <ul style="list-style-type: none"> • Discontinue non-ARV, marrow-toxic drugs, if feasible. • Treat coexisting iron deficiency, OIs, and malignancies. • For persistent, severe anemia that is thought to be associated with ARV drugs (typically macrocytic anemia), switch to a regimen that does not contain ZDV.
Macrocytosis	ZDV	<p><u>Onset:</u></p> <ul style="list-style-type: none"> • Within days to weeks of starting therapy <p><u>Presentation:</u></p> <ul style="list-style-type: none"> • Asymptomatic but MCV is often >100 fL • Sometimes associated with anemia 	<p><u>All Ages:</u></p> <ul style="list-style-type: none"> • >90% to 95% 	None	<p>No monitoring required—macrocytosis can be detected if CBC is obtained as part of routine care (see Clinical and Laboratory Monitoring of Pediatric HIV Infection).</p>	No management required.

Table 15d. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Hematologic Effects (Last updated April 16, 2019; last reviewed April 16, 2019) (page 2 of 2)

Adverse Effects	Associated ARVs	Onset/ Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Neutropenia ^a	ZDV	<p><u>Onset:</u></p> <ul style="list-style-type: none"> • Variable <p><u>Presentation:</u></p> <ul style="list-style-type: none"> • Asymptomatic 	<p><u>Newborns Exposed to HIV:</u></p> <ul style="list-style-type: none"> • Rare <p><u>Children with HIV Who Are Taking ARV Drugs:</u></p> <ul style="list-style-type: none"> • 2% to 4% of children on ARV drugs • Highest rates occur in children on ZDV-containing regimens 	<p><u>Newborns Exposed to HIV:</u></p> <ul style="list-style-type: none"> • <i>In utero</i> exposure to ARV drugs • Combination ARV prophylaxis, particularly with ZDV plus 3TC <p><u>Children with HIV Who Are Taking ARV Drugs:</u></p> <ul style="list-style-type: none"> • Advanced or poorly controlled HIV infection • Myelosuppressive drugs (e.g., TMP-SMX, ganciclovir, hydroxyurea, rifabutin) 	<p><u>Children with HIV Who Are Taking ARV Drugs:</u></p> <ul style="list-style-type: none"> • Obtain CBC as part of routine care. 	<p><u>Newborns Exposed to HIV:</u></p> <ul style="list-style-type: none"> • No established threshold for intervention; some experts would consider using an alternative NRTI for prophylaxis if ANC reaches <500 cells/mm³. ZDV administration can be limited to 4 weeks in low-risk neonates (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV). <p><u>Children with HIV Who Are Taking ARV Drugs:</u></p> <ul style="list-style-type: none"> • Discontinue non-ARV, marrow-toxic drugs, if feasible. • Treat coexisting OIs and malignancies. • For persistent, severe neutropenia that is thought to be associated with ARV drugs, change to a regimen that does not contain ZDV.

^a HIV infection itself, OIs, and medications used to prevent OIs (e.g., TMP-SMX) may all contribute to anemia and neutropenia.

Key to Acronyms: 3TC = lamivudine; ANC = absolute neutrophil count; ARV = antiretroviral; CBC = complete blood count; dL = deciliter; fL = femtoliter; G6PD = glucose-6-phosphate dehydrogenase; Hgb = hemoglobin; MCV = mean cell volume; NRTI = nucleoside reverse transcriptase inhibitor; OI = opportunistic infection; TMP-SMX = trimethoprim-sulfamethoxazole; ZDV = zidovudine

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Table 15e. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Hepatic Events

(Last updated April 16, 2019; last reviewed April 16, 2019) (page 1 of 2)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Hepatitis	<p>Most ARV drugs have been associated with hepatitis, but there is a strong association between hepatitis, NVP, and EFV.</p> <p>NVP, EFV, ABC, RAL, DTG, and MVC have been associated with hepatitis in the context of HSRs.</p> <p>NRTIs have been associated with lactic acidosis and hepatic steatosis, especially ZDV.</p>	<p><u>Onset:</u></p> <ul style="list-style-type: none"> Acute toxic hepatitis most commonly occurs within the first few months of therapy, but it can occur later. Steatosis presents after months to years of therapy. Patients with HBV coinfection may develop flare of hepatitis with the initiation or withdrawal of 3TC, FTC, TDF, or TAF. Flare may also occur with the emergence of resistance to 3TC or FTC (especially if the patient is receiving only one anti-HBV agent). Note that HBV has a high genetic barrier for resistance to TDF and TAF. Hepatitis may be a manifestation of IRIS if it occurs early in therapy, especially in patients with HBV or HCV coinfection. <p><u>Presentation:</u></p> <ul style="list-style-type: none"> Asymptomatic elevation of AST and ALT levels Symptomatic hepatitis with nausea, fatigue, and jaundice Hepatitis may present in the context of HSR with rash, lactic acidosis, and hepatic steatosis. 	Uncommon	<p>HBV or HCV coinfection</p> <p>Underlying liver disease</p> <p>Use of other hepatotoxic medications and supplements (e.g., St. John's wort [<i>Hypericum perforatum</i>], chaparral [<i>Larrea tridentata</i>], germander [<i>Teucrium chamaedrys</i>])</p> <p>Alcohol use</p> <p>Pregnancy</p> <p>Obesity</p> <p>Higher drug concentrations of PIs</p> <p><u>For NVP-Associated Hepatic Events in Adults:</u></p> <ul style="list-style-type: none"> Female sex with pre-NVP CD4 count >250 cells/mm³ Male sex with pre-NVP CD4 count >400 cells/mm³ Population-specific HLA types^a 	<p><u>Prevention:</u></p> <ul style="list-style-type: none"> Avoid concomitant use of hepatotoxic medications. In patients with elevated levels of hepatic enzymes (>5 times to 10 times ULN) or chronic liver disease, most clinicians would avoid NVP. <p><u>Monitoring</u></p> <p><i>For ARV Drugs Other Than NVP:</i></p> <ul style="list-style-type: none"> Obtain AST and ALT levels at baseline and at least every 3 months–4 months thereafter;^b monitor at-risk patients more frequently (e.g., those with HBV or HCV coinfection or elevated baseline AST and ALT levels). <p><i>For NVP:</i></p> <ul style="list-style-type: none"> Obtain AST and ALT levels at baseline, at 2 weeks, 4 weeks, and then every 3 months. 	<p>Evaluate the patient for other infectious and non-infectious causes of hepatitis and monitor the patient closely.</p> <p><u>Asymptomatic Hepatitis:</u></p> <ul style="list-style-type: none"> Potentially offending ARV drugs should be discontinued if ALT or AST level is >5 times ULN. <p><u>Symptomatic Hepatitis:</u></p> <ul style="list-style-type: none"> Discontinue all ARV drugs and other potentially hepatotoxic drugs. If a patient experiences hepatitis that is attributed to NVP, NVP should be permanently discontinued. Consider viral causes of hepatitis: HAV, HBV, HCV, EBV, and CMV.

Table 15e. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Hepatic Events

(Last updated April 16, 2019; last reviewed April 16, 2019) (page 2 of 2)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Indirect Hyperbilirubinemia	ATV	<p><u>Onset:</u></p> <ul style="list-style-type: none"> • Within the first months of therapy <p><u>Presentation:</u></p> <ul style="list-style-type: none"> • May be asymptomatic or associated with jaundice • Levels of direct bilirubin may be normal or slightly elevated when levels of indirect bilirubin are very high. • Normal AST and ALT 	In long-term follow-up, 9% of children receiving ATV had at least one total bilirubin level >5 times ULN and 1.4% of children experienced jaundice.	N/A	<p><u>Monitoring:</u></p> <ul style="list-style-type: none"> • No ongoing monitoring needed. • After an initial rise over the first few months of therapy, unconjugated bilirubin levels generally stabilize; levels may improve over time. 	<p>Isolated indirect hyperbilirubinemia is not an indication for cessation of the potentially offending ARV drug.</p> <p>Psychological impact of jaundice should be evaluated, and alternative agents should be considered.</p> <p>Jaundice may result in nonadherence, particularly in adolescents; this side effect should be discussed.</p>
Non-Cirrhotic Portal Hypertension	d4T, ddl The Panel no longer recommends the use of these agents.	<p><u>Onset:</u></p> <ul style="list-style-type: none"> • Generally after years of therapy; may occur years after stopping therapy. <p><u>Presentation:</u></p> <ul style="list-style-type: none"> • GI bleeding, esophageal varices, and hypersplenism • Mild elevations in AST and ALT levels, moderate increases in ALP levels, and pancytopenia <p><u>Liver Biopsy Findings:</u></p> <ul style="list-style-type: none"> • Most commonly seen findings include nodular regenerative hyperplasia and hepatportal sclerosis. 	Rare	Prolonged exposure to ddl and the combination of d4T and ddl.	<p><u>Monitoring:</u></p> <ul style="list-style-type: none"> • No specific monitoring 	Manage complications of GI bleeding and esophageal varices.

^a For example, HLA-DRB1*0101 in white people, HLA-DRB1*0102 in South Africans, and HLA-B35 in Thai people and white people.

^b Less-frequent monitoring can be considered in children whose clinical status is stable for >2 years to 3 years (see [Clinical and Laboratory Monitoring of Pediatric HIV Infection](#)).

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ALP = alkaline phosphatase; ALT = alanine transaminase; ARV = antiretroviral; AST = aspartate aminotransferase; ATV = atazanavir; CD4 = CD4 T lymphocyte; CMV = cytomegalovirus; COBI = cobicistat; d4T = stavudine; ddl = didanosine; **DTG = dolutegravir**; EBV = Epstein-Barr virus; EFV = efavirenz; FTC = emtricitabine; GI = gastrointestinal; HAV = hepatitis A virus; HBV = hepatitis B virus; HCV = hepatitis C virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; IRIS = immune reconstitution inflammatory syndrome; MVC = maraviroc; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ULN = upper limit of normal; ZDV = zidovudine

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Table 15f. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Insulin Resistance, Asymptomatic Hyperglycemia, Diabetes Mellitus (Last updated April 16, 2019; last reviewed April 16, 2019)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Insulin Resistance, Asymptomatic Hyperglycemia, DM^a	ZDV, LPV/r, and possibly other PIs	<p><u>Onset:</u></p> <ul style="list-style-type: none"> Weeks to months after beginning therapy <p><u>Presentation:</u></p> <ul style="list-style-type: none"> Asymptomatic fasting hyperglycemia (which sometimes occurs in the setting of lipodystrophy), metabolic syndrome, or growth delay Symptomatic DM (rare) 	<p><u>Children:</u></p> <ul style="list-style-type: none"> Insulin resistance, 6% to 12% (incidence is higher during puberty, 20% to 30%) Impaired fasting glucose, 0% to 7% Impaired glucose tolerance, 3% to 4% DM, 0.2 per 100 child-years 	<p><u>Risk Factors for Type 2 DM:</u></p> <ul style="list-style-type: none"> Lipodystrophy Metabolic syndrome Family history of DM High BMI (obesity) 	<p><u>Prevention:</u></p> <ul style="list-style-type: none"> Lifestyle modification <p><u>Monitoring:</u></p> <ul style="list-style-type: none"> Monitor for signs of DM, change in body habitus, and acanthosis nigricans. <p><i>Obtain RPG Levels at:</i></p> <ul style="list-style-type: none"> Initiation of ARV therapy 3 months–6 months after therapy initiation Once a year thereafter <p><i>For RPG ≥140 mg/dL:</i></p> <ul style="list-style-type: none"> Obtain FPG after an 8-hour fast and consider referring the patient to an endocrinologist. 	<p>Counsel patient on lifestyle modification (e.g., implementing a diet low in saturated fat, cholesterol, trans fat, and refined sugars; increasing physical activity; ceasing smoking). Recommend that the patient consult with a dietician.</p> <p>If patient is receiving ZDV, change to TAF, TDF, or ABC.</p> <p><u>For Either RPG ≥200 mg/dL Plus Symptoms of DM or FPG ≥126 mg/dL:</u></p> <ul style="list-style-type: none"> Patient meets diagnostic criteria for DM; consult an endocrinologist. <p><u>FPG 100–125 mg/dL:</u></p> <ul style="list-style-type: none"> Impaired FPG suggests insulin resistance; consult endocrinologist. <p><u>FPG <100 mg/dL:</u></p> <ul style="list-style-type: none"> This FPG is normal, but a normal FPG does not exclude insulin resistance. Recheck FPG in 6 months–12 months.

^a Insulin resistance, asymptomatic hyperglycemia, and DM form a spectrum of increasing severity.

Insulin Resistance: Often defined as elevated insulin levels for the level of glucose observed.

Impaired FPG: Often defined as an FPG of 100–125 mg/dL.

Impaired Glucose Tolerance: Often defined as an elevated 2-hour PG of 140–199 mg/dL in a 75-g OGTT (or, if the patient weighs <43 kg, 1.75 g per kg of glucose up to a maximum of 75 g).

Diabetes Mellitus: Often defined as either an FPG ≥126 mg/dL, and RPG ≥200 mg/dL in a patient with hyperglycemia symptoms, an HgbA1c of ≥6.5%, or a 2-hour PG ≥200 mg/dL after an OGTT.

However, the Panel does not recommend performing routine measurements of insulin levels, HgbA1c, or glucose tolerance without consulting an endocrinologist. These guidelines are instead based on the readily available RPG and FPG levels.

Key to Acronyms: ABC = abacavir; ARV = antiretroviral; BMI = body mass index; dL = deciliter; DM = diabetes mellitus; FPG = fasting plasma glucose; HgbA1c = glycosylated hemoglobin; LPV/r = lopinavir/ritonavir; OGTT = oral glucose tolerance test; PG = plasma glucose; PI = protease inhibitor; RPG = random plasma glucose; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

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Table 15g. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Lactic Acidosis

(Last updated April 16, 2019; last reviewed April 16, 2019)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Lactic Acidosis	<p>NRTIs:</p> <ul style="list-style-type: none"> ZDV Less likely with 3TC, FTC, ABC, TAF, and TDF <p>Other Drugs:</p> <ul style="list-style-type: none"> See Risk Factors and Prevention/Monitoring columns for information regarding the toxicity of propylene glycol when LPV/r oral solution is used in neonates. 	<p>Onset:</p> <ul style="list-style-type: none"> Generally, after years of exposure <p>Presentation:</p> <ul style="list-style-type: none"> Lactic acidosis may be clinically asymptomatic. <p><i>Insidious Onset of a Combination of Signs and Symptoms:</i></p> <ul style="list-style-type: none"> Generalized fatigue, weakness, and myalgias Vague abdominal pain, weight loss, unexplained nausea, or vomiting Dyspnea Peripheral neuropathy <p>Note: Patients may present with acute multi-organ failure (e.g., fulminant hepatic failure, pancreatic failure, respiratory failure).</p>	<p>Lactic acidosis is associated with use of ddl and d4T. Cases are rare now that these NRTIs are no longer recommended.</p> <p>3TC, FTC, ABC, TAF, and TDF are less likely to induce clinically significant mitochondrial dysfunction than ZDV.</p>	<p>Adults:</p> <ul style="list-style-type: none"> Female sex High BMI Chronic HCV infection African-American race Coadministration of TDF with metformin Overdose of propylene glycol CD4 cell count <350 cells/mm³ Acquired riboflavin or thiamine deficiency Possibly pregnancy <p><u>Preterm Infants or Any Neonates Who Have Not Attained a Post-Menstrual Age of 42 Weeks and a Postnatal Age of ≥14 Days:</u></p> <ul style="list-style-type: none"> Exposure to propylene glycol (e.g., present as a diluent in LPV/r oral solution). A diminished ability to metabolize propylene glycol may lead to accumulation and potential adverse events. 	<p>Prevention:</p> <ul style="list-style-type: none"> Due to the presence of propylene glycol as a diluent, LPV/r oral solution should not be used in preterm neonates or any neonate who has not attained a postmenstrual age of 42 weeks and a postnatal age of ≥14 days. Monitor for clinical manifestations of lactic acidosis and promptly adjust therapy. <p><u>Monitoring</u></p> <p><i>Asymptomatic Patients:</i></p> <ul style="list-style-type: none"> Measurement of serum lactate is not recommended. <p><i>Patients with Clinical Signs or Symptoms Consistent with Lactic Acidosis:</i></p> <ul style="list-style-type: none"> Obtain blood lactate level.^a Additional diagnostic evaluations should include serum bicarbonate, anion gap, and/or arterial blood gas; amylase and lipase; serum albumin; and hepatic transaminases. 	<p>Lactate 2.1–5.0 mmol/L (Confirmed with a Second Test):</p> <ul style="list-style-type: none"> Consider discontinuing all ARV drugs temporarily while conducting additional diagnostic workup. <p>Lactate >5.0 mmol/L (Confirmed With a Second Test)^b or >10.0 mmol/L (Any One Test):</p> <ul style="list-style-type: none"> Discontinue all ARV drugs. Provide supportive therapy (e.g., IV fluids; some patients may require sedation and respiratory support to reduce oxygen demand and ensure adequate oxygenation of tissues). <p><u>Anecdotal (Unproven) Supportive Therapies:</u></p> <ul style="list-style-type: none"> Administer bicarbonate infusions, THAM, high doses of thiamine and riboflavin, oral antioxidants (e.g., L-carnitine, co-enzyme Q10, vitamin C) <p>Following the resolution of clinical and laboratory abnormalities, resume therapy, either with a NRTI-sparing regimen or a revised NRTI-containing regimen. Institute a revised NRTI-containing regimen with caution, using NRTIs that are less likely to induce mitochondrial dysfunction (ABC, TAF, or TDF preferred; possibly FTC or 3TC). Lactate should be monitored monthly for ≥3 months.</p>

^a Blood for lactate determination should be collected, without prolonged tourniquet application or fist clenching, into a pre-chilled, gray-top, fluoride-oxalate-containing tube and transported on ice to the laboratory to be processed within 4 hours of collection.

^b Management can be initiated before receiving the results of the confirmatory test.

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; BMI = body mass index; CD4 = CD4 T lymphocyte; d4T = stavudine; ddl; didanosine; FTC = emtricitabine; HCV = hepatitis C virus; IV = intravenous; LPV/r = lopinavir/ritonavir; NRTI = nucleoside reverse transcriptase inhibitor; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; THAM = tris (hydroxymethyl) aminomethane; ZDV = zidovudine

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Table 15h. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Lipodystrophy, Lipohypertrophy, Lipoatrophy (Last updated April 16, 2019; last reviewed April 16, 2019) (page 1 of 2)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
<p>Lipodystrophy (Fat Maldistribution)</p> <p>General Information</p>	See below for specific associations.	<p><u>Onset:</u></p> <ul style="list-style-type: none"> Trunk and limb fat are the first sign; peripheral fat wasting may not appear for 12 months–24 months after ART initiation. 	Frequency is low (<5%) with current regimens.	<p>Genetic predisposition</p> <p>Puberty</p> <p>HIV-associated inflammation</p> <p>Older age</p> <p>Longer duration of ART</p> <p>Body habitus</p>	<p><u>Prevention:</u></p> <ul style="list-style-type: none"> Initiating a calorically appropriate, low-fat diet and exercise <p><u>Monitoring:</u></p> <ul style="list-style-type: none"> BMI measurement Body circumference and waist-hip ratio 	<p>Physicians should perform a regimen review and consider changing the regimen when lipodystrophy occurs.</p> <p>Improvement in fat maldistribution following a regimen change is variable. Improvement may occur after several months or years, or it may not occur at all.</p>
<p>Central Lipohypertrophy</p> <p>or</p> <p>Lipo-accumulation</p>	Can occur in the absence of ART, but these conditions are most often associated with the use of PIs and EFV.	<p><u>Presentation:</u></p> <ul style="list-style-type: none"> Central fat accumulation with increased abdominal girth, which may include a dorsocervical fat pad (buffalo hump). Gynecomastia in males or breast hypertrophy in females, particularly with the use of EFV. 	<5% with current regimens	<p>Obesity before initiation of therapy</p> <p>Sedentary lifestyle</p>	<p><u>Prevention:</u></p> <ul style="list-style-type: none"> Initiating a calorically appropriate, low-fat diet and exercise <p><u>Monitoring:</u></p> <ul style="list-style-type: none"> BMI measurement Body circumference and waist-hip ratio 	<p>Counsel patient on lifestyle modification and dietary interventions (e.g., maintaining a calorically appropriate, healthy diet that is low in saturated fats and simple carbohydrates, and starting an exercise regimen, especially strength training).</p> <p>Recommend smoking cessation (if applicable) to decrease future CVD risk.</p> <p>Consider using an INSTI instead of a PI or EFV.</p> <p><u>Data are Insufficient to Allow the Panel to Safely Recommend Use of Any of the Following Modalities in Children:</u></p> <ul style="list-style-type: none"> Recombinant human growth hormone Growth hormone-releasing hormone Metformin Thiazolidinediones Recombinant human leptin Anabolic steroids Liposuction

Table 15h. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Lipodystrophy, Lipohypertrophy, Lipoatrophy (Last updated April 16, 2019; last reviewed April 16, 2019) (page 2 of 2)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Facial/Peripheral Lipoatrophy	Most cases are associated with the use of ZDV, a thymidine analogue NRTI.	<p>Presentation:</p> <ul style="list-style-type: none"> • Thinning of subcutaneous fat in the face, buttocks, and extremities, measured as a decrease in trunk/limb fat by DXA or triceps skinfold thickness. Preservation of lean body mass distinguishes lipoatrophy from HIV-associated wasting. 	<5% with currently used regimens	Underweight before ART	<p>Prevention:</p> <ul style="list-style-type: none"> • Limit the use of ZDV. <p>Monitoring:</p> <ul style="list-style-type: none"> • Patient self-report and physical examination are the most sensitive methods of monitoring lipoatrophy. 	<p>Replace ZDV with another NRTI if possible.</p> <p><u>Data are Insufficient to Allow the Panel to Safely Recommend Use of Any of the Following Modalities in Children:</u></p> <ul style="list-style-type: none"> • Injections of poly-L-lactic acid • Recombinant human leptin • Autologous fat transplantation • Thiazolidinediones

Key to Acronyms: ART = antiretroviral therapy; ARV = antiretroviral; BMI = body mass index; CVD = cardiovascular disease; DXA = dual energy x-ray absorptiometry; EFV = efavirenz; INSTI = integrase strand transfer inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; ZDV = zidovudine

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See the archived version of [Supplement III, February 23, 2009, Pediatric Guidelines](#) on the [AIDSinfo website](#) for a more complete discussion and reference list.

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Table 15i. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Nephrotoxic Effects
 (Last updated April 16, 2019; last reviewed April 16, 2019) (page 1 of 2)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Urolithiasis/ Nephrolithiasis	ATV DRV causes crystalluria, but it is not associated with nephrolithiasis.	<u>Onset:</u> <ul style="list-style-type: none"> Weeks to months after starting therapy <u>Clinical Findings:</u> <ul style="list-style-type: none"> Crystalluria Hematuria Pyuria Flank pain Increased creatinine in some cases 	ATV-related nephrolithiasis occurs in <10% of patients.	In adults, elevated urine pH (>5.7) The risk factors in children are unknown.	<u>Prevention:</u> <ul style="list-style-type: none"> Maintain adequate hydration. <u>Monitoring:</u> <ul style="list-style-type: none"> Obtain urinalysis at least every 6 months–12 months. 	Provide adequate hydration and pain control. Consider using another ARV in place of ATV.
Renal Dysfunction	TDF	<u>Onset:</u> <ul style="list-style-type: none"> Variable; in adults, renal dysfunction may occur weeks to months after initiating therapy. Hypophosphatemia appears at a median of 18 months. Glucosuria may occur after a year of therapy. Abnormal urine protein/osmolality ratio may be an early indicator. <u>Presentation</u> <i>More Common:</i> <ul style="list-style-type: none"> Increased serum creatinine, proteinuria, normoglycemic glucosuria Increased urinary protein/creatinine ratio and albumin/creatinine ratio Hypophosphatemia, usually asymptomatic; may present with bone and muscle pain, or muscle weakness <i>Less Common:</i> <ul style="list-style-type: none"> Renal failure, acute tubular necrosis, Fanconi syndrome, proximal renal tubulopathy, interstitial nephritis, nephrogenic diabetes insipidus with polyuria 	<u>Adults:</u> <ul style="list-style-type: none"> Approximately 2% experience increased serum creatinine levels. Approximately 0.5% experience severe renal complications <u>Children:</u> <ul style="list-style-type: none"> Approximately 4% experience hypophosphatemia or proximal tubulopathy; frequency increases with prolonged TDF therapy and advanced HIV infection. 	<u>Risk May Increase in Children with the Following Characteristics:</u> <ul style="list-style-type: none"> Aged >6 years Black race, Hispanic/Latino ethnicity Advanced HIV infection Hypertension Diabetes Concurrent use of PIs (especially LPV/r) and preexisting renal dysfunction Risk increases with longer duration of TDF treatment. 	Monitor urine protein, urine glucose and serum creatinine at 3-month to 6-month intervals. For patients taking TDF, some Panel members routinely monitor serum phosphate levels. Measure serum phosphate if the patient experiences persistent proteinuria or glucosuria, or has symptoms of bone pain, muscle pain, or weakness. Because toxicity risk increases with the duration of TDF treatment, do not decrease the frequency of monitoring over time.	If TDF is the likely cause, consider using an alternative ARV drug. TAF has significantly less toxicity than TDF.

Table 15i. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Nephrotoxic Effects
 (Last updated April 16, 2019; last reviewed April 16, 2019) (page 2 of 2)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Elevation in Serum Creatinine	DTG, COBI, RPV	<p>Onset:</p> <ul style="list-style-type: none"> • Within a month of starting treatment <p>Presentation:</p> <ul style="list-style-type: none"> • Asymptomatic. These drugs decrease renal tubular secretion of creatinine, leading to an increase in serum creatinine levels without a true change in eGFR. 	<p>Common</p> <p>Need to distinguish between a true change in eGFR and other causes. A true change may be associated with other medical conditions, the continuing rise of serum creatinine levels over time, and albuminuria.</p>	N/A	<p>Monitor serum creatinine. Assess for renal dysfunction if serum creatinine increases by >0.4 mg/dL or if increases continue over time.</p>	<p>No need to change therapy.</p> <p>Reassure the patient about the benign nature of the laboratory abnormality.</p>

Key to Acronyms: ARV = antiretroviral; ATV = atazanavir; COBI = cobicistat; **dL = deciliter**; DRV = darunavir; DTG = dolutegravir; eGFR = estimated glomerular filtration rate; LPV/r = lopinavir/ritonavir; PI = protease inhibitor; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

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Table 15j. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Osteopenia and Osteoporosis (Last updated April 16, 2019; last reviewed April 16, 2019)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Osteopenia and Osteoporosis	Any ART regimen <u>Specific Agents of Concern:</u> • TDF, especially when used in a regimen that includes a boosting agent (i.e., RTV, COBI) • PIs, especially LPV/r	<u>Onset:</u> • Any age; decrease in BMD is usually seen soon after initiation of ART. <u>Presentation:</u> • Usually asymptomatic • Rarely presents as osteoporosis, a clinical diagnosis defined by evidence of bone fragility (e.g., fracture with minimal trauma)	<u>BMD z Score Less Than -2.0:</u> • <10% in U.S. cohorts • Approximately 20% to 30% in international cohorts	Longer duration and greater severity of HIV disease Vitamin D insufficiency/deficiency Delayed growth or pubertal delay Low BMI Lipodystrophy Non-black race Smoking Prolonged systemic corticosteroid use Medroxyprogesterone use Lack of weight-bearing exercise	<u>Prevention:</u> • Ensure that the patient has sufficient intake and levels of both calcium and vitamin D • Encourage weight-bearing exercise. • Minimize modifiable risk factors (e.g., smoking, low BMI, use of steroids or medroxyprogesterone). • Use TAF instead of TDF whenever possible. • Use TDF with EFV or an unboosted INSTI. • When using TDF in a regimen, consider supplementing with vitamin D3 at a daily dose of 1,000–4,000 IU <u>Monitoring:</u> • Assess nutritional intake (calcium, vitamin D, and total calories). • Strongly consider measuring serum 25-OH-vitamin D levels, particularly in patients who are taking ARV drugs of concern. ^a • Obtain a DXA. ^b	Same options as for prevention. Consider changing the ARV regimen (e.g., switching from TDF to TAF, and/or from LPV/r to EFV or an un-boosted INSTI whenever possible). Treat patient with vitamin D3 to raise serum 25-OH-vitamin D concentrations to >30 ng/mL. Vitamin D3 levels should be monitored in patients who are receiving a daily dose of vitamin D3 >4,000 IU. The role of bisphosphonates in managing osteopenia and osteoporosis in children with HIV has not been established.

^a Some experts periodically measure 25-OH-vitamin D. This is especially important in children and adolescents with HIV who live in urban areas; the prevalence of vitamin D insufficiency is high in that population.

^b Until more data are available on the long-term effects of TDF on bone mineral acquisition in childhood, DXA scanning is not usually recommended for children who are being treated with TDF. Obtaining a DXA could be considered for adolescent women who are receiving TDF and medroxyprogesterone and for children with indications that are not uniquely related to HIV infection (such as cerebral palsy).

Key to Acronyms: ART = antiretroviral therapy; ARV = antiretroviral; BMD = bone mineral density; BMI = body mass index; COBI = cobicistat; DXA = dual-energy x-ray absorptiometry; EFV = efavirenz; INSTI = integrase strand transfer inhibitor; IU = international unit; LPV/r = lopinavir/ritonavir; PI = protease inhibitor; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

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Table 15k. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Rash and Hypersensitivity Reactions (Last updated April 16, 2019; last reviewed April 16, 2019) (page 1 of 4)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Rash	Any ARV drug can cause rash	<p><u>Onset:</u></p> <ul style="list-style-type: none"> • First few days to weeks after starting new ARV drug(s) <p><u>Presentation:</u></p> <ul style="list-style-type: none"> • Most rashes are mild-to-moderate, diffuse maculopapular eruptions. <p>Note: A rash can be the initial manifestation of systemic hypersensitivity (see the SJS/TEN/EM Major and HSR sections below).</p>	<p><u>Common (>10%):</u></p> <ul style="list-style-type: none"> • EFV • ETR • FTC • NVP <p><u>Less Common (5% to 10%):</u></p> <ul style="list-style-type: none"> • ABC • ATV • DRV • TDF <p><u>Unusual (2% to 4%):</u></p> <ul style="list-style-type: none"> • LPV/r • MVC • RAL • RPV 	<p>Sulfonamide allergy is a risk factor for rash in patients who are taking PIs that contain a sulfonamide moiety (e.g., DRV).</p> <p>Polymorphisms in CYP2B6 and multiple HLA loci may confer an increased risk of rash in patients who are taking NVP.</p>	<p><u>When Starting NVP or Restarting After Interruptions of >14 Days:</u></p> <ul style="list-style-type: none"> • Utilize once-daily lead-in dosing.^a This may not be necessary in children aged <2 years.^b • Avoid the use of systemic corticosteroids during NVP dose escalation. • Assess patient for rash severity, mucosal involvement, and other signs of systemic reaction. 	<p><u>Mild-to-Moderate Maculopapular Rash Without Systemic or Mucosal Involvement:</u></p> <ul style="list-style-type: none"> • Most rashes will resolve without intervention; ARV drugs can be continued while monitoring.^a • Antihistamines may provide some relief. <p><u>Severe Rash and/or Rash Accompanied by Systemic Symptoms:</u></p> <ul style="list-style-type: none"> • Manage as SJS/TEN/EM major, DRESS, or HSR as applicable (see below). <p><u>Rash in Patients Receiving NVP:</u></p> <ul style="list-style-type: none"> • Given the elevated risk of HSR, measure hepatic transaminases. • If hepatic transaminases are elevated, NVP should be discontinued and not restarted (see the HSR section below).
SJS/TEN/EM Major	Many ARV drugs, especially NNRTIs (see the Estimated Frequency column)	<p><u>Onset:</u></p> <ul style="list-style-type: none"> • First few days to weeks after starting new ARV drug(s) <p><u>Presentation:</u></p> <ul style="list-style-type: none"> • Initial rash may be mild, but it often becomes painful, evolving to blister/bulla formation with necrosis in severe cases. Usually involves mucous membrane ulceration and/or conjunctivitis. Systemic symptoms may also include fever, tachycardia, malaise, myalgia, and arthralgia. 	<p><u>Infrequent:</u></p> <ul style="list-style-type: none"> • NVP (0.3%) • EFV (0.1%) • ETR (<0.1%) <p><u>Case Reports:</u></p> <ul style="list-style-type: none"> • ABC • ATV • DRV • LPV/r • RAL • ZDV 	<p><u>Adults:</u></p> <ul style="list-style-type: none"> • Female sex • Patients who are black, Asian, or Hispanic are at higher risk. 	<p><u>When Starting NVP or Restarting After Interruptions of >14 Days:</u></p> <ul style="list-style-type: none"> • Utilize once-daily lead-in dosing.^a This may not be necessary in children aged <2 years.^b • Counsel families to report symptoms as soon as they appear. 	<p>Discontinue all ARV drugs and other possible causative agents (e.g., TMP-SMX).</p> <p>Provide intensive supportive including care, IV hydration, aggressive wound care, eye care, labial adhesion preventative care, pain management, and antipyretics. Parenteral nutrition and antibiotics may also be necessary.</p> <p>Corticosteroids and/or IVIG are sometimes used, but the use of these interventions is controversial.</p> <p>Do not reintroduce the offending medication.</p> <p>When SJS/TEN/EM major occurs with the use of one NNRTI, many experts would avoid the use of other NNRTIs.</p>

Table 15k. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Rash and Hypersensitivity Reactions (Last updated April 16, 2019; last reviewed April 16, 2019) (page 2 of 4)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
DRESS	DRV, DTG, EFV, ETR, NVP, RAL, RPV	<p><u>Onset:</u></p> <ul style="list-style-type: none"> • 1–8 weeks after starting new ARV drug(s) <p><u>Presentation:</u></p> <ul style="list-style-type: none"> • Fever • Lymphadenopathy • Facial swelling • Morbilliform to polymorphous rash • Peripheral eosinophilia • Atypical circulating lymphocytes • Internal organ involvement (particularly the liver and/or kidneys) 	Rare	Unknown	Obtain a CBC and AST, ALT, and creatinine levels from a patient who presents with suggestive symptoms.	<p>Discontinue all ARV drugs and other possible causative agents (e.g., TMP-SMX).</p> <p>The role of systemic steroids in treatment unclear; consultation with a specialist is recommended.</p> <p>Provide supportive care for end-organ disease.</p> <p>Do not reintroduce the offending medication.</p>
HSR With or without skin involvement and excluding SJS/TEN	ABC	<p><u>Onset</u></p> <p><i>With First Use:</i></p> <ul style="list-style-type: none"> • Within first 6 weeks <p><i>With Reintroduction:</i></p> <ul style="list-style-type: none"> • Within hours <p><u>Presentation:</u></p> <ul style="list-style-type: none"> • Symptoms include high fever, diffuse skin rash, malaise, nausea, headache, myalgia, arthralgia, diarrhea, vomiting, abdominal pain, pharyngitis, and respiratory symptoms (e.g., dyspnea). • With continuation of ABC, symptoms may progress to hypotension and vascular collapse. With rechallenge, symptoms can mimic anaphylaxis. 	<1% to 9% (varies by ethnicity)	<p>HLA-B*5701 (HSR is very uncommon in people who are HLA-B*5701 negative).</p> <p>The risk of HSR is higher in patients who are white compared to patients who are black or East Asian.</p>	<p>Screen for HLA-B*5701. ABC should not be prescribed if HLA-B*5701 is present. The medical record should clearly indicate that ABC is contraindicated.</p> <p>When starting ABC, counsel patients and families about the signs and symptoms of HSR to ensure prompt reporting of reactions.</p>	<p>Discontinue ARV drugs and investigate other causes of the symptoms (e.g., a concurrent viral illness).</p> <p>Provide symptomatic treatment.</p> <p>Most symptoms resolve within 48 hours after discontinuing ABC.</p> <p>Do not rechallenge with ABC even if the patient is HLA-B*5701 negative.</p>

Table 15k. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Rash and Hypersensitivity Reactions (Last updated April 16, 2019; last reviewed April 16, 2019) (page 3 of 4)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
HSR, continued	NVP	<p><u>Onset:</u></p> <ul style="list-style-type: none"> Occurs most frequently in the first few weeks of therapy, but can occur through 18 weeks <p><u>Presentation:</u></p> <ul style="list-style-type: none"> Flu-like symptoms (including nausea, vomiting, myalgia, fatigue, fever, abdominal pain, and jaundice) with or without skin rash that may progress to hepatic failure with encephalopathy 	Occurs in 4% of patients on average, with a range of 2.5% to 11%	<p><u>Adults:</u></p> <ul style="list-style-type: none"> Treatment-naive with a higher CD4 count (>250 cells/mm³ in women; >400 cells/mm³ in men) Female sex (risk is three-fold higher in females than in males) <p><u>Children:</u></p> <ul style="list-style-type: none"> NVP hepatotoxicity and HSR are less common in prepubertal children than in adults, and both are uncommon in infants. High CD4 percentage is associated with an increased risk of NVP toxicity. In the PREDICT study, the risk of NVP toxicity (rash, hepatotoxicity, hypersensitivity) was 2.65 times greater in children who had CD4 percentages ≥15% than in children who had CD4 percentages <15%. 	<p><u>When Starting NVP or Restarting After Interruptions of >14 Days:</u></p> <ul style="list-style-type: none"> A 2-week lead-in period with once-daily dosing, followed by dose escalation to twice daily as recommended, may reduce the risk of reaction.^a This may not be necessary in children aged <2 years.^b Counsel families about signs and symptoms of HSR to ensure prompt reporting of reactions. Obtain AST and ALT levels in patients with rash. Obtain AST and ALT levels at baseline, before dose escalation, 2 weeks after dose escalation, and thereafter at 3-month intervals. Avoid NVP use in women with CD4 counts >250 cells/mm³ and in men with CD4 counts >400 cells/mm³, unless benefits outweigh risks. Do not use NVP as PEP outside of the neonatal period. 	<p>Discontinue ARV drugs.</p> <p>Consider other causes for hepatitis and discontinue all hepatotoxic medications. Provide supportive care as indicated and monitor the patient closely.</p> <p>Do not re-introduce NVP. The safety of other NNRTIs is unknown following symptomatic hepatitis due to NVP, and many experts would avoid the NNRTI drug class when restarting treatment.</p>

Table 15k. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Rash and Hypersensitivity Reactions (Last updated April 16, 2019; last reviewed April 16, 2019) (page 4 of 4)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
HSR, continued	ETR	<p><u>Onset:</u></p> <ul style="list-style-type: none"> Any time during therapy <p><u>Presentation:</u></p> <ul style="list-style-type: none"> Symptoms may include rash, constitutional findings, and sometimes organ dysfunction, including hepatic failure. 	Rare	Unknown	Evaluate for hypersensitivity if the patient is symptomatic.	Discontinue ARV drugs. Rechallenge with ETR is not recommended .
	MVC	Rash preceding hepatotoxicity	Rare	Unknown	Obtain AST and ALT levels in patients with rash or other symptoms of hypersensitivity.	Discontinue all ARV drugs. Rechallenge with MVC is not recommended .
	DTG	Rash with hepatic dysfunction	Rare	Unknown	Obtain AST and ALT levels in patients with rash or other symptoms of hypersensitivity.	Discontinue all ARV drugs. Rechallenge with DTG is contraindicated .

^a The prescribing information for NVP states that patients who experience rash during the 14-day lead-in period should not have the NVP dose increased until the rash has resolved. However, prolonging the lead-in phase beyond 14 days may increase the risk of NVP resistance because of subtherapeutic drug levels. Children who have persistent mild or moderate rash after the lead-in period should receive individualized care. Consult an expert in HIV care when managing these patients. **NVP should be stopped and not restarted** if the rash is severe or progressing. See the [NVP section](#) of the Drug Appendix.

^b Lead-in dosing **is not recommended** when using nevirapine for either empiric or definitive HIV therapy in newborns with perinatal HIV exposure or perinatal HIV. See the [NVP section](#) of the Drug Appendix and [Table 12](#).

Key to Acronyms: ABC = abacavir; ALT = alanine transaminase; ARV = antiretroviral; AST = aspartate aminotransferase; ATV = atazanavir; CBC = complete blood count; CD4 = CD4 T lymphocyte; CYP = cytochrome P450; DRESS = drug reaction (or rash) with eosinophilia and systemic symptoms; DRV = darunavir; DTG = dolutegravir; EFV = efavirenz; EM = erythema multiforme; ETR = etravirine; FTC = emtricitabine; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; IV = intravenous; IVIG = intravenous immune globulin; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PEP = post-exposure prophylaxis; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; SJS = Stevens-Johnson syndrome; TDF = tenofovir disoproxil fumarate; TEN = toxic epidermal necrolysis; TMP-SMX = trimethoprim-sulfamethoxazole; ZDV = zidovudine

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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 ddI 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; ddI = didanosine; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = 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; TDF = tenofovir; ZDV = zidovudine

Table 17. Discordance Among Virologic, Immunologic, and Clinical Responses

Differential Diagnosis of Poor Immunologic Response Despite Virologic Suppression
<p><u>Poor Immunologic Response Despite Virologic Suppression and Good Clinical Response:</u></p> <ul style="list-style-type: none"> • Lab error (in CD4 or viral load measurement) • Misinterpretation of normal, age-related CD4 decline (i.e., the immunologic response is not actually poor) • Low pretreatment CD4 cell count or percentage • Adverse effects of using ZDV • Use of systemic corticosteroids or chemotherapeutic agents • Conditions that can cause low CD4 values, such as HCV, acute viral infections, TB, malnutrition, Sjogren’s syndrome, sarcoidosis, and syphilis <p><u>Poor Immunologic and Clinical Responses Despite Virologic Suppression:</u></p> <ul style="list-style-type: none"> • Lab error • Falsely low viral load result for an HIV strain/type that is not detected by viral load assay (HIV-1 non-M groups, non-B subtypes; HIV-2) • Persistent immunodeficiency soon after initiation of ART but before ART-related reconstitution • Primary protein-calorie malnutrition • Untreated TB • Malignancy
Differential Diagnosis of Poor Clinical Response Despite Adequate Virologic and Immunologic Responses
<ul style="list-style-type: none"> • IRIS • A previously unrecognized, pre-existing infection or condition (e.g., TB, malignancy) • Malnutrition • Clinical manifestations of previous organ damage: brain (e.g., strokes, vasculopathy), lungs (e.g., bronchiectasis), cardiac (cardiomyopathy), renal (HIV-related kidney disease) • A new clinical event due to a non-HIV illness or condition • A new, otherwise unexplained HIV-related clinical event (treatment failure)

Key to Acronyms: ART = antiretroviral therapy; CD4 = CD4 T lymphocyte; HCV = hepatitis C virus; IRIS = immune reconstitution inflammatory syndrome; TB = tuberculosis; ZDV = zidovudine

Table 18. Options for Regimens with at Least Two Fully Active Agents to Achieve Virologic Suppression in Patients with Virologic Failure and Evidence of Viral Resistance^a

Prior Regimen	New Regimen Options ^a
Two NRTIs plus NNRTI	Two NRTIs plus PI Two NRTIs plus INSTI
Two NRTIs plus PI	Two NRTIs plus INSTI Two NRTIs plus a different RTV-boosted PI INSTI plus a different RTV-boosted PI plus or minus an NNRTI and plus or minus NRTI(s)
Two NRTIs plus INSTI	Two NRTIs plus RTV-boosted PI DTG ^b (if not used in the prior regimen) plus RTV-boosted PI plus or minus one or two NRTIs. DTG must be given twice daily if a patient has certain documented INSTI mutations, or if there is concern about certain mutations (see the dolutegravir section).
Failed Regimen(s) That Included NRTI(s), NNRTI(s), and PI(s)	INSTI plus two NRTIs (if NRTIs are fully active) INSTI plus two NRTIs plus or minus RTV-boosted PI (if NRTIs are not fully active) INSTI plus or minus RTV-boosted PI plus or minus (ETR or RPV) plus or minus NRTI(s) (if there is minimal NRTI activity). Consider adding T-20 and/or MVC if additional active drug(s) are needed.

^a Clinicians should evaluate a patient's treatment history and drug-resistance test results when choosing an ART regimen in order to optimize ARV drug effectiveness. This is particularly important in selecting the NRTI components of an NNRTI-based regimen, where drug resistance to the NNRTI can occur rapidly if the virus is not sufficiently sensitive to the NRTIs. Regimens should contain at least two, but preferably three, fully active drugs for durable and potent virologic suppression. If the M184V/I mutation associated with FTC and 3TC is present, these medications should be continued if the new regimen contains TDF, TAF, or ZDV as the presence of this mutation may increase susceptibility to these NRTIs. **Please see individual drug profiles for information about age limitations (e.g., do not use DRV in children aged <3 years), drug interactions, and dose adjustments when devising a regimen for children with multiclass drug resistance.** Collaboration with a pediatric HIV specialist is especially important when choosing regimens for children with multiclass drug resistance. Regimens in this table are provided as examples, but the list is not exhaustive.

^b 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 dolutegravir in women of childbearing potential and in pregnant women are available in the [Adult and Adolescent Antiretroviral Guidelines](#) (see [Adolescents and Young Adults with HIV and Management of the Treatment-Experienced Patient](#)) and in the [Perinatal Guidelines](#) (see [Teratogenicity and Recommendations for Use of Antiretroviral Drugs During Pregnancy](#)).

Key to Acronyms: 3TC = lamivudine; ART = antiretroviral therapy; ARV = antiretroviral; DRV = darunavir; DTG = dolutegravir; ETR = etravirine; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RPV = rilpivirine; RTV = ritonavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

Appendix A: Pediatric Antiretroviral Drug Information

Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets

Brand Name by Class	NRTIs						NNRTIs			INSTIs			PIs			PK Enhancers	
	ABC	3TC	ZDV	FTC	TDF	TAF ^a	DOR	EFV	RPV	BIC ^a	DTG	EVG ^a	ATV	DRV	LPV ^b	COBI	RTV
NRTI																	
Cimduo		X			X												
Combivir, Generic		X	X														
Descovy				X		X											
Epzicom, Generic	X	X															
Temixys		X			X												
Trizivir, Generic	X	X	X														
Truvada				X	X												
NRTI/NNRTI																	
Atripla				X	X			X									
Complera				X	X				X								
Delstrigo		X			X		X										
Odefsey				X		X			X								
Symfi or Symfi Lo		X			X				X								
NRTI/INSTI																	
Biktarvy				X		X				X							
Dovato		X									X						
Triumeq	X	X									X						
NNRTI/INSTI																	
Juluca									X		X						
NRTI/INSTI/COBI																	
Genvoya				X		X						X				X	
Stribild				X	X							X				X	
NRTI/PI/COBI																	
Symtuza				X		X								X		X	
PI/COBI																	
Evotaz													X			X	
Prezcobix														X		X	
PI/RTV																	
Kaletra															X		X

Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets

^a TAF, BIC, and EVG are only available in FDC tablets. However, TAF 25 mg tablets (Vemlidy) are FDA-approved for treatment of HBV. In select circumstances, TAF might be used as one component of a combination ARV regimen, with dosing recommendations similar to those for Descovy.

^b LPV is only available in FDC tablets or solution.

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; BIC = bictegravir; COBI = cobicistat; DOR = doravirine; DRV = darunavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; FDA = Food and Drug Administration; FDC = fixed-dose combination; FTC = emtricitabine; HBV = hepatitis B virus; LPV = lopinavir; LPV/r = lopinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside and nucleotide reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

Appendix A, Table 2. Antiretroviral Fixed-Dose Combination Tablets: Minimum Body Weights and Considerations for Use in Children and Adolescents (page 1 of 3)

This table may include recently approved FDCs that have not yet been added to individual drug sections in the [Pediatric Antiretroviral Drug Information Appendix](#) (see individual drug components for details).

General Considerations When Considering an FDC Tablet:

- For children weighing ≥ 25 kg, the Panel recommends using one of the following single-tablet, once-daily regimens: Triumeq (ABC/DTG/3TC), Genvoya (EVG/COBI/FTC/TAF), and Biktarvy (BIC/FTC/TAF).
- ABC and TAF are favored over ZDV because of lower risk of NRTI-associated mitochondrial toxicity.
- TDF is more potent than ABC at high viral loads when used in regimens that do not contain an INSTI.
- TAF is favored over TDF because of the lower risk of TDF-associated bone and renal toxicity.
- TDF is generally **not recommended** for children with SMR 1–3 because of TDF-associated bone toxicity; however, for a child weighing < 25 kg who can swallow pills, Truvada (FTC/TDF) low-strength tablets offer a reasonable, once daily combination alternative to twice daily ZDV plus 3TC or an alternative to ABC.
- RPV has low potency at high viral loads, a low barrier to resistance, and requires a high fat meal for optimal absorption, so EFV or an INSTI are favored.
- BIC and DTG, second-generation INSTIs, have a higher barrier to resistance than EVG and RAL, first-generation INSTIs.
- For images of most of the FDCs 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 FDCs and individual ARVs (see the [Intro ARV Chart](#)). Although most of the drugs listed in that chart are the same as those in the United States, a few of the brand names are not the same as those listed in Appendix A, Table 2 below.
- FDCs and individual ARVs can also be looked up by drug (brand name and generic) at [DailyMed](#); size is listed under Ingredients and Appearance in the Product Characteristics section.

INSTI FDC Dosing for Children and Adolescents:

- [Elvitegravir](#):
 - Genvoya (EVG/COBI/FTC/TAF) is FDA approved for children and adolescents weighing ≥ 25 kg.
- [Dolutegravir](#):
 - The Panel recommends DTG 50 mg for children and adolescents weighing ≥ 20 kg, see the [dolutegravir](#) section. The FDA-approved dose is DTG 35 mg for patients weighing ≥ 30 kg to 40 kg, and DTG 50 mg for patients weighing ≥ 40 kg.
 - For children weighing ≥ 25 kg, DTG 50 mg can be given as Triumeq (ABC/DTG/3TC) in 1 large pill or as Descovy (FTC/TAF) plus DTG which requires 2 small pills.
 - Recent data identified a possible increased risk of NTDs among women who were receiving DTG at the time of conception. Specific recommendations about the initiation and use of DTG in adolescents and 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

Appendix A, Table 2. Antiretroviral Fixed-Dose Combination Tablets: Minimum Body Weights and Considerations for Use in Children and Adolescents (page 2 of 3)

Perinatal Guidelines (see [Teratogenicity](#) and [Recommendations for the Use of Antiretroviral Drugs in Pregnancy](#)).

- **Bictegravir:**
 - Biktarvy (BIC/FTC/TAF) **is now approved by the FDA for use in children and adolescents weighing ≥ 25 kg.**

FDC by Class Brand name and generic ^a products, when available	FDC Components	Minimum Body Weight (kg) or Age^b	Pill Size (mm x mm) or Largest Dimension (mm)	Food Requirements
NRTI				
Cimduo	3TC 300 mg/TDF 300 mg	35 kg	19	Take with or without food
Combivir and Generic 3TC/ZDV	3TC 150 mg/ZDV 300 mg (scored tablet)	30 kg	18 x 7	Take with or without food
Descovy	FTC 200 mg/TAF 25 mg	25 kg: With INSTI or NNRTI 35 kg: With boosted PI	12.5 x 6.4	Take with or without food
Epzicom and Generic ABC/3TC	ABC 600 mg/3TC 300 mg	25 kg	21 x 9	Take with or without food
Temixys	3TC 300 mg/TDF 300 mg	35 kg	N/A	Take with or without food
Trizivir and Generic ABC/3TC/ZDV	ABC 300 mg/3TC 150 mg/ZDV 300 mg	40 kg (FDA) 30 kg (Panel) ^c	21 x 10	Take with or without food
Truvada	FTC 200 mg/TDF 300 mg	35 kg	19 x 8.5	Take with or without food
Truvada Low Strength	FTC 167 mg/TDF 250 mg	28 kg	18	Take with or without food
	FTC 133 mg/TDF 200 mg	22 kg	16	Take with or without food
	FTC 100 mg/TDF 150 mg	17 kg	14	Take with or without food
NRTI/NNRTI				
Atripla	EFV 600 mg/FTC 200 mg/TDF 300 mg	40 kg	20	Take on an empty stomach
Complera	FTC 200 mg/RPV 25 mg/TDF 300 mg	35 kg and aged ≥ 12 years	19	Take on an empty stomach
Delstrigo	DOR 100 mg/3TC 300 mg/TDF 300 mg	Adults	19	Take with or without food
Odefsey	FTC 200 mg/RPV 25 mg/TAF 25 mg	35 kg and aged ≥ 12 years	15	Take with a meal
Symfi	EFV 600 mg/3TC 300 mg/TDF 300 mg (scored tablet)	40 kg	23	Take on an empty stomach
Symfi Lo	EFV 400 mg/3TC 300 mg/TDF 300 mg	35 kg ^d	21	Take on an empty stomach
NRTI/INSTI				
Biktarvy	BIC 50 mg/FTC 200 mg/TAF 25 mg	≥ 25 kg	15 x 8	Take with or without food

Appendix A, Table 2. Antiretroviral Fixed-Dose Combination Tablets: Minimum Body Weights and Considerations for Use in Children and Adolescents (page 3 of 3)

FDC by Class Brand name and generic ^a products, when available	FDC Components	Minimum Body Weight (kg) or Age^b	Pill Size (mm x mm) or Largest Dimension (mm)	Food Requirements
NRTI/INSTI, continued				
Dovato	DTG 50 mg/3TC 300 mg	Adults	19	Take with or without food
Triumeq	ABC 600 mg/DTG 50 mg/3TC 300 mg	≥40 kg (FDA) 25 kg (Panel) ^e	22 x 11	Take with or without food
NNRTI/INSTI				
Juluca	DTG 50 mg/RPV 25 mg	Adults	14	Take with a meal
NRTI/INSTI/COBI				
Genvoya	EVG 150 mg/COBI 150 mg/FTC 200 mg/TAF 10 mg	25 kg	19 x 8.5	Take with food
Stribild	EVG 150 mg/COBI 150 mg/FTC 200 mg/TDF 300 mg	35 kg	20	Take with food
NRTI/PI/COBI				
Symtuza	DRV 800 mg/COBI 150 mg/FTC 200 mg/TAF 10 mg	Adults	22	Take with food
PI/COBI				
Evotaz	ATV 300 mg/COBI 150 mg	35 kg	19	Take with food
Prezcobix	DRV 800 mg/COBI 150 mg	40 kg	23	Take with food
PI/RTV				
Kaletra	<u>LPV/r Oral Solution:</u> • LPV 80 mg/mL and RTV 20 mg/mL <u>Tablets:</u> • LPV 200 mg/RTV 50 mg • LPV 100 mg/RTV 25 mg	<u>Post-Menstrual Age of 42 Weeks and a Postnatal Age of ≥14 Days:</u> • No minimum weight	19	Take with or without food

^a Size or largest dimension of generic drugs are not listed because they may vary by manufacturer; this information is available by looking up one of the drug components using [DailyMed](#).

^b Minimum body weight and age are those recommended by the FDA unless otherwise noted.

^c Based on the current FDA-approved minimum body weights for Trizivir component drugs, the Panel suggests Trizivir may be used at a minimum body weight of ≥30 kg, although it is FDA approved for use in children and adolescents ≥40 kg. However, the Panel does not recommend regimens containing NRTI's only, or 3-NRTI regimens, for use in children.

^d Due to pharmacokinetic concerns, the Panel recommends caution when using Symfi Lo in children and adolescents who have a SMR 1-3 and weigh ≥40 kg, see the [efavirenz](#) section.

^e The Panel recommends using DTG 50 mg for children and adolescents weighing ≥20 kg based on available data. **However, the doses of ABC and 3TC in Triumeq are too high for children weighing <25 kg** (see the [dolutegravir](#) section).

Key to Abbreviations: 3TC = lamivudine; ABC = abacavir; ATV = atazanavir; ARV = antiretroviral; BIC = bictegravir; COBI = cobicistat; DRV = darunavir; DTG = dolutegravir; DOR = doravirine; EFV = efavirenz; EVG = elvitegravir; FDA = Food and Drug Administration; FDC = fixed-dose combination; FTC = emtricitabine; INSTI = integrase inhibitor; LPV = lopinavir; LPV/r = lopinavir/ritonavir; mm = millimetre; N/A = information not available; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside and nucleotide reverse transcriptase inhibitor; **NTD = neural tube defect**; RPV = rilpivirine; RTV = ritonavir; SMR = sexual maturity rating; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine