Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

Developed by the HHS Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV—A Working Group of the NIH Office of AIDS Research Advisory Council (OARAC)

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It is emphasized that concepts relevant to HIV management evolve rapidly. The Panels have a mechanism to update recommendations on a regular basis, and the most recent information is available on the Clinicalinfo website (https://clinicalinfo.hiv.gov/).

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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 in the United States on the optimal use of antiretroviral (ARV) agents when treating infants, children, and adolescents in early to mid-puberty (sexual maturity rating [SMR] 1–3) with HIV.
Panel Members	The Panel on Antiretroviral Therapy and Medical Management of Children Living With HIV (the Panel) is composed of approximately 30 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 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, the U.S. Food and Drug Administration (FDA), the Health Resources and Services Administration (HRSA), and the National Institutes of Health (NIH). A representative from the Canadian Paediatric and Perinatal HIV/AIDS Research Group and a representative from the Australasian Society for HIV, Viral Hepatitis, and Sexual Health Medicine participate as nonvoting, *ex officio* members 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 Guidelines Panel Members.
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 Clinicalinfo website.
Users of the Guidelines	Providers of care to infants, children, and adolescents 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	NIH Office of AIDS Research 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 working groups. The recommendations generally are 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

Topic	Comment
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	These guidelines focus on infants, children, and adolescents in early to mid-puberty (SMR 1–3) 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. Separate guidelines outline the use of antiretroviral therapy (ART) during pregnancy and interventions to reduce perinatal HIV transmission, including maternal and infant interventions to prevent perinatal transmission (the Perinatal Guidelines); ART for nonpregnant adults and postpubertal adolescents with HIV; and ARV prophylaxis for those who experience occupational or nonoccupational exposure to HIV. These and other HIV guidelines are also available on the Clinicalinfo website.
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: Initial Combination Antiretroviral Regimens for People with HIV). Updates may be prompted by new drug approvals (or new indications, formulations, or frequency of dosing), new 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 Clinicalinfo website until the guidelines can be updated with appropriate changes. All sections of the guidelines are 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 Clinicalinfo 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 via the Contact Us webpage.

Table 2. Rating Scheme for Recommendations

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

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

Table 3. Recommended Virologic Testing Schedules for Infants Who Were Exposed to HIV According to Risk of Perinatal HIV Acquisition at and After Birth[a]

Infants at High Risk	
Criteria for Infants at High Risk	**Age at HIV NAT[b] Testing for Infants at High Risk**
Infants born to mothers with HIV who— • Did not receive prenatal care; • Received no antepartum ARVs or only intrapartum ARV drugs; • Initiated ART late in pregnancy (during the late second or third trimester); • Received a diagnosis of acute HIV infection during pregnancy or in labor; and/or • Had detectable HIV viral loads (≥50 copies/mL) close to the time of delivery, including those who received ART but did not achieve sustained viral suppression	Birth 14–21 days 1–2 months 2–3 months[c] 4–6 months All infants at high risk of perinatal HIV transmission should have specimens obtained for HIV testing at birth before initiating an ARV drug regimen; however, presumptive HIV therapy should not be delayed. If an infant's NAT test result is positive, a repeat test should be performed as soon as possible and ART should be initiated.
Infants at Low Risk	
Criteria for Infants at Low Risk	**Age at HIV NAT[b] Testing for Infants at Low Risk**
Infants born to mothers who— • Received ART during pregnancy; • Had sustained viral suppression (usually defined as <50 copies/mL); *and* • Were adherent to their ARV regimens	14–21 days 1–2 months[d] 4–6 months
Infants With Perinatal HIV Exposure Who Are Being Breastfed	
Age at HIV NAT[b] Testing for Infants With Perinatal HIV Exposure Who Are Being Breastfed	
Birth 14–21 days 1–2 months 2–4 months[e] 4–6 months If breastfeeding continues beyond 6 months of age, NAT testing should be performed every 3 months during breastfeeding. In addition to the standard time points after birth, NAT testing also should be performed at 4 to 6 weeks, 3 months, and 6 months after cessation of breastfeeding, regardless of the age at when breastfeeding ends.	

Consultation with an expert is recommended to determine additional testing time points that may be needed for infants with risk factors for HIV acquisition at birth who are being breastfed.

Prompt NAT testing of the infant is indicated if maternal viral load becomes detectable during breastfeeding.

If the mother has a detectable viral load and continues breastfeeding, some Panel members would recommend monthly virologic testing of the infant as an approach to early detection of HIV infection during ongoing exposure.

See Infant Feeding for Individuals With HIV in the United States. Consultation with an expert and/or the Perinatal HIV Hotline (888-448-8765) is recommended for questions about HIV diagnostic testing for infants with perinatal HIV exposure who are being breastfed.

[a] This table summarizes standard time points for HIV virologic diagnostic testing of infants according to risk of perinatal acquisition.

[b] HIV RNA or HIV DNA NATs that directly detect HIV.

[c] For high-risk infants, virologic diagnostic testing is recommended at birth. For infants treated with multiple ARVs in the first 2 to 4 weeks of life, additional virologic testing is recommended 2 to 6 weeks after ARV drugs are discontinued (i.e., at 8–12 weeks of life).

[d] For low-risk infants, testing may be timed to occur at least 2 weeks after cessation of ARV prophylaxis.

[e] An additional virologic test should be performed at age 2 to 4 months if the gap between the tests at ages 1 to 2 months and 4 to 6 months is greater than 3 months.

Key: ART = antiretroviral therapy; ARV = antiretroviral; NAT = nucleic acid test

Table 4. Characteristics and Requirements for In-Person Clinic Visits vs. Telemedicine Visits

	In-Person Visits	Telemedicine Visits
Patient/caregiver convenience		✓
Flexibility (time and locations) of appointments		✓
Confidentiality concerns	✓	✓
Directly observed therapy in home settings		✓
Physical assessment (e.g., skin rashes)	✓	✓
Physical exam, including weight and height	✓	✓[a]
Adherence support and counseling	✓	✓
Mental health assessment and counseling	✓	✓
Multidisciplinary support (assessment and coordination of nutritional and social services)	✓	✓
Laboratory testing on site	✓	
Travel to clinic	✓	
Technology requirements (internet access, equipment, skills)		✓
Legal and administrative guidelines for visit documentation and billing	✓	✓

[a] Cooperative children can be weighed and have their height measured at home if a scale and measuring tape are available, with simple instructions for continuity, or directly observed during a synchronous visit or obtained from a recent pediatric or other specialty in-office visit.

Table 5. CD4 Cell Counts and Percentages in Healthy Children: Distribution by Age

	Age						
	0–3 months	3–6 months	6–12 months	1–2 years	2–6 years	6–12 years	12–18 years
CD4 cell count[a,b]	2,600 (1,600–4,000)	2,850 (1,800–4,000)	2,670 (1,400–4,300)	2,160 (1,300–3,400)	1,380 (700–2,200)	980 (650–1,500)	840 (530–1,300)
CD4 percentage[a,c]	52 (35–64)	46 (35–56)	46 (31–56)	41 (32–51)	38 (28–47)	37 (31–47)	41 (31–52)

[a] Values presented as median (10th to 90th percentile)

[b] n = 699;

[c] n = 709

Source: Shearer WT, Rosenblatt HM, Gelman RS, et al. Lymphocyte subsets in healthy children from birth through 18 years of age: the Pediatric AIDS Clinical Trials Group P1009 study. *J Allergy Clin Immunol.* 2003;112(5):973-980.

Table 6. Sample Schedule for Clinical and Laboratory Monitoring of Children Before and After Initiation of Antiretroviral Therapy[a]

Laboratory Testing	Entry Into Care[a,b]	ART Initiation[c]	Weeks 1–2 on Therapy	Weeks 2–4 on Therapy	Every 3–4 Months[d]	Every 6–12 Months[e]	Virologic Failure (Prior to Switching ARV Regimens)
Medical History and Physical Examination[f,g]	✓	✓	✓	✓	✓		✓
Adherence Evaluation[g]		✓	✓	✓	✓		✓
CD4 Count	✓	✓			✓		✓
Plasma Viral Load[h]	✓	✓		✓	✓		✓
Resistance Testing	✓						✓
CBC with Differential[d]	✓	✓		✓	✓		✓
Chemistries[d,i]	✓	✓		✓	✓		✓
Lipid Panel[e]	✓	✓				✓	
Random Plasma Glucose[j]		✓				✓	
Urinalysis	✓	✓				✓	
HBV Screening[k]	✓						✓
Pregnancy Test for Girls and Young Women of Childbearing Potential[l]	✓	✓					✓
HLA-B*5701[m]	✓						

[a] See the texts on immunologic, virologic, general laboratory, and clinical monitoring of children with HIV for details on recommended laboratory tests to perform.

[b] If a child does not initiate ART after receiving an HIV diagnosis, the child's CD4 count and plasma viral load should be monitored at least every 3 to 4 months.

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

[d] CD4 count, CBC, and chemistries can be monitored less frequently (every 6–12 months) in children and youth who are adherent to therapy, who have CD4 count values that are well above the threshold for opportunistic infection risk, and who have

had sustained virologic suppression and stable clinical status for more than 2 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 may be needed. For patients treated with TDF, more frequent urinalysis should be considered.

[f] Pay special attention to changes in weight that might occur after altering an ARV regimen. Weight gain or weight loss may occur when using some ARV drugs (see Table 17h. Lipodystrophies and Weight Gain).

[g] Virtual visits may be appropriate at some time points, particularly for adherence assessments and for visits for established patients, see Table 4 above.

[h] Some experts monitor viral load more often (with each injection) in adolescents initiating injectable CAB and RPV. Viral load monitoring should be performed 4 to 8 weeks after a switch to long-acting CAB and RPV. HIV-RNA also should be checked in patients with unplanned missed visits and delayed dosing of long-acting CAB and RPV. When viremia develops during long-acting therapy, resistance testing, including integrase resistance testing, should be performed. Follow-up dosing in patients with missed doses should not be delayed while waiting for viral load and resistance test results. However, regimen changes should be prompted if resistance to CAB and/or RPV is discovered (see Optimizing Antiretroviral Therapy in the Setting of Viral Suppression in the Adult and Adolescent Antiretroviral Guidelines).

[i] Chemistries refer to a comprehensive metabolic panel. Some experts perform a comprehensive panel at entry and routinely test Cr, ALT, AST, with additional tests tailored to the history of the individual patient.

[j] Random plasma glucose is collected in a gray-top blood collection tube or other designated tube. Some experts would consider monitoring HgbA1C, rather than routine blood glucose, in children at risk for prediabetes/diabetes.

[k] This screening is only recommended for individuals who have previously demonstrated no immunity to HBV and who are initiating a regimen that contains ARV drugs with activity against HBV, specifically 3TC, FTC, TAF, or TDF.

[l] See the Prepregnancy Counseling and Care for Persons of Childbearing Age with HIV in the Perinatal Guidelines.

[m] Conduct HLA-B*5701 on entry or prior to initiating ABC if not done previously. Choose an alternative ARV drug if the patient is HLA-B*5701 positive (see the Abacavir section in Appendix A: Pediatric Antiretroviral Drug Information).

Key: 3TC = lamivudine; ABC = abacavir; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; CBC = complete blood count; CD4 = CD4 T lymphocyte; Cr = creatinine; FTC = emtricitabine; HBV = hepatitis B virus; HgbA1C = glycosylated hemoglobin; OI = opportunistic infection; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Table 7. 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	Aptima HIV-1 Quant Assay
Method	Real-time RT-PCR	Real-time NASBA	Real-time RT-PCR	Real-time RT-PCR	Real-time TMA
Dynamic Range	40–10^7 copies/mL	25–10^7 copies/mL	20–10^7 copies/mL	37–11×10^7 copies/mL	30–10^7 copies/mL
Specimen Volume[a]	0.2–1 mL	0.1–1 mL	1 mL	0.5 mL	≥0.4 mL
Manufacturer	Abbott Laboratories	bioMerieux	Roche	Siemens	Hologic, Inc.

[a] Laboratories often request large blood volumes for standard viral load testing. Consider contacting the local laboratory to determine minimum blood volume required to run the assay. Smaller volumes for children can be accommodated.

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

Figure 1. Preferred Regimen by Age, Weight, and Drug Class

<table>
<tr><th colspan="6">Patient Age and Weight Class</th></tr>
<tr><th></th><th>Birth to <14 Days of Age[a,b,c]</th><th>Aged ≥ 14 Days and ≥2 kg to <4 Weeks</th><th>Aged ≥4 Weeks and ≥3 kg to <2 Years</th><th>Aged ≥2 Years and ≥14 kg</th><th>Aged ≥6 Years and ≥25 kg</th></tr>
<tr><td rowspan="2">INSTI-Based Regimens</td><td colspan="2">Two NRTIs plus RAL[c]</td><td colspan="3"></td></tr>
<tr><td colspan="3"></td><td colspan="2">Two NRTIs plus BIC[d]</td></tr>
<tr><td></td><td colspan="3"></td><td colspan="2">Two NRTIs plus DTG[e]</td></tr>
<tr><td>NNRTI-Based Regimens</td><td>Two NRTIs plus NVP[a,f]</td><td colspan="4"></td></tr>
<tr><td>PI-Based Regimens</td><td></td><td>Two NRTIs plus LPV/r[b]</td><td colspan="3"></td></tr>
</table>

[a] Preferred NRTIs are listed in Table 8 below.

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. Although many pediatric experts favor initiating antiretroviral therapy as soon as possible after birth to limit the establishment of viral reservoirs, available clinical trial data do 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 HIV Infection. 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 than NVP in studies of children aged <3 years. Data are limited on the clinical outcomes of using RAL in infants and children aged <2 years.

[b] In general, LPV/r should not be administered to neonates before a postmenstrual age of 42 weeks and a postnatal age of ≥14 days (see the Lopinavir/Ritonavir section in Appendix A: Pediatric Antiretroviral Drug Information).

[c] RAL granules can be administered to infants and children weighing ≥2 kg from birth to age 2 years. Oral RAL granules can be used up to a dose of 100 mg in the 14 kg to <20 kg weight band. RAL pills or chewable tablets can be used in children aged ≥2 years. Chewable RAL tablets can be crushed and dispersed in liquid to infants as young as 4 weeks of age who weigh at least 3 kg.

[d] BIC is available only as part of a fixed-dose combination (FDC) tablet that contains BIC/FTC/TAF; this FDC tablet is recommended as a *Preferred* regimen for children aged ≥ 2 years and weighing ≥14 kg. Two strengths of BIC/FTC/TAF are available, with dosing according to a child's weight (see Bictegravir).

[e] DTG is recommended as a *Preferred* agent for infants, children, and adolescents aged ≥4 weeks and weighing ≥3 kg. DTG dispersible tablets can be administered in infants and children aged ≥4 weeks and weighing ≥3 kg. DTG film-coated tablets can be used in children weighing ≥14 kg. An FDC that contains ABC/DTG/3TC is available in dispersible tablets (Triumeq PD) for children weighing ≥10 kg to <25 kg and in a single tablet to be swallowed (Triumeq) for children weighing ≥25 kg. See Dolutegravir for information about dosing and administration.

[f] NVP should not be used in post-pubertal girls with CD4 T lymphocyte cell counts >250/mm^3, unless the benefit clearly outweighs the risk. NVP is approved by the U.S. Food and Drug Administration for the treatment of infants aged ≥15 days.

Key: BIC = bictegravir; DTG = dolutegravir; 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; TAF = tenofovir alafenamide

Table 8. Antiretroviral Regimens Recommended for *Initial* Therapy for HIV Infection in Children

An antiretroviral (ARV) regimen for treatment-naive children is generally made up of a two– nucleoside reverse transcriptase inhibitor (NRTI) backbone and either one non-nucleoside reverse transcriptase inhibitor (NNRTI) **or** one integrase strand transfer inhibitor (INSTI) **or** one protease inhibitor (PI) boosted with ritonavir or cobicistat (COBI). Regimens are designated *Preferred* based on efficacy, ease of administration, and acceptable toxicity. *Alternative* regimens also have 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. Refer to Appendix A: Pediatric Antiretroviral Drug Information for additional information and recommended doses and formulations (also see Table 8 below). In addition, many drugs that are recommended for use in newborns do not have dosing recommendations for premature infants. Additional information regarding dosing recommendations in this population can be found in Antiretroviral Management of Newborns With Perinatal HIV Exposure or HIV Infection.

Children who are receiving effective and tolerable ARV regimens can continue using those regimens as they age, even if the combinations they are receiving are no longer *Preferred* regimens. Refer to the Management of Children Receiving Antiretroviral Therapy sections for decisions about transitioning children to other regimens as they grow.

Preferred Initial Regimens Based on Age and Weight at Time of Treatment Initiation			
Age	Weight Restriction	Regimens	FDC Available (see Appendix A, Table 1)
Newborns, Birth to Age <14 Days[a,b]	None	Two NRTIs plus NVP	No
	≥2 kg	Two NRTIs plus RAL[c]	No
Neonates ≥14 Days to Age <4 Weeks	None	Two NRTIs plus LPV/r[b]	No
	≥2 kg	Two NRTIs plus RAL[c]	No
Infants and Children Aged **≥4** Weeks	≥3 kg	Two NRTIs plus DTG[d]	No
		Two NRTIs plus DTG[d]	Yes (≥10 kg)
Children Aged ≥2 Years	≥14 kg	Two NRTIs plus BIC[e]	Yes
Adolescents Aged ≥12 Years With SMRs of 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
Neonates Aged Birth to 1 Month	ABC plus (3TC or FTC)[f]		No[g]
	ZDV plus (3TC or FTC)[h]		No[g]
Infants and Children Aged >1 Month to <2 Years	ABC plus (3TC or FTC)[f]		Yes
	ABC plus (3TC or FTC)[f]		Yes

Children and Adolescents Aged **≥2** Years With SMRs of 1–3	FTC/TAF[i] in children and adolescents weighing ≥14 kg and receiving a regimen that contains an INSTI or an NNRTI FTC/TAF[i] in children and adolescents weighing ≥35 kg and receiving a regimen that contains a boosted PI	Yes
Adolescents Aged **≥12 Years** With SMRs of 4 or 5	Refer to the Adult and Adolescent Antiretroviral Guidelines.	Yes

Alternative Regimens Based on Age and Weight at Time of Treatment Initiation			
Age	Weight Restriction	Regimens	FDC Available
Neonates, Infants, and Children **Aged ≥14 Days to <3 Years**	None	Two NRTIs **plus** NVP[j]	No
Infants and Children Aged ≥4 Weeks to <3 Months	None	Two NRTIs **plus** LPV/r[b]	No
	≥2 kg	Two NRTIs **plus** RAL[c]	No
Infants and Children Aged **≥3** Months to <3 Years	None	Two NRTIs **plus** ATV/r	No
	None	Two NRTIs **plus** LPV/r[b]	No
	None	Two NRTIs **plus** RAL[c]	No
Children Aged ≥3 Years	None	Two NRTIs **plus** ATV/r	No
	None	Two NRTIs **plus** DRV/r[k]	No
	None	Two NRTIs **plus** EFV[l]	No[g]
	None	Two NRTIs **plus** LPV/r[b]	No
	≥25 kg	Two NRTIs **plus** EVG/c[m]	Yes
	≥35 kg	Two NRTIs **plus** DOR[n]	Yes
Adolescents Aged ≥12 Years With SMRs of 1–3	None	Two NRTIs **plus** ATV/r	No
	None	Two NRTIs **plus** DRV/r[k]	No
	None	Two NRTIs **plus** EFV[l]	Yes
	None	Two NRTIs **plus** LPV/r[b]	No
	None	Two NRTIs **plus** RAL[c]	No
	≥25 kg	Two NRTIs **plus** EVG/c[m]	Yes
	≥35 kg	Two NRTIs **plus** ATV/c[o]	No
		Two NRTIs **plus** DOR[n]	Yes
		Two NRTIs **plus** RPV[p]	Yes
	≥40 kg	Two NRTIs **plus** DRV/c[q]	Yes

Adolescents Aged ≥12 Years With SMRs of 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**
Infants and Children Aged ≥1 Month to <6 Years	ZDV plus (3TC or FTC)[h]	No[g]
	ZDV plus ABC[f]	No
Children Aged ≥2 Years to 12 Years	TDF plus (3TC or FTC)[r]	Yes
Children and Adolescents Aged **≥6** Years and SMRs of 1–3	ZDV plus (3TC or FTC)[h]	Yes
	ZDV plus ABC[f]	No

[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. Although many pediatric experts favor initiating antiretroviral therapy as soon as possible after birth to limit the establishment of viral reservoirs, available clinical trial data do 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 HIV Infection. 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 than NVP in studies of children aged <3 years. Data are limited on the clinical outcomes of using RAL in infants and children aged <2 years.

[b] In general, LPV/r should not be administered to neonates before a postmenstrual age of 42 weeks and a postnatal age of ≥14 days (see the Lopinavir/Ritonavir section in Appendix A: Pediatric Antiretroviral Drug Information). Some experts would choose not to start with LPV/r as a *Preferred* initial regimen in neonates aged ≥14 days to <4 weeks but would choose to start with NVP instead.

[c] RAL granules can be administered to infants and children weighing ≥2 kg from birth to age 2 years. Oral RAL granules can be used up to a dose of 100 mg in the 14 kg to <20 kg weight band. RAL pills or chewable tablets can be used in children aged ≥2 years. Chewable RAL tablets can be crushed and dispersed in liquid and administered to infants as young as 4 weeks of age who weigh at least 3 kg.

[d] DTG is recommended as a *Preferred* agent for infants, children, and adolescents aged ≥4 weeks and weighing ≥3 kg. DTG dispersible tablets can be administered in infants and children aged ≥4 weeks and weighing ≥3 kg. DTG film-coated tablets can be used in children weighing ≥14 kg. An FDC that contains ABC/DTG/3TC is available in dispersible tablets (Triumeq PD) for children weighing ≥10 kg to <25 kg and in a single tablet to be swallowed (Triumeq) for children weighing ≥25 kg. See Dolutegravir for information about dosing and administration.

[e] BIC is available only as part of an FDC tablet that contains BIC/FTC/TAF; this FDC tablet is recommended as a *Preferred* regimen for children weighing ≥14 kg. Two strengths of BIC/FTC/TAF are available, with dosing according to a child's weight (see Bictegravir).

[f] ABC is not approved by the U.S. Food and Drug Administration (FDA) for use in full-term neonates and infants aged <3 months. Recent data from the IMPAACT P1106 trial and two observational cohorts provide reassuring data on the safety of ABC in infants when initiated at the age of <3 months (see Abacavir). Before ABC administration, a negative HLA-B 5701 allele test should be available. An FDC tablet that contains ABC/3TC (Epzicom and generic) is available for use in children weighing ≥25 kg.

[g] FDA-approved FDC tablets are not included in this table when they are not approved for use in the specific patient populations being discussed.

[h] An FDC tablet that contains 3TC/ZDV (Combivir and generic) is available for use in children weighing ≥30 kg. Some members of the Panel on Antiretroviral Therapy and Medical Management of Children Living With HIV (the Panel) prefer ABC over ZDV because ABC can be dosed once daily.

[i] FTC plus TAF is recommended as a *Preferred* NRTI combination for children and adolescents weighing ≥14 kg when used with an INSTI or NNRTI; an FDC tablet that contains FTC/TAF (Descovy) is available in two strengths, with dosage determined by a child's weight (see Tenofovir Alafenamide). FTC/TAF is approved by the FDA for children weighing ≥14 kg when used in the regimen BIC/FTC/TAF, which is also available in two strengths, with dosage determined by a child's weight. EVG/c/FTC/TAF is approved for use in children weighing ≥25 kg. FTC/TAF is a *Preferred* NRTI combination for children and adolescents weighing ≥35 kg when used with a boosted PI; FTC/TAF is not approved or recommended for use with a boosted PI in children weighing <35 kg.

[j] NVP should not be used in post-pubertal girls with T lymphocyte cell counts >250/mm^3, unless the benefit clearly outweighs the risk. NVP is approved by the FDA for the treatment of infants aged ≥15 days.

[k] 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).

[l] 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. FDC tablets that contain EFV/FTC/TDF (Atripla) and EFV 600 mg/3TC/TDF (Symfi) are available. See the Efavirenz section in Appendix A: Pediatric Antiretroviral Drug Information for information about use of the FDC EFV 400 mg/3TC/TDF (Symfi Lo).

[m] EVG is currently recommended only as a component of FDC tablets. Tablets that contain EVG/c/FTC/TAF (Genvoya) are recommended as an *Alternative* regimen for children and adolescents weighing ≥25 kg due to multiple drug–drug interactions from COBI and a lower barrier to the development of resistance to EVG.

[n] DOR is not FDA approved for pediatric use. Based on data from studies that evaluated the efficacy and tolerability of DOR in adults, as well as early findings from pediatric PK studies, the Panel recommends DOR as an *Alternative* ARV for children and adolescents weighing ≥35 kg. An FDC tablet containing DOR/3TC/TDF is available.

[o] ATV/c is available as an FDC tablet containing ATV/c (Evotaz) that has been approved by the FDA for use in children and adolescents weighing ≥35 kg.

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

[q] DRV/c is available as part of an FDC tablet containing DRV/c/FTC/TAF (Symtuza) that has been approved by the FDA for use in children and adolescents weighing ≥40 kg.

[r] An FDC tablet that contains FTC/TDF (Truvada) is available.

Key: 3TC = lamivudine; ABC = abacavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; 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; PK = pharmacokinetic; RAL = raltegravir; RPV = rilpivirine; SMR = sexual maturity rating; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended for *Initial* Therapy in Children

See Appendix A: Pediatric Antiretroviral Drug Information and Table 8. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios in the Adult and Adolescent Antiretroviral Guidelines for more information.

ARV Class/ Agent(s)	Advantages	Disadvantages
All INSTIs	INSTI Class Advantages • Few drug–drug interactions • Well tolerated	INSTI Class Disadvantages • Limited data on pediatric dosing or safety • Possible weight gain in adults, especially Black/African American women
BIC	Once-daily administration Can give with or without food Available in FDC tablets (see Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets)	The FDC tablet **is not recommended** for patients with hepatic impairment or an estimated CrCl <30 mL/min. The FDC tablet **should not be coadministered** with rifampin or dofetilide.
DTG	Once-daily administration Can give with food Available in FDC tablets (see Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets) Single-agent DTG pills are available in several doses and are small in size. DTG and the FDC ABC/DTG/3TC are available as dispersible tablets for suspension.	Drug interactions with EFV, FPV/r, TPV/r, and rifampin, necessitating twice-daily dosing of DTG CNS side effects, particularly sleep disturbances Early concerns about a possible increased risk of NTDs in infants born to women who were receiving DTG at the time of conception have decreased substantially. The Panel for Antiretroviral Guidelines for Adults and Adolescents and the Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission include DTG among the preferred ARV agents for use in people of childbearing potential and for use in people who are pregnant or are trying to conceive. Risks and benefits should be discussed to support informed decision-making (see Dolutegravir, Appendix C: Antiretroviral Counseling Guide for Health Care Providers).
EVG	Once-daily administration Available in FDC tablets (see Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets)	Among INSTIs, EVG has the lowest barrier to the development of resistance. If EVG is coadministered with COBI, the potential exists for multiple drug interactions because COBI is metabolized by hepatic enzymes (e.g., CYP3A4). COBI inhibits tubular secretion of creatinine, and this may result in increased serum creatinine but normal glomerular clearance.
RAL	Can give with food	Potential for rare systemic allergic reaction or hepatitis

ARV Class/ Agent(s)	Advantages	Disadvantages
	Available in tablet, chewable tablet, and powder formulations Chewable tablets can be crushed and mixed with various liquids for infants ≥4 weeks of age who weigh ≥3 kg. Once-daily administration (with RAL HD) can be used for treatment-naive or virologically suppressed children weighing ≥40 kg.	Granule formulation requires a multistep preparation before administration; caregiver must be taught how to properly prepare this formulation.
All NNRTIs	NNRTI Class Advantages • 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	NNRTI Class Disadvantages • 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; these toxic effects have not been reported in neonates. • Potential for multiple drug interactions due to metabolism via hepatic enzymes (e.g., CYP3A4). Information about drug interactions is available in the Adult and Adolescent Antiretroviral Guidelines and the HIV Drug Interaction Checker.
DOR	Once-daily administration Available in FDC tablets (see Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets) Can be taken with or without food Has continued antiviral activity in the setting of some NNRTI mutations	Neuropsychiatric AEs, but fewer than reported for EFV DOR is contraindicated when co-administered with drugs that are strong cytochrome P450 (CYP)3A enzyme inducers (see Doravirine). Drug interactions between DOR and rifabutin induce the metabolism of DOR and require an additional dose of DOR 100 mg to be administered 12 hours after a fixed-dose combination of DOR/3TC/TDF or an increase of the DOR dose to 100 mg twice daily (see Doravirine).
EFV	Once-daily administration Available in FDC tablets (see Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets) 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

ARV Class/ Agent(s)	Advantages	Disadvantages
NVP	Liquid formulation is available. Dosing information for young infants is available. Can give with food Extended-release formulation that allows once-daily dosing in older children is available.	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 to resistance
RPV	Once-daily dosing Available in FDC tablets (see Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets)	Should not use in patients with 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 to resistance
All PIs	PI Class Advantages • 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 that contains a PI targets HIV at two steps of viral replication by inhibiting the activity of viral reverse transcriptase and protease enzymes.	PI Class Disadvantages • 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 the PR interval of an ECG) RTV is associated with a large number of drug interactions.

ARV Class/ Agent(s)	Advantages	Disadvantages
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 Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets)	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 be used only 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 food, but they may be better tolerated when taken with a meal or snack.	Poor palatability of liquid formulation (bitter taste) 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 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) 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 an ECG)
ABC plus (3TC or FTC)	Palatable liquid formulations Can give with food Available in FDC tablets (see Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets)	Risk of ABC HSR; perform HLA-B*5701 screening before initiating ABC.
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 Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets)	Limited data on the safety and efficacy of this combination in children Increased lipid levels

ARV Class/ Agent(s)	Advantages	Disadvantages
TDF plus (3TC or FTC) for adolescents with SMRs of 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 Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets)	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.
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 and lipoatrophy with ZDV ZDV requires twice-daily dosing.
ZDV plus ABC	Palatable liquid formulations Can give with food	Risk of ABC HSR; perform HLA-B*5701 screening before initiating ABC. Bone marrow suppression and lipoatrophy with ZDV ZDV requires twice-daily dosing.

Key: 3TC = lamivudine; ABC = abacavir; AE = adverse event; ARV = antiretroviral; ATV = atazanavir; BIC = bictegravir; BSA = body surface area; CNS = central nervous system; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P450; ddI = didanosine; DOR = doravirine; DRV = darunavir; DTG = dolutegravir; ECG = electrocardiogram; EFV = efavirenz; EVG = elvitegravir; FDC = fixed-dose combination; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; HD = high dose; 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; NTD = neural tube defect; 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 = triglyceride; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine

Table 10. Antiretroviral Regimens or Components That Are Not Recommended for Initial Treatment of HIV Infection in Children and Adolescents

ARV Regimen	Rationale
Regimens containing only NRTIs	Inferior virologic efficacy
Regimens containing three drug classes	Potential to induce multiclass resistance Use as an initial regimen in children has not been studied
Regimens containing three NRTIs and one NNRTI	Added cost and complexity outweighs any benefit
Full-dose, dual-PI regimens	Insufficient data to recommend; potential for added toxicities
Oral regimens containing only two ARVs	Not FDA approved for pediatric use
ARV Component	**Rationale**
Unboosted ATV-containing regimens in children	Inadequate drug exposure
CAB	Not FDA approved for use in ARV-naive individuals or in children aged <12 years and weighing <35 kg
DRV/r in children <3 years	Potential for seizures
Once-daily DRV-based regimens in children aged ≥3 years to <12 years	Insufficient data to recommend
EFV-based regimens for children aged <3 years	CYP2B6 genotyping required to determine appropriate dosing
ETR-based regimens	Insufficient data to recommend; unlikely to be used as initial therapy
FTR	Not FDA approved for use in ARV-naive adults or for pediatric use
IBA	Not FDA approved for use in ARV-naive adults or for pediatric use
LPV/r dosed once daily	Inadequate drug exposure
MVC-based regimens	Only effective for CCR5-tropic virus
TDF-containing regimens in children aged <2 years	Potential bone toxicity Appropriate dose has yet to be determined

Key: ARV = antiretroviral; ATV = atazanavir; CAB = cabotegravir; DRV = darunavir; DRV/r = darunavir/ritonavir; FDA = U.S. Food and Drug Administration; EFV = efavirenz; ETR = etravirine; FTR = fostemsavir; GI = gastrointestinal; IBA = ibalizumab; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; TDF = tenofovir disoproxil fumarate

Table 11. Antiretroviral Regimens or Components That Are Never Recommended for Treating HIV in Children and Adolescents[a]

ARV Regimen or Component	Rationale	Exceptions
One ARV Drug Alone (Monotherapy)	Rapid development of resistance Inferior antiviral activity compared with regimens that include ≥3 ARV drugs Monotherapy "holding" regimens are associated with more rapid CD4 count declines than nonsuppressive ART.	Infants with perinatal HIV exposure and negative virologic tests who are receiving 4–6 weeks of ZDV prophylaxis to prevent perinatal transmission of HIV
Two NRTIs Alone	Rapid development of resistance Inferior antiviral activity compared with regimens that include ≥3 ARV drugs	Not recommended for initial therapy Some clinicians may opt to continue using two NRTIs alone in patients who achieve virologic goals with this regimen.
Any Regimen Containing Both 3TC Plus FTC	Similar resistance profile and no additive benefit	No exceptions
Any Regimen Containing Both TDF and TAF	No data to support potential additive efficacy or toxicity	No exceptions
Dual-NNRTI Combinations	Enhanced toxicity	No exceptions
TDF Plus ABC Plus (3TC *or* 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
NVP as Component of Initial ARV Therapy Regimen in Adolescent Girls With CD4 Counts >250 cells/mm^3 or Adolescent Boys With CD4 Counts >400 cells/mm^3	Increased incidence of symptomatic (including serious and potentially fatal) hepatic events in these patient groups	Only if benefit clearly outweighs risk

[a] Several ARV drugs that are no longer available or that have not been recommended for use in children for several years have been removed from this chapter, including the NRTIs stavudine and didanosine; the protease inhibitors fosamprenavir indinavir, nelfinavir, saquinavir, and tipranavir; and the fusion inhibitor enfuvirtide (see Archived Drugs).

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; CD4 = CD4 T lymphocyte; FTC = emtricitabine; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

Table 12. 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 (1-888-448-8765) or from an expert in pediatric HIV infection.

Level of Perinatal HIV Transmission Risk	Description	Neonatal ARV Management
Low Risk of Perinatal HIV Transmission	**Infants ≥37 weeks gestation when the** mother— • Is currently receiving and has received at least 10 consecutive weeks of ART during pregnancy, *and* • Has achieved and maintained *or* maintained viral suppression (defined as at least two consecutive tests with HIV RNA levels <50 copies/mL obtained at least 4 weeks apart) for the remainder of the pregnancy, *and* • Has HIV RNA <50 copies/mL at or after 36 weeks and within 4 weeks of delivery, *and* • Did not have acute HIV infection during pregnancy, *and* • Has reported good ART adherence, and adherence concerns have not been identified.	ZDV for 2 weeks[a]
	Infants born to mothers who do not meet the criteria above but who have a HIV RNA <50 copies/mL at or after 36 weeks gestation	ZDV for 4 to 6 weeks[a]
	Premature infants (<37 weeks gestation) who are not at high risk of perinatal acquisition of HIV	ZDV for 4 to 6 weeks[a]
High Risk of Perinatal HIV Transmission[a,b]	Mothers who did not receive antepartum ARV drugs, *or* Mothers who received only intrapartum ARV drugs, *or* Mothers who received antepartum ARV drugs but did not have viral suppression (defined as at least two consecutive tests with HIV RNA level <50 copies/mL obtained at least 4 weeks apart) within 4 weeks prior to delivery, *or* Mothers with acute or primary HIV infection during pregnancy or breastfeeding (in which case, breastfeeding should be immediately discontinued)[c]	Presumptive HIV therapy using either ZDV, 3TC, and NVP (treatment dose) *or* ZDV, 3TC, and RAL administered together from birth for 2 to 6 weeks; if the duration of the 3-drug regimen is shorter than 6 weeks, ZDV should be continued alone, to complete a total of 6 weeks of prophylaxis[d]

Level of Perinatal HIV Transmission Risk	Description	Neonatal ARV Management
Presumed Newborn HIV Exposure	Mothers with unconfirmed HIV status who have at least one positive HIV test at delivery or postpartum, *or* Mothers whose newborn has a positive HIV antibody test	ARV management as described above for newborns with a high risk of perinatal HIV acquisition Infant ARV drugs should be discontinued immediately if supplemental testing confirms that the mother does not have HIV.
Newborn with HIV[e]	Positive newborn HIV virologic test/NAT	Three-drug ARV regimen using treatment doses. Refer to the What to Start: Regimens Recommended for Initial Therapy of Antiretroviral-Naive Children in the Pediatric Antiretroviral Guidelines for specific treatment recommendations.

[a] ZDV prophylaxis is recommended for infants born to mothers with HIV-2 mono-infection; see HIV-2 Infection and Pregnancy. If the mother has HIV-1 and HIV-2 infection, the infant ARV regimen should be based on the determination of low or high risk of HIV-1 transmission as described in the above table. Because HIV-2 is not susceptible to NVP, RAL should be considered for infants at high risk of perinatal HIV-2 acquisition. See text for evidence that supports the use of presumptive HIV therapy and a two-drug ARV prophylaxis regimen.

[b] See Intrapartum Care for People With HIV for guidance on indications for scheduled cesarean delivery and intrapartum intravenous 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 presumptive HIV therapy to infants born to mothers with acute HIV infection during pregnancy because of the higher risk for *in utero* transmission. If acute HIV is diagnosed during breastfeeding, the mother should immediately discontinue breastfeeding.

[d] The optimal duration of presumptive HIV therapy in newborns who are at a high risk for HIV acquisition is unknown. Newborns who are at a high risk for HIV acquisition should receive the ZDV component of the three-drug presumptive HIV therapy regimen for 6 weeks. The other two ARVs (3TC and NVP *or* 3TC plus RAL) may be administered for 2 to 6 weeks; the recommended duration for treatment with three ARVs varies depends on infant HIV NAT results, maternal viral load at the time of delivery, and additional risk factors for HIV transmission including breastfeeding (see sections below). Consultation with an expert in pediatric HIV is recommended when selecting a therapy duration because this decision should be based on case-specific risk factors and interim infant HIV NAT results.

[e] Infant ART should be initiated without waiting for the results of confirmatory HIV NAT testing, given the low likelihood of a false-positive HIV NAT. However, the specimen for confirmatory HIV testing should be obtained prior to ART initiation.

Note: ARV drugs should be initiated as close to the time of birth as possible, preferably within 6 hours of delivery. See Table 13 for dosing specifics.

Key: 3TC = lamivudine; ART = antiretroviral therapy; ARV =antiretroviral; NAT = nucleic acid test; NVP = nevirapine; Panel = Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission and Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV; RAL = raltegravir; ZDV = zidovudine

Table 13. Antiretroviral Drug Dosing Recommendations for Newborns

<table>
<tr><th>Drug</th><th>Drug Doses by Gestational Age at Birth</th></tr>
<tr><td rowspan="3">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.</td><td>≥35 Weeks Gestation at Birth

Birth to Age 4 Weeks

• ZDV 4 mg/kg per dose orally twice daily or alternative simplified weight-band dosing (see below)

Age >4 Weeks

• ZDV 12 mg/kg per dose orally twice daily; only make this dose increase for infants with confirmed HIV infection.

Simplified Weight-Band Dosing for Newborns Aged ≥35 Weeks Gestation From Birth to 4 Weeks
<table>
<tr><th>Weight Band</th><th>Volume of ZDV 10 mg/mL Oral Syrup Twice Daily</th></tr>
<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>
</table></td></tr>
<tr><td>≥30 to <35 Weeks' Gestation at Birth

Birth to Age 2 Weeks

• ZDV 2 mg/kg per dose orally twice daily

Age 2 Weeks to 6 to 8 Weeks

• ZDV 3 mg/kg per dose orally twice daily

Age >6 to 8 Weeks

• ZDV 12 mg/kg per dose orally twice daily; make this dose increase only for infants with confirmed HIV infection.</td></tr>
<tr><td><30 Weeks' Gestation at Birth

Birth to Age 4 Weeks

• ZDV 2 mg/kg per dose orally twice daily

Age 4 to 8 to 10 Weeks

• ZDV 3 mg/kg per dose orally twice daily

Age >8 to 10 Weeks

• ZDV 12 mg/kg per dose orally twice daily; only make this dose increase for infants with confirmed HIV infection.</td></tr>
</table>

Drug	Drug Doses by Gestational Age at Birth
ABC[c] Note: ABC is not approved by the FDA for use in neonates and infants aged <1 month. However, dosing recommendations have been modeled using PK simulation. Because of ABC-associated hypersensitivity, negative testing for HLA-B5701 allele should be confirmed prior to administration of ABC.	**≥37 Weeks' Gestation at Birth** *Birth to 1 Month* • ABC 2 mg/kg per dose orally twice daily *Age 1 Month to <3 Months* • ABC 4 mg/kg per dose orally twice daily
3TC	**≥32 Weeks' Gestation at Birth** *Birth to Age 4 Weeks* • 3TC 2 mg/kg per dose orally twice daily *Age >4 Weeks* • 3TC 4 mg/kg per dose orally twice daily
NVP[d]	**≥37 Weeks' Gestation at Birth** *Birth to Age 4 Weeks* • NVP 6 mg/kg per dose orally twice daily *Age >4 Weeks* • NVP 200 mg/m^2 BSA per dose orally twice daily; only make this dose increase for infants with confirmed HIV infection.
	≥34 to <37 Weeks' Gestation at Birth *Birth to Age 1 Week* • NVP 4 mg/kg per dose orally twice daily *Age 1 to 4 Weeks* • NVP 6 mg/kg per dose orally twice daily *Age >4 Weeks* • NVP 200 mg/m^2 BSA per dose orally twice daily; only make this dose increase for infants with confirmed HIV infection.
	≥32 to <34 Weeks' Gestation at Birth *Birth to Age 2 Weeks* • NVP 2 mg/kg per dose orally twice daily

<table>
<tr><th>Drug</th><th>Drug Doses by Gestational Age at Birth</th></tr>
<tr><td></td><td>Age 2 to 4 Weeks
• NVP 4 mg/kg per dose orally twice daily
Age 4 to 6 Weeks
• NVP 6 mg/kg per dose orally twice daily
Age >6 Weeks
• NVP 200 mg/m^2 BSA per dose orally twice daily; only make this dose increase for infants with confirmed HIV infection.</td></tr>
<tr><td>RAL

Note: If the mother has taken RAL 2 to 24 hours prior to delivery, the neonate's first dose of RAL should be delayed until 24 to 48 hours after birth; additional ARV drugs should be started as soon as possible.[7]</td><td>≥37 Weeks' Gestation at Birth and Weighing ≥2 kg[e]
Birth to Age 6 Weeks
<table>
<tr><th>Body Weight</th><th>Volume (Dose) of RAL 10 mg/mL Suspension</th></tr>
<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>
</table></td></tr>
</table>

[a] The optimal duration of presumptive HIV therapy in newborns who are at a high risk for perinatal HIV acquisition is unknown. Newborns who are at a high risk for HIV acquisition should receive the ZDV component of the three-drug presumptive HIV therapy regimen for 6 weeks. The other two ARVs (3TC and NVP *or* 3TC plus RAL) may be administered for 2 to 6 weeks; the recommended duration for these ARVs varies depending on infant HIV NAT results, maternal viral load at the time of delivery, and additional risk factors for HIV transmission. Consultation with an expert in pediatric HIV is recommended when selecting a therapy duration because this decision should be based on case-specific risk factors and interim infant HIV NAT results.

[b] For ARV management of infants with HIV infection, see the What to Start: Regimens Recommended for Initial Therapy of Antiretroviral-Naive Children section in the Pediatric Antiretroviral Guidelines.

[c] ABC is approved by the FDA for use in children aged ≥3 months when administered as part of an ARV regimen. ABC also has been reported to be safe in infants and children ≥1 month of age. More recently, an ABC dosing recommendation using PK simulation models has been endorsed by the WHO using weight-band dosing for full-term infants from birth to 1 month of age. See Abacavir in Appendix A: Pediatric Antiretroviral Drug Information in the Pediatric Antiretroviral Guidelines for additional information about the use of ABC between birth and 1 month of age. At this time, the Panels do not recommend ABC as part of a presumptive HIV therapy regimen. However, in situations where ZDV is not available or the infant has ZDV-associated toxicity, ABC could be considered an alternative to ZDV. This substitution should be considered in circumstances where increased risk of ZDV toxicity may exist, such as in infants with anemia or neutropenia. Because of ABC-associated hypersensitivity, negative testing for HLA-B5701 allele should be confirmed prior to administration of ABC.

[d] The NVP doses for infants ≥32 to <37 weeks gestation at birth and infants ≥37 weeks gestation at birth are not yet approved by the FDA. The FDA also has not approved a dose of NVP for infants aged <1 month. The doses for infants ≥32 to <34 weeks gestation at birth are based on modeling and might underestimate potential toxicity in infants of 32 to <34 weeks gestational age because the doses used to develop the model were lower than the doses now recommended. See Nevirapine in Appendix A: Pediatric Antiretroviral Drug Information in the Pediatric Antiretroviral Guidelines for additional information about dosing.

[e] RAL dosing is increased at 1 week and 4 weeks of age because metabolism by UGT1A1 is low at birth and increases rapidly during the next 4 to 6 weeks of life. No dosing information is available for preterm infants or infants weighing <2 kg at birth. In infants with HIV infection, twice-daily RAL can be replaced with once-daily DTG at ≥ 4 weeks of age (see Dolutegravir and What to Start: Regimens Recommended for Initial Therapy of Antiretroviral-Naive Children in the Pediatric Antiretroviral Guidelines). The current dosing regimen with two dose changes in the first month of life may be challenging for some families. To minimize dosing changes, some experts increase to the 3 mg/kg twice daily dose upon discharge on day 4 or 5 of life.

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; BSA = body surface area; DTG = dolutegravir; FDA = U.S. Food and Drug Administration; IV = intravenous; NVP = nevirapine; the Panels = the Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission and the Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV; PK = pharmacokinetic; RAL = raltegravir; UGT = uridine diphosphate glucotransferase; WHO = World Health Organization; ZDV = zidovudine

Table 14. Infant Antiretroviral Prophylaxis for Newborns of Mothers With Sustained Viral Suppression Who Breastfeed

<table>
<tr><th colspan="2">Newborns at Low Risk of HIV Acquisition During Breastfeeding</th></tr>
<tr><th>Recommended Regimen</th><th>Recommended Duration</th></tr>
<tr><td>ZDV</td><td>ZDV administered for 2 weeks (see Table 13 for dosing)</td></tr>
<tr><th colspan="2">Optional Extended Postnatal Prophylaxis for Newborns at Low Risk of HIV Transmission During Breastfeeding</th></tr>
<tr><th>Optional Regimen</th><th>Optional Recommended Duration</th></tr>
<tr><td>ZDV</td><td>ZDV administered for 4 to 6 weeks (see Table11 for dosing)</td></tr>
<tr><td>NVP</td><td>Simplified Age-Based Dosing for Newborns ≥32 Weeks Gestation Receiving Extended NVP Prophylaxis During Breastfeeding[a]
<table>
<tr><th>Age</th><th>Volume of NVP 10 mg/mL Oral Syrup Daily</th></tr>
<tr><td>Birth to 6 weeks</td><td>1.5 mL</td></tr>
<tr><td>6 weeks to 6 months</td><td>2.0 mL</td></tr>
<tr><td>6 months to 9 months</td><td>3.0 mL</td></tr>
<tr><td>9 months to 1 to 4 weeks post-weaning</td><td>4.0 mL</td></tr>
</table></td></tr>
</table>

[a] Extended NVP prophylaxis during breastfeeding recommendations are adapted from the Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery and Monitoring: Recommendations for a Public Health Approach. If prescribed, these simplified doses should start following confirmation of a negative infant NAT test and completion of a presumptive HIV therapy regimen in infants at high risk of HIV acquisition. For infants at low risk of transmission, these doses can be given from birth. Geneva: World Health Organization; 2021 Jul. Simplified Age-Based Dosing for Newborns ≥32 Weeks Gestation Receiving Extended NVP Prophylaxis During Breastfeeding in Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service delivery and Monitoring: Recommendations for a Public Health Approach

[b] For breastfeeding parents with viral resistance to NVP, alternative regimens for infant prophylaxis after completion of the 4 to 6 weeks of presumptive HIV therapy include daily 3TC or LPV/r; see Table 13. Antiretroviral Drug Dosing Recommendations for Newborns for dosing information.

Table 15. 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 a 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).
Request a description of the 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 potential barriers to adherence and strategies to overcome them.
Monitor pharmacy refills.	Approaches include a pharmacy-based or clinic-based assessment of on-time medication refills.
Employ telemedicine to monitor and support medication administration.	Telemedicine visits allow remote and often face-to-face contact and provide new opportunities to support families; to visualize ART preparation, handling, and swallowing; and to conduct DOT in the home setting.
Conduct announced and unannounced pill counts.	Approaches include asking patients to bring medications to the clinic, conducting home visits, or providing referral to community health nursing.
Targeted Approaches to Monitoring Adherence in Special Circumstances	**Description**
Implement DOT in person and via telemedicine.	Include a brief period of hospitalization if indicated.
Measure drug concentration in plasma or DBS.	Measuring drug concentrations can be considered for particular drugs.
Approaches to Monitoring Medication Adherence in Research Settings	**Description**
Measure drug concentrations in hair.	Measuring hair drug concentrations can be considered for particular drugs; it provides a good measure of adherence over time.[23,64,65]
Use electronic monitoring devices.	Approaches include MEMS caps and Wisepill.
Use mobile phone-based technologies.	Approaches 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: apps = applications; ART = antiretroviral therapy; DBS = dried blood spots; DOT = directly observed therapy; MEMS = Medication Event Monitoring System

Table 16. Strategies to Improve Adherence to Antiretroviral Medications

Initial Intervention Strategies
• Establish trust and identify mutually acceptable goals for care. • Obtain explicit agreement on the need for treatment and adherence. • Determine whether the child is aware of their HIV status. Consider talking to the child's caregivers about disclosing this information to the child in a developmentally appropriate way. • Identify psychosocial, behavioral, or structural barriers that may affect adherence and help child and/or family access resources to help eliminate these barriers. • 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. • With the patient and family together, develop a treatment plan that they believe is achievable. • Work with the patient and family to make specific plans for taking medications as prescribed and for supporting adherence. Assist them in arranging administration during day care, school, and in other settings, when needed. Consider home delivery of medications. • Identify barriers—such as co-pays and insurance access—related to medication access to help prevent interruptions in ART. • Schedule a home visit or telemedicine 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
• Choose the simplest regimen possible; reduce dosing frequency, pill size, and number of pills (see Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets or as a Co-packaged Formulation, by Drug Class and Appendix A, Table 2. Antiretroviral Fixed-Dose Combination Tablets and Co-packaged Formulations: Minimum Body Weights and Considerations for Use in Children and Adolescents). • When choosing a regimen, consider the patient's 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 improve palatability). • Choose drugs with the fewest AEs; provide anticipatory guidance for managing 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. • Choose ARV regimens with high genetic barriers to resistance, when available, if there are concerns about adherence.
Follow-Up Intervention Strategies
• Members of the multidisciplinary team should monitor adherence at each visit. In between visits, adherence can be monitored and supported by telephone, email, text, and other secure applications; confidentiality of any communication approach must be ensured.

- Provide ongoing support, encouragement, and understanding of the difficulties associated with maintaining adherence to daily medication regimens.
- Provide education and counseling that explain the meaning and significance of viral load results.
- Use patient education aids, including pictures, calendars, and stickers.
- Encourage the use of pill boxes, reminders, mobile apps, alarms, and resources such as the CDC's Every Dose, Every Day (E2D2) Toolkit and App.
- Provide follow-up clinic visits, telephone calls, text messages, and telemedicine visits to support and assess adherence.
- Provide access to support groups, peer groups, summer camp programs, or one-on-one counseling for caregivers and patients.
- Provide referrals and support access to counseling and treatment services for individuals with identified mental health problems, including depression and substance abuse.
- 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, during a brief period of 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.

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

Table 17a. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Central Nervous System Toxicity

Updated: April 11, 2023
Reviewed: April 11, 2023

Adverse Effects	Associated ARVs	Onset/ Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Global CNS Depression	LPV/r oral solution which contains both ethanol (42.4% v/v) and propylene glycol (15.3% w/v) as excipients	Onset • 1–6 days after starting LPV/r Presentation *Neonates/Premature Infants* • Global CNS depression (e.g., abnormal EEG, altered state of consciousness, somnolence)	Unknown; rare case reports have been published.	Prematurity Low birth weight Aged <14 days (whether birth was premature or term)	Avoid use of LPV/r until a postmenstrual age of 42 weeks and a postnatal age of ≥14 days unless no other alternatives are available. See Lopinavir/Ritonavir.	Discontinue LPV/r; symptoms should resolve in 1–5 days. If needed, reintroduction of LPV/r can be considered when the patient is outside the vulnerable period (i.e., postmenstrual age of 42 weeks and a postnatal age ≥14 days).
Neuropsychiatric Symptoms and Other CNS Manifestations	EFV	Onset • For many symptoms, onset is 1–2 days after starting EFV. • Many symptoms subside or diminish by 2–4 weeks, but symptoms may persist in a significant proportion of patients. Presentation (May Include One or More of the Following) *Neuropsychiatric Symptoms* • Abnormal dreams	Variable, depending on age, symptoms, and assessment method Children • 24% of patients experienced any EFV-related CNS manifestation in one case series, with 18% of participants requiring drug discontinuation. • Five of 45 participants (11%) experienced new-onset seizures in one study of children aged <36 months; two of these participants	Insomnia is associated with elevated EFV trough concentration (≥4 mcg/mL). CYP2B6 polymorphisms that decrease EFV metabolism and cause increased EFV serum concentrations (CYP2B6 516 T/T genotype or co-carriage of CYP2B6 516 G/T	Avoid use of EFV for initial ARV treatment in children and adolescents to prevent EFV-associated CNS side effects. See What to Start: Regimens Recommended for Initial Therapy of Antiretroviral-Naive Children. In situations where EFV treatment may be indicated,	If symptoms are excessive or persistent, obtain EFV trough concentration. If EFV trough concentration is >4 mcg/mL and/or symptoms are severe, strongly consider drug substitution if a suitable alternative exists. Alternatively, consider dose reduction with repeat TDM and dose adjustment (with input from an expert pharmacologist).

Adverse Effects	Associated ARVs	Onset/ Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
		• Psychosis • Suicidal ideation or attempted/ completed suicide *Other CNS Manifestations* • Dizziness • Somnolence • Insomnia or poor sleep quality • Impaired concentration • Seizures (including absence seizures) • Cerebellar dysfunction (e.g., tremor, dysmetria, ataxia) Note: CNS side effects (e.g., impaired concentration, abnormal dreams, sleep disturbances) may be more difficult to assess in children.	had alternative causes for seizures. • Cases of cerebellar dysfunction have been reported in children with very high EFV plasma levels. Adults • 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.	and 983 T/C variants) History of psychiatric illness or use of psychoactive drugs	consider the following: • Administer EFV on an empty stomach, preferably at bedtime. • Prescreen for psychiatric illness; avoid use in the presence of psychiatric illness, including depression or suicidal thoughts. Avoid concomitant use of psychoactive drugs. • Consider using TDM in children with mild or moderate EFV-associated toxicities.	
	RPV	Onset • Most symptoms occur in the first 4–8 weeks of treatment. Presentation	Children • Depressive disorders of all severity grades were reported in 19.4% of pediatric patients aged	History of neuropsychiatric illness	• Monitor carefully for depressive disorders and other CNS symptoms.	Consider drug substitution in cases of severe symptoms.

Adverse Effects	Associated ARVs	Onset/ Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
		Neuropsychiatric Symptoms • Depressive disorders • Suicidal ideation • Abnormal dreams/nightmares *Other CNS Manifestations* • Headache • Dizziness • Insomnia • Somnolence	12–17 years. Severe depressive disorders were reported in 5.6% of patients, including one suicide attempt. • Somnolence was reported in 5 of 36 children (14%). Adults • CNS/neuropsychiatric adverse events of all severity grades were reported in 43% of patients at 96 weeks (most were Grade 1). Depressive disorders of all severity grades were reported in 9% of patients; 1% of patients discontinued RPV because of severe depressive disorders. Higher frequency of depression and dizziness reported when coadministered with DTG.			
	RAL	Onset • As early as 3–4 days after starting RAL Presentation	Children • Increased psychomotor activity was reported in one child. Adults	Elevated RAL concentrations Co-treatment with TDF, a PPI, or	Prescreen for psychiatric symptoms. Monitor carefully for CNS symptoms.	Consider drug substitution (RAL or coadministered drug) in cases of severe insomnia or other neuropsychiatric symptoms.

Adverse Effects	Associated ARVs	Onset/ Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
		• Increased psychomotor activity • Headaches • Insomnia • Depression • Cerebellar dysfunction (e.g., tremor, dysarthria, ataxia)	• Headache • Insomnia (<5% in adult trials) • Rare case reports of cerebellar dysfunction in adults	inhibitors of UGT1A1 Prior history of insomnia or depression	Use with caution in the presence of drugs that increase RAL concentration.	
	DTG	Onset • 7–30 days after starting DTG Presentation *Neuropsychiatric Symptoms* • Depression or exacerbation of preexisting depression • Anxiety • Self-harm thoughts, suicidal ideation or attempted/ completed suicide • Drowsiness • Neurocognitive deficits (lower total competence and school performance) *Other CNS Manifestations (Generally Mild)* • Sleep disturbances	Children • In a retrospective cohort analysis, neuropsychiatric events that resulted in discontinuation occurred in 2 of 29 (6.8%) children who initiated DTG. • Significantly higher frequency of self-harm or suicidal thoughts reported in children in the ODYSSEY trial receiving DTG (23%) compared to SOC ARVs (5%). They were transient, self-resolved, and did not lead to treatment changes. Adults • 2.7% of the neuropsychiatric AEs	Preexisting depression or other psychiatric illness History of ARV-related neuropsychiatric symptoms Higher frequency of overall neuropsychiatric symptoms reported when DTG is coadministered with ABC, and of depression and dizziness when DTG is coadministered with RPV. However, evidence is conflicting for ABC association.	Use with caution in the presence of psychiatric illness, especially in patients with depression or a history of ARV-related neuropsychiatric symptoms. Consider morning dosing of DTG.	For persistent or severe neuropsychiatric symptoms, consider discontinuing DTG if a suitable alternative exists. For mild symptoms, continue DTG and counsel patient that symptoms likely will resolve with time.

Adverse Effects	Associated ARVs	Onset/ Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
		• Dizziness • Headache	reported in a large prospective cohort resulted in treatment discontinuation. • Higher frequency of neuropsychiatric symptoms reported with DTG than with other INSTIs. A class effect has been suggested.			
	BIC	Onset • 1–63 days after starting BIC (as late as 233 days for schizoaffective disorders) Presentation *Neuropsychiatric Symptoms* • Depression or exacerbation of preexisting depression • Suicidal ideation or attempted suicide • Schizoaffective disorders • Anxiety *Other CNS Manifestations (Generally Mild)* • Sleep disturbances • Dizziness • Insomnia	Children • One child (1%) had Grade 2 insomnia and anxiety that led to drug discontinuation in clinical trials. Adults • Overall, the frequency of neuropsychiatric events in BIC and DTG comparator arms appeared similar in adult clinical trials. • Abnormal dreams, dizziness, and insomnia occurred in 1% to 5% of adults.	Preexisting depression or other psychiatric conditions History of ARV-related neuropsychiatric symptoms	Use with caution in the presence of psychiatric conditions or in patients with a history of ARV-related neuropsychiatric symptoms.	For persistent or severe neuropsychiatric symptoms, consider discontinuing BIC if a suitable alternative exists. For mild symptoms, continue BIC and counsel patient that symptoms likely will resolve with time.

Adverse Effects	Associated ARVs	Onset/ Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
			• Suicidal ideation, suicide attempts, schizoaffective disorders, and depression occurred in <1% of adults. • A recent study reported a 3.3% short-term BIC-related discontinuation rate due to neuropsychiatric AEs after ART switch in a large cohort of adults with HIV in routine clinical practice setting.			
	CAB	Presentation *Neuropsychiatric Symptoms (Generally Mild or Moderate, Occasionally Serious)* • Mood disorders, including depression and suicidal ideation or attempt • Anxiety disorders *Other CNS Manifestations (Generally Mild or Moderate)* • Sleep disorders • Dizziness • Headache • Somnolence	Children • Insomnia was reported in 1 of 8 adolescents in the ongoing MOCHA trial. Adults • 2–4% pooled incidence reported in Phase 3 trials for CNS AEs, including sleep disorders, dizziness, and headache. • Less than 2% incidence reported for depressive disorders, including suicidal ideation, in Phase 3	Preexisting depression or other psychiatric conditions could be contributing factors, but causal links have not clearly been identified. CAB exposure did not differ between subjects with or without CNS or neuropsychiatric manifestations.	Monitor individuals for depressive symptoms or self-injurious thoughts or behavior, especially if prior history of such.	Promptly evaluate severe depressive symptoms, self-injurious behavior, or other CNS symptoms for a possible relationship with CAB, and assess risks and benefits of continued CAB treatment. If CAB is discontinued— • Counsel the individual about prolonged residual CAB levels in the blood for 52 weeks or longer, and monitor frequently for symptom resolution. • Ensure that a new suppressive regimen is

Adverse Effects	Associated ARVs	Onset/ Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
			trials, with comparable incidence in CAB and control groups.			started within 30 days of last injection.

Key: ABC = abacavir; AE = adverse event; ARV = antiretroviral; BIC = bictegravir; CAB = cabotegravir; CNS = central nervous system; CYP2B6 = cytochrome P450 2B6; DTG = dolutegravir; EEG = electroencephalogram; EFV = efavirenz; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; MOCHA = More Options for Children and Adolescents; PPI = proton pump inhibitor; RAL = raltegravir; RPV = rilpivirine; SOC = standard of care; TDF = tenofovir disoproxil fumarate; TDM = therapeutic drug monitoring; UGT1A = uridine diphosphate(UDP)-glucuronosyltransferase Family 1 Member A Complex; % v = volume; w = weight

Table 17b. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Dyslipidemia

Updated: April 11, 2022
Reviewed: April 11, 2023

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Dyslipidemia	PIs • All PIs, especially RTV-boosted PIs; lower incidence reported with DRV/r and ATV, with or without RTV NRTIs • Lower incidence reported with TDF than with TAF NNRTIs • Lower incidence reported with NVP, RPV, and ETR than with EFV INSTIs • EVG/c	Onset • As early as 2 weeks to months after beginning therapy Presentation *PIs* • ↑ LDL-C, TC, and TG *NRTIs* • ↑ LDL-C, TC, and TG. Significant increase in plasma lipid values was observed in adults switching from TDF to TAF, regardless of third agent or presence of a boosting agent.	Reported frequency varies with specific ARV regimen, duration of ART, and the specific laboratory parameters used to diagnose lipid abnormalities. 10% to 20% of young children receiving LPV/r will have lipid abnormalities. 40% to 75% of older children and adolescents with prolonged ART history will have lipid abnormalities. Pooled dyslipidemia prevalence of 39.5% and an incidence of 32% (191 per 1,000 person-years) reported in a recent meta-	Advanced-stage HIV disease High-fat, high-cholesterol diet Sedentary lifestyle Obesity Hypertension Smoking Family history of dyslipidemia or premature ASCVD Metabolic syndrome Fat maldistribution	Prevention • Low-fat diet • Exercise • Smoking-prevention counseling • Use of ARVs is associated with a lower prevalence of dyslipidemia, such as INSTIs, and to a lesser extent, newer PIs (e.g., ATV, DRV). • When considering a TDF-based or TAF-based regimen, the lipid-lowering beneficial effect of TDF should be weighed against its potential for increased renal and bone toxicities. Monitoring[a] • Obtain fasting (or non-fasting) lipid profile (TC, HDL-C, non-HDL-C, LDL-C, and TG) twice (>2 weeks but ≤3 months apart) and average these results. Monitor every 6 months (for abnormal results) or every	Assess all patients for additional ASCVD risk factors. Patients with HIV are considered to be at moderate risk for ASCVD.[b] ARV regimen changes should be considered, especially when the patient is receiving older PIs (e.g., LPV/r) and/or RTV boosting. Switching to 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. The lipid-lowering effect of an ARV regimen switch on LDL-C is less pronounced than with statin therapy but may be enough to re-establish a healthy lipid profile. Refer patients to a lipid specialist early if LDL-C is ≥250 mg/dL or TG is ≥500 mg/dL. If LDL-C is ≥130 mg/dL but <250 mg or TG is ≥150 mg/dL but <500 mg/dL, the following staged treatment approach is recommended by the NHLBI guidelines[b]:

		NNRTIs • ↑ LDL-C, TC, and HDL-C	analysis and a recent review of a large consortium of prospective observational cohorts, respectively.		12 months (for normal results). • If TG or LDL-C is elevated or if a patient has additional risk factors, obtain FLP. *Children With Lipid Abnormalities and/or Additional Risk Factors* • Obtain 12-hour fasting lipid profile (FLP) before initiating or changing therapy and every 6 months thereafter (more often if indicated). *Children Receiving Lipid-Lowering Therapy With Statins or Fibrates* • Obtain 12-hour FLP, LFT, and CK at 4 weeks, 8 weeks, and 3 months after starting lipid therapy. • If minimal alterations in AST, ALT, and CK are indicated, monitor every 3–4 months during the first year and every 6 months thereafter (or as clinically indicated). • Repeat FLP 4 weeks after increasing doses of antihyperlipidemic agents.	• Implement diet, nutrition, and lifestyle management for 6–9 months. Consult with a dietician if one is available. • If a 6- 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. • Statin therapy should be considered for patients with elevated LDL-C levels. NHLBI guidelines provide recommendations for statin therapy in patients with specific LDL-C levels and risk factors.[b] Concurrent substitution—preferably to ARVs with no inhibitory or inducing effect on CYP3A4 or OATP1B1 (e.g., INSTI)—also should be considered as appropriate to limit drug–drug interaction potential. • Drug therapy can be considered in cases of severe hypertriglyceridemia (TG ≥500 mg/dL). Fibrates (gemfibrozil and fenofibrate) may be used. The long-term risks of lipid abnormalities in children who are receiving ART are unclear. However, persistent dyslipidemia in children may lead to premature ASCVD.

[a] Because of the burden of collecting fasting blood samples, some practitioners routinely measure cholesterol and TG 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 Symbol:
↑ = increase

Key: ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; ASCVD = atherosclerotic cardiovascular disease; AST = aspartate aminotransferase; ATV = atazanavir; CK = creatine kinase; COBI = cobicistat; CYP3A4 = cytochrome P450 3A4; DRV = darunavir; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FLP = fasting lipid profile; 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; OATP1B1 = organic anion transporter polypeptide 1B1; PI = protease inhibitor; PUFA = polyunsaturated fatty acid; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglycerides

Table 17c. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Gastrointestinal Effects

Updated: April 11, 2022
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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	Onset • Early Presentation • Nausea and emesis, both of which may be associated with anorexia and/or abdominal pain	Varies by ARV agent; generally <15%	Unknown	Instruct patient to take PIs with food. Monitor for weight loss and ARV adherence.	Reassure the patient that these adverse effects generally improve over time (usually in 6–8 weeks). Consider switching to ARV drugs with smaller tablet sizes (see Appendix A,Table 2. Antiretroviral Fixed-Dose Combination Tablets: Minimum Body Weights and Considerations for Use in Children and Adolescents). Provide supportive care. In extreme or persistent cases, use antiemetics or switch to another ARV regimen.
Diarrhea	All ARV drugs, but most notably RTV-boosted PIs	Onset • Early Presentation • More frequent bowel movements and stools that are generally soft	Varies by ARV agent; generally <15%	Unknown	Monitor for weight loss and dehydration.	In prolonged or severe cases, exclude infectious or noninfectious (e.g., lactose intolerance) causes of diarrhea. Reassure patient that this adverse effect generally improves over time (usually in 6–8 weeks). Consider

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
						switching to another ARV regimen in persistent and severe cases. Treatment data in children are lacking; however, the following strategies may be useful when the ARV regimen cannot be changed: • Modifying the diet • 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.
Pancreatitis	Rare, but may occur with NRTIs or RTV-boosted PIs	Onset • Any time, usually after months of therapy Presentation • Emesis, abdominal pain, elevated amylase and lipase levels (asymptomatic hyperamylasemia or elevated lipase	<2%	Use of concomitant medications that are associated with pancreatitis (e.g., TMP-SMX, pentamidine, ribavirin) Hypertriglyceridemia Advanced HIV infection	Measure serum amylase and lipase concentrations if persistent abdominal pain develops.	Discontinue offending agent and avoid reintroduction. Manage symptoms of acute episodes. If pancreatitis is associated with hypertriglyceridemia, consider using interventions to lower TG levels.

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
		do not in and of themselves indicate pancreatitis)		Previous episode of pancreatitis Alcohol use		

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

Table 17d. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Hematologic Effects

Updated: April 11, 2022
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Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Anemia[a]	ZDV	Onset • Variable; weeks to months after starting therapy Presentation *More Common* • Asymptomatic • Mild fatigue • Pallor • Tachypnea *Rare* • Congestive heart failure	Newborns Exposed to HIV • Severe anemia is uncommon but might be coincident with physiologic Hgb nadir. Children With HIV Who Are Taking ARV Drugs • Anemia is two to three times more common with ZDV-containing regimens than with all other regimens.	Newborns Exposed to HIV • Premature birth is the most common risk factor. • *In utero* exposure to ZDV-containing regimens • Advanced maternal HIV • Neonatal blood loss • Combination ARV prophylaxis or presumptive HIV therapy, although no particular regimen has been identified as being worse than others. Children With HIV Who Are Taking ARV Drugs • Underlying hemoglobinopathy (e.g., sickle cell disease, G6PD deficiency)	Newborns Exposed to HIV • 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. Children With HIV Who Are Taking ARV Drugs • Avoid using 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).	Newborns Exposed to HIV • Anemia rarely requires intervention unless it is symptomatic or Hgb <7.0 g/dL. • ZDV administration can be limited to 4 weeks in low-risk neonates (see Antiretroviral Management of Newborns With Perinatal HIV Exposure or HIV Infection). Children With HIV Who Are Taking ARV Drugs • 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.

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
				• Myelosuppressive drugs (e.g., TMP-SMX, rifabutin) • Iron deficiency • Advanced or poorly controlled HIV disease • OIs of the bone marrow • Malnutrition		
Macrocytosis	ZDV	Onset • Within days or weeks of starting therapy Presentation • Asymptomatic, but MCV often is >100 fL • Sometimes associated with anemia	>90% to 95% for all ages	None	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).	No management required.
Neutropenia[a]	ZDV	Onset • Variable Presentation • Asymptomatic	Newborns Exposed to HIV • Rare Children With HIV Who Are Taking ARV Drugs • 2% to 4% of children on ARV drugs	Newborns Exposed to HIV • *In utero* exposure to ARV drugs • Combination ARV prophylaxis, particularly ZDV plus 3TC and NVP	Children With HIV Who Are Taking ARV Drugs • Obtain CBC as part of routine care.	Newborns Exposed to HIV • No established threshold for intervention; some experts would consider using an alternative NRTI for prophylaxis if ANC reaches <500 cells/mm^3. ZDV administration can be limited to 4 weeks in low-risk neonates (see Antiretroviral Management of Newborns With Perinatal HIV Exposure or HIV Infection).

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
			• Highest rates occur in children on ZDV-containing regimens	Children With HIV Who Are Taking ARV Drugs • Advanced or poorly controlled HIV infection • Myelosuppressive drugs (e.g., TMP-SMX, ganciclovir, hydroxyurea, rifabutin)		Children With HIV Who Are Taking ARV Drugs • Discontinue non-ARV, marrow-toxic drugs, if feasible. • Treat coexisting OIs and malignancies. • In cases of persistent, severe neutropenia that is thought to be associated with ARV drugs, switch to a regimen that does not contain ZDV.

[a] HIV infection itself, OIs, and medications that are used to prevent OIs (e.g., TMP-SMX) can all contribute to anemia and neutropenia. Prolonged use of NVP with ZDV in three drug regimens for the prevention of perinatal HIV transmission has been associated with increased rates of anemia and neutropenia in some, but not all, studies. The effects are of uncertain clinical significance and appear to be transient.

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

Table 17e. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Hepatic Events

Updated: April 11, 2022
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Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Hepatitis	Most ARV drugs have been associated with hepatitis, but a strong association exists between hepatitis and the use of NVP and EFV. NVP, EFV, ABC, RAL, DTG, and MVC have been associated with hepatitis in the context of HSRs. NRTIs, especially ZDV, have been associated with lactic acidosis and hepatic steatosis.	Onset • Acute toxic hepatitis occurs most commonly within the first few months of therapy, but it can occur later. • Steatosis presents after months or years of therapy. • Patients with HBV coinfection can experience a hepatitis flare with the initiation or withdrawal of 3TC, FTC, TDF, or TAF. A flare also can occur with the emergence of resistance to 3TC or FTC (especially if the patient is receiving only one anti-HBV agent). Note that TDF and TAF have high barriers to resistance when used to treat HBV. • Hepatitis can be a manifestation of IRIS	Uncommon	HBV or HCV coinfection Underlying liver disease Use of other hepatotoxic medications and supplements (e.g., St. John's wort [*Hypericum perforatum*], chaparral [*Larrea tridentata*], germander [*Teucrium chamaedrys*]) Alcohol use Pregnancy Obesity Higher drug concentrations of PIs For NVP-Associated Hepatic Events in Adults • Female sex with pre-NVP CD4 count >250 cells/mm^3 • Male sex with pre-NVP CD4 count >400 cells/mm^3	Prevention • 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. Monitoring *For ARV Drugs Other than NVP* • Obtain AST and ALT levels at baseline and at least every 3–4 months thereafter[b]; monitor at-risk patients more frequently (e.g., those with HBV or HCV coinfection or elevated baseline AST and ALT levels).	Evaluate the patient for other infectious and noninfectious causes of hepatitis and monitor the patient closely. Asymptomatic Hepatitis • Potentially offending ARV drugs should be discontinued if ALT or AST level is >5 times ULN. Symptomatic Hepatitis • Discontinue all ARV drugs and other potentially hepatotoxic drugs. • If a patient experiences hepatitis that is attributed to NVP, NVP should be discontinued permanently.

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
		if it occurs early in therapy, especially in patients with HBV or HCV coinfection. Presentation • 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.		• Population-specific HLA types[a]	*For NVP* • Obtain AST and ALT levels at baseline, at 2 weeks, 4 weeks, and then every 3 months.	• Consider viral causes of hepatitis: HAV, HBV, HCV, EBV, and CMV.
Indirect Hyperbilirubinemia	ATV	Onset • Within the first months of therapy Presentation • Can be asymptomatic or associated with jaundice. • Levels of direct bilirubin can be normal or slightly elevated when levels of indirect bilirubin are very high.	In long-term follow-up, 9% of children who were receiving ATV had at least one total bilirubin level >5 times ULN, and 1.4% of children experienced jaundice.	None established	Monitoring • No ongoing monitoring needed. • After an initial rise over the first few months of therapy, unconjugated bilirubin levels generally stabilize; levels can improve over time.	Isolated indirect hyperbilirubinemia is not an indication to stop ATV. Psychological impact of jaundice should be evaluated, and alternative agents should be considered. Jaundice can result in nonadherence, particularly in adolescents; this side effect should be

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
		• Normal AST and ALT				discussed with patients.

[a] For example, HLA-DRB1*0101 in White people, HLA-DRB1*0102 in South African people, and HLA-B35 in Thai people and White people.

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

Key: 3TC = lamivudine; ABC = abacavir; ALT = alanine transaminase; ARV = antiretroviral; AST = aspartate aminotransferase; ATV = atazanavir; CD4 = CD4 T lymphocyte; CMV = cytomegalovirus; DTG = dolutegravir; EBV = Epstein-Barr virus; EFV = efavirenz; FTC = emtricitabine; 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; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ULN = upper limit of normal; ZDV = zidovudine

Table 17f. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Insulin Resistance, Asymptomatic Hyperglycemia, and Diabetes Mellitus

Updated: April 11, 2022
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Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Insulin Resistance, Asymptomatic Hyperglycemia, and Diabetes Mellitus[a]	ZDV, LPV/r and, possibly, other PIs and INSTIs	Onset • Weeks to months after beginning therapy Presentation • Asymptomatic fasting hyperglycemia (which sometimes occurs in the setting of lipodystrophy), metabolic syndrome, or growth delay • Symptomatic DM (rare)	Children • IR, 6% to 12% (incidence is higher during puberty, 20% to 30%) • IFPG, 0% to 7% • IGT, 3% to 4% • DM, 0.2 per 100 child-years	Risk Factors for Type 2 DM • Lipodystrophy • Metabolic syndrome • Family history of DM • High BMI (obesity)	Prevention • Lifestyle modification Monitoring • Monitor for signs of DM, change in body habitus, and acanthosis nigricans. • Obtain RPG levels at initiation of ART, 3–6 months after ART initiation, and yearly thereafter. • In patients with an RPG ≥140 mg/dL, obtain FPG after an 8-hour fast and consider referring the patient to an endocrinologist.	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. If the patient is receiving ZDV, switch to TAF, TDF, or ABC. For Patients With Either an **RPG ≥200** mg/dL Plus Symptoms of DM or an **FPG ≥126** mg/dL • These patients meet diagnostic criteria for DM; consult an endocrinologist. For Patients With an FPG of 100–125 mg/dL • Impaired FPG suggests insulin resistance; consult an endocrinologist.

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
						For Patients With an FPG <100 mg/dL • This FPG is normal, but a normal FPG does not exclude IR. Recheck FPG in 6–12 months.

[a] IR, asymptomatic hyperglycemia, IFPG, IGT, and DM form a spectrum of increasing severity.

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

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

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

DM: Often defined as either an FPG ≥126 mg/dL, an RPG ≥200 mg/dL in a patient with hyperglycemia symptoms, a glycosylated hemoglobin (HgbA1c) of ≥6.5%, or a 2-hour PG ≥200 mg/dL in an OGTT.

However, the Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV 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. The HgbA1c test may underestimate glycemia in people with HIV; it is not recommended for diagnosis and may present challenges for monitoring.

Key: ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; BMI = body mass index; DM = diabetes mellitus; FPG = fasting plasma glucose; IFPG = impaired fasting plasma glucose; IGT = impaired glucose tolerance; INSTI = integrase strand transfer inhibitor; IR = insulin resistance; LPV/r = lopinavir/ritonavir; mg/dL = milligrams per deciliter; PI = protease inhibitor; RPG = random plasma glucose; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

Table 17g. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Lactic Acidosis

Updated: April 11, 2022
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Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Lactic Acidosis	NRTIs • ZDV • Less likely with 3TC, FTC, ABC, TAF, and TDF Other Drugs • See the Risk Factors and Prevention/ Monitoring columns for information regarding the toxicity of propylene glycol when LPV/r oral solution is used in neonates.	Onset • Generally after years of exposure Presentation • Lactic acidosis may be clinically asymptomatic. *Lactic Acidosis May Also Present With Insidious Onset of a Combination of Signs and Symptoms* • Generalized fatigue, weakness, and myalgias • Vague abdominal pain, weight loss, unexplained nausea, or vomiting • Dyspnea • Peripheral neuropathy Note: Patients may present with acute multiorgan failure (e.g., fulminant hepatic failure, pancreatic failure, respiratory failure).	3TC, FTC, ABC, TAF, and TDF are less likely to induce clinically significant mitochondrial dysfunction than ZDV.	Adults • Female sex • High BMI • Chronic HCV infection • African American race • Coadministration of TDF with metformin • Overdose of propylene glycol • CD4 count <350 cells/mm^3 • Acquired riboflavin or thiamine deficiency • Possible pregnancy • Overdose in setting of renal insufficiency (e.g., 3TC) Preterm Infants or Any Neonates Who Have Not Attained a Postmenstrual Age of 42 Weeks and a Postnatal Age of ≥14 Days	Prevention • 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. Monitoring *Asymptomatic Patients* • Routine measurement of serum lactate is not recommended. *Patients With Clinical Signs or Symptoms Consistent With Lactic Acidosis* • Obtain blood lactate level.[a] • Additional diagnostic evaluations should include	For Patients With Lactate 2.1–5.0 mmol/L (Confirmed With a Second Test) • Consider discontinuing all ARV drugs temporarily while conducting additional diagnostic work-up. For Patients With Lactate >5.0 mmol/L (Confirmed With a Second Test)[b] or >10.0 mmol/L (Any One Test) • 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). Anecdotal (Unproven) Supportive Therapies • Administer bicarbonate infusions, THAM, high doses of thiamine and riboflavin, and oral antioxidants

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
				• Exposure to propylene glycol, which is used as a diluent in LPV/r oral solution, because these newborns have a diminished ability to metabolize propylene glycol may lead to accumulation, increasing the risk of adverse events.	serum bicarbonate, anion gap, and/or arterial blood gas; amylase and lipase; serum albumin; and hepatic transaminases.	(e.g., L-carnitine, co-enzyme Q10, vitamin C). Following the resolution of clinical and laboratory abnormalities, resume therapy either with an 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, TDF, FTC, or 3TC). Lactate should be monitored monthly for ≥3 months.

[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: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; BMI = body mass index; CD4 = CD4 T lymphocyte; 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

Table 17h. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Lipodystrophies and Weight Gain

Updated: April 11, 2022
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Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Lipodystrophy (Fat Maldistribution) General Information	See below for specific associations.	Onset • Increase in trunk and limb fat is the first sign; peripheral fat wasting may not appear for 12–24 months after ART initiation.	Frequency is low (<5%) with current regimens.	• Genetic predisposition • Puberty • HIV-associated inflammation • Older age • Longer duration of ART • Body habitus	Prevention • Initiate a calorically appropriate low-fat diet and an exercise regimen. Monitoring • BMI measurement • Waist circumference and waist-hip ratio	• Physicians should perform a regimen review and consider changing the regimen when lipodystrophy occurs. • Improvement in fat maldistribution can vary following a regimen change. Improvement may occur after several months or years, or it may not occur at all.
Central Lipohypertrophy or Lipo-Accumulation	Can occur in the absence of ART, but these conditions most often are associated with the use of PIs and EFV.	Presentation • Central fat accumulation with increased abdominal girth, which may include a dorsocervical fat pad (buffalo hump). Gynecomastia may occur in males, or breast hypertrophy may occur in females,	Frequency is low (<5%) with current regimens.	• Obesity before initiation of therapy • Sedentary lifestyle	Prevention • Initiate a calorically appropriate low-fat diet and an exercise regimen. Monitoring • BMI measurement • Waist circumference and waist-hip ratio measurements	• Counsel patient on lifestyle modification and dietary interventions (e.g., maintaining a calorically appropriate diet that is low in saturated fats and simple carbohydrates and starting an exercise regimen, especially strength training).

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
		particularly with the use of EFV.				• Recommend smoking cessation (if applicable) to decrease future CVD risk. • Consider using an INSTI instead of a PI or EFV, although some INSTIs may be associated with generalized weight gain (see below). Data Are Insufficient to Allow the Panel to Safely Recommend Use of Any of the Following Modalities in Children • Recombinant human growth hormone • Growth hormone–releasing hormone • Metformin • Thiazolidinediones • Recombinant human leptin • Anabolic steroids • Liposuction
Facial/Peripheral Lipoatrophy	Most cases are associated with the use of ZDV, a	Presentation • Thinning of subcutaneous fat in	Frequency is low (<5%) with current regimens.	Underweight before ART initiation.	Prevention • Limit the use of ZDV.	• Replace ZDV with another NRTI when possible.

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
	thymidine analogue NRTI.	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.			Monitoring • Patient self-report and physical examination are the most sensitive methods of monitoring lipoatrophy.	Data Are Insufficient to Allow the Panel to Safely Recommend Use of Any of the Following Modalities in Children • Injections of poly-L-lactic acid • Recombinant human leptin • Autologous fat transplantation • Thiazolidinediones
Weight Gain	Significant weight gain may occur with all ARV regimens, but it appears to be more pronounced with DTG, BIC, and TAF.	Onset • Gradual weight gain after initiating ARV drugs is common with all currently used regimens. The mechanism for weight gain is unclear and under investigation.	Rate of development of obesity is unclear.	In Infants and Children • Have not been evaluated yet In Adolescents • Female sex • Pre-treatment obesity In Adults • Low pre-treatment BMI • Older age • Female sex • Black race	Prevention • Initiate a calorically appropriate low-fat diet and an exercise regimen. Monitoring • BMI measurement • Waist circumference and waist-hip ratio measurements	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).

Key: ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; BMI = body mass index; CVD = cardiovascular disease; DTG = dolutegravir; DXA = dual energy X-ray absorptiometry; EFV = efavirenz; INSTI = integrase strand transfer inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; TAF = tenofovir alafenamide; ZDV = zidovudine

See the archived version of Supplement III, February 23, 2009, Pediatric Guidelines on the Clinicalinfo website for a more complete discussion and reference list.

Table 17i. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Nephrotoxic Effects

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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.	Onset • Weeks to months after starting therapy Clinical Findings • Crystalluria • Hematuria • Pyuria • Flank pain • Increased creatinine levels in some cases	ATV-related nephrolithiasis occurs in <10% of patients and has been reported after stopping ATV.	In adults, elevated urine pH (>5.7) The risk factors in children are unknown.	Prevention • Maintain adequate hydration. Monitoring • Obtain urinalysis at least every 6–12 months.	Provide adequate hydration and pain control. Consider using another ARV drug in place of ATV.
Renal Dysfunction	TDF	Onset • 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 1 year of therapy. • Abnormal urine protein/osmolality ratio may be an early indicator.	Adults • Approximately 2% of adults experience increased serum creatinine levels. • Approximately 0.5% of adults experience severe renal complications. Children • Approximately 4% of children experience	Risk May Increase in Children With the Following Characteristics • Aged >6 years • Black race, Hispanic/Latino ethnicity • Advanced HIV infection • Hypertension • Diabetes	Monitor urine protein, urine glucose, and serum creatinine at 3- to 6-month intervals. Some Panel members routinely monitor serum phosphate levels in patients who are taking TDF. Measure serum phosphate if the patient experiences persistent proteinuria or glucosuria or has	If TDF is the likely cause, consider using an alternative ARV drug. TAF has significantly less toxicity than TDF. Changing from TDF to TAF may improve renal function.

		Presentation *More Common* • Increased serum creatinine levels, 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 *Less Common* • Renal failure, acute tubular necrosis, Fanconi syndrome, proximal renal tubulopathy, interstitial nephritis, nephrogenic diabetes insipidus with polyuria	hypophosphatemia or proximal tubulopathy; frequency increases with prolonged TDF therapy and advanced HIV infection.	• Concurrent use of PIs (especially LPV/r) and preexisting renal dysfunction • Longer duration of TDF treatment • The presence of the apolipoprotein L1 variants G1 and G2 appears to increase the risk of renal abnormality in children with HIV. These alleles are more common in persons of Black descent.	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.	
Elevation in Serum Creatinine	DTG, COBI, RPV, BIC	Onset • Within 1 month of starting treatment Presentation • Asymptomatic. These drugs decrease renal tubular secretion of creatinine, leading to an increase in serum creatinine levels without a true change in eGFR. • Clinicians need to distinguish between a true	Common laboratory finding.	The risk factors in children are unknown.	Monitor serum creatinine. Assess for renal dysfunction if serum creatinine increases by >0.4 mg/dL or if increases continue over time.	No need to change therapy. Reassure the patient about the benign nature of the laboratory abnormality.

		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.				

Key: ARV = antiretroviral; ATV = atazanavir; BIC = bictegravir; COBI = cobicistat; DRV = darunavir; DTG = dolutegravir; eGFR = estimated glomerular filtration rate; LPV/r = lopinavir/ritonavir; mg/dL = milligrams per deciliter; Panel = The Panel on Antiretroviral Therapy and Medical Management of Children Living With HIV; PI = protease inhibitor; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Table 17j. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Osteopenia and Osteoporosis

Updated: April 11, 2023
Reviewed: April 11, 2023

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Osteopenia and Osteoporosis	Any ARV regimen Specific Agents of Concern • TDF, especially when used in a regimen that includes a boosting agent (i.e., RTV, COBI) • PIs (LPV, ATV>DRV) • EFV	Onset • Any age; decrease in BMD is usually seen soon after initiating ART. Presentation • Usually asymptomatic • Rarely presents as osteoporosis, a clinical diagnosis defined by evidence of bone fragility (e.g., a fracture with minimal trauma).	BMD *z score* Less **Than −2.0** • <10% in U.S. cohorts • Approximately 10% to 20% in international cohorts	• Longer duration and greater severity of HIV disease • Detectable viral load • Vitamin D insufficiency/deficiency • Delayed growth or pubertal delay • Low BMI • Lipodystrophy • Smoking • Prolonged systemic corticosteroid use • Medroxyprogesterone use • Lack of weight-bearing exercise	Prevention • 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 RPV or an unboosted INSTI. • When using TDF or EFV in a regimen, consider measuring vitamin D levels and supplementing with vitamin D3 if deficiency is identified.	• Same options as for prevention • Consider changing the ARV regimen (e.g., switching from TDF to TAF and/or from LPV/r to RPV or an unboosted INSTI whenever possible). • Supplement with vitamin D3 to raise serum 25-OH-vitamin D concentrations to >30 ng/mL. There is no clear benefit to administering daily supplemental vitamin D3 doses that are >4,000 IU. If patients are receiving a daily dose of vitamin D3 that is >4,000 IU, consider monitoring levels of 25-OH-vitamin D. • An increase in BMD was seen in one trial that evaluated the use of alendronate in youth with HIV and low BMD. However, the role of bisphosphonates in managing osteopenia and osteoporosis in children with

					Monitoring • Assess nutritional intake (calcium, vitamin D, and total calories). • Consider measuring serum 25-OH-vitamin D levels, particularly in patients who are taking ARV drugs of concern.[a] • DXA is rarely indicated.[b]	HIV has not been established.

[a] Drugs of greatest concern are TDF and EFV. Some experts measure 25-OH-vitamin D in children with HIV with additional risk factors, including living at high latitudes, sun avoidance, low dietary intake, and obesity.

[b] DXA scanning is not routinely recommended for children and youth who are being treated with TDF. DXA scanning can be considered for children and youth who are receiving additional medications that also affect bone density or have non-HIV related conditions for which DXA scans may be indicated (e.g., cerebral palsy).

Key: 25-OH-vitamin D = 25-hydroxy vitamin D; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; BMD = bone mineral density; BMI = body mass index; COBI = cobicistat; DRV = darunavir; DXA = dual-energy X-ray absorptiometry; EFV = efavirenz; INSTI = integrase strand transfer inhibitor; IU = international unit; LPV = lopinavir; LPV/r = lopinavir/ritonavir; PI = protease inhibitor; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Table 17k. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Rash and Hypersensitivity Reactions

Updated: April 11, 2023
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Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Rash	Any ARV drug can cause rash.	Onset • First few days to weeks after starting new ARV drug(s) Presentation • Most rashes mild to moderate diffuse maculopapular eruptions Note: A rash can be the initial manifestation of systemic hypersensitivity (see the SJS/TEN/EM major and HSR sections below).	Common (>10%) • EFV • ETR • FTC • NVP Less Common (5% to 10%) • ABC • ATV • DRV • TDF Unusual (2% to 4%) • BIC • LPV/r • MVC • RAL • RPV	• Sulfonamide allergy is a risk factor for rash in patients who are taking PIs that contain a sulfonamide moiety (i.e., DRV). • Polymorphisms in CYP2B6 and multiple HLA loci are associated with an increased risk of rash in patients who are taking NVP.	When Starting NVP or Restarting NVP After Interruptions of >14 Days • Utilize once-daily lead-in dosing.[a] This may not be necessary in children ages <2 years.[b] • Avoid the use of systemic corticosteroids during NVP dose escalation. • Assess the patient for rash severity, mucosal involvement, and other signs of systemic reaction.	Mild-to-Moderate Maculopapular Rash Without Systemic or Mucosal Involvement • Most rashes will resolve without intervention; ARV drugs can be continued while monitoring.[a] • Antihistamines may provide some relief. Severe Rash and/or Rash Accompanied by Systemic Symptoms • Manage as SJS/TEN/EM major, DRESS, or HSR as applicable (see below). Rash in Patients Receiving NVP • Given the elevated risk of HSR, measure hepatic transaminases. • If hepatic transaminases are elevated, NVP should be discontinued and not

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
						restarted (see the HSR section below).
SJS/TEN/EM Major	Many ARV drugs, especially NNRTIs (see the Estimated Frequency column)	Onset • First few days to weeks after starting new ARV drug(s) Presentation • 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.	Infrequent • NVP (0.3%) • EFV (0.1%) • ETR (<0.1%) Case Reports • ABC • ATV • DRV • LPV/r • RAL • ZDV	Adults • Female sex Patients who are Black, Asian, or Hispanic at higher risk	When Starting NVP or Restarting NVP After Interruptions of >14 Days • 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.	• Discontinue all ARV drugs and other possible causative agents (e.g., TMP- SMX). • Provide intensive supportive care, including IV hydration, aggressive wound care, eye care, labial adhesion preventive care, pain management, and antipyretics. Parenteral nutrition and antibiotics may also be necessary. • Corticosteroids and/or IVIG are sometimes used, but the use of these interventions is controversial. • Do not reintroduce the offending medication. • In cases where a patient experiences SJS/TEN/EM major while taking an NNRTI, many experts would avoid using other NNRTIs when restarting ART.
DRESS	DRV, DTG, EFV, ETR, NVP, RAL, RPV	Onset • 1–8 weeks after starting new ARV drug(s).	Rare	• Unknown • Potential association with HLA-B*53:01 and RAL-induced DRESS	Obtain a CBC and AST, ALT, and creatinine levels from patients who present with suggestive symptoms.	• Discontinue all ARV drugs and other possible causative agents (e.g., TMP-SMX). • The role of systemic steroids or IVIG in treatment is

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
		Presentation • Fever • Lymphadenopathy • Facial swelling • Morbilliform to polymorphous rash • Peripheral eosinophilia • Atypical circulating lymphocytes • Internal organ involvement (particularly the liver and/or kidneys)				unclear; consultation with a specialist is recommended. • Provide supportive care for end-organ disease. • Do not reintroduce the offending medication.
HSR With or without skin involvement and excluding SJS/TEN	ABC	Onset *With First Use* • Within first 6 weeks of initiating ABC *With Reintroduction* • Within hours of initiating ABC Presentation • Symptoms include high fever, diffuse skin rash, malaise,	<1% to 9% (varies by ethnicity)	• HLA-B*5701 (HSR is very uncommon in people who are HLA-B*5701 negative). • The risk of HSR is higher in patients who are white than in patients who are Black or East Asian.	• 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 in these patients. • When starting ABC, counsel patients and families about the signs and symptoms of HSR to ensure prompt reporting of reactions.	• Discontinue all ARV drugs and investigate other causes of the symptoms (e.g., a concurrent viral illness). • Provide symptomatic treatment. • Most symptoms resolve within 48 hours after discontinuing ABC. Do not rechallenge with ABC even if the patient is HLA-B*5701 negative.

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
		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.				
	NVP	Onset • Occurs most frequently in the first few weeks of therapy but can occur through 18 weeks. Presentation • Flu-like symptoms (including nausea, vomiting, myalgia, fatigue, fever, abdominal pain, and jaundice) with or without skin rash that may progress to hepatic	Occurs in 4% of patients on average, with a range of 2.5% to 11%.	Adults • ARV-naive with a higher CD4 count (>250 cells/mm^3 in women; >400 cells/mm^3 in men) • Female sex (risk is threefold higher in females than in males). Children • NVP hepatotoxicity and HSR are less common in prepubertal children than in adults, and	When Starting NVP or Restarting NVP After Interruptions of >14 Days • 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.	• Discontinue all ARV drugs. • Consider other causes of hepatitis and discontinue all hepatotoxic medications. • Provide supportive care as indicated and monitor the patient closely. • Do not reintroduce NVP. It is unclear whether it is safe to use other NNRTIs after a patient experiences symptomatic hepatitis due to NVP, and many experts would avoid the NNRTI drug class when restarting treatment.

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
		failure with encephalopathy.		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, and hypersensitivity) was 2.65 times greater in children who had CD4 percentages ≥15% than in children who had CD4 percentages <15%.	• 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/mm^3 and in men with CD4 counts >400 cells/mm^3, unless benefits outweigh risks. • Do not use NVP as PEP outside of the neonatal period.	
	ETR	Onset • Any time during therapy Presentation • Symptoms may include rash, constitutional findings, and sometimes organ dysfunction, including hepatic failure.	Rare	Unknown	Evaluate for hypersensitivity if the patient is symptomatic.	• Discontinue all ARV drugs. • Rechallenge with ETR is not recommended.

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
	MVC	Rash preceding hepatotoxicity	Rare	Unknown	Obtain AST and ALT levels from 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 from 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 Nevirapine section of the Drug Appendix.

[b] Lead-in dosing **is not recommended** when using NVP for either presumptive or definitive HIV therapy in newborns with perinatal HIV exposure or perinatal HIV infection. See the Nevirapine section of the Drug Appendix and Table 13. Antiretroviral Drug Dosing Recommendations for Newborns in Antiretroviral Management of Newborns With Perinatal HIV Exposure or HIV Infection.

Key: ABC = abacavir; ALT = alanine transaminase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; ATV = atazanavir; BIC = bictegravir; CBC = complete blood count; CD4 = CD4 T lymphocyte; CYP2B6 = Cytochrome P450 Family 2 Subfamily B Member 6; 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; HLA-B*5701 = human leucocyte antigen gene variant; 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; PREDICT Study = Personalised Responses to Dietary Composition Trial Study; RAL = raltegravir; RPV = rilpivirine; SJS = Stevens-Johnson syndrome; TDF = tenofovir disoproxil fumarate; TEN = toxic epidermal necrolysis; TMP-SMX = trimethoprim-sulfamethoxazole; ZDV = zidovudine

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

This list is not exhaustive and does not necessarily contain all potential treatment options. Instead, it provides examples of changes that could be made. The table includes information only about switching between ARV drugs; **it does not include all the information that clinicians should consider before prescribing these drugs, such as drug cost and the patient's insurance coverage.** Refer to the individual drug sections, Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets or as a Co-Packaged Formulation, by Drug Class, and Appendix A, Table 2. Antiretroviral Fixed-Dose Combination Tablets and Co-packaged Formulations: Minimum Body Weights and Considerations for Use in Children and Adolescents in Appendix A: Pediatric Antiretroviral Drug Information for further information about the use and administration of specific ARV drugs and FDC formulations. For images of most of the ARV drugs listed in this table, see the Antiretroviral Medications section of the National HIV Curriculum. In addition, a resource from the United Kingdom illustrates the relative sizes of individual ARV drugs FDC tablets (see the ARV Chart in HIV i-Base). Although most of the drugs listed in that chart are the same as those in the United States, not all formulations available in the United States are included, and there are differences in a few of the brand names.

Current ARV Drug(s)	Age, Weight, and Sexual Maturity Rating Requirements	Potential ARV Drug Switch[a]	Comment
NRTIs			
ABC Twice Daily	Aged ≥3 months[b]	ABC once daily	See the Abacavir[b] section.
3TC Twice Daily	Aged ≥3 years	3TC once daily	See the Lamivudine section.
	Any age (starting at full-term birth) Any weight	FTC once daily	See the Emtricitabine section.
ZDV	Aged ≥1 months[b]	ABC	Less long-term mitochondrial toxicity Children aged ≥3 months can take ABC once daily.
	Weighing 17 kg to <25 kg	TDF	TDF is a reasonable, once-daily option for HLA-B*5701-positive children for whom ABC is not recommended and in whom ZDV is not tolerated. TDF is available as an oral powder and as low-strength tablets alone or in combination with FTC.
	Weighing ≥14 kg	TAF[c]	Less long-term mitochondrial toxicity. Once-daily dosing. Only available in coformulation with other ARV drugs; can further reduce pill burden. TAF is preferred over TDF because of the lower risk of bone and renal toxicity, but it may be associated with weight gain and lipid abnormalities.
	Weighing ≥14 kg	FTC/TAF[c] (Descovy)	Once-daily dosing. This combination NRTI medication may be more desirable because of smaller pill size

Current ARV Drug(s)	Age, Weight, and Sexual Maturity Rating Requirements	Potential ARV Drug Switch[a]	Comment
			and reduced pill burden. Benefits as described for TAF.
Any NRTI	Aged ≥12 years Weighing ≥35 kg	CAB and RPV co-packaged regimen as Cabenuva	NRTI-sparing regimen. Long-acting injectable, complete ARV regimen requiring two IM injections every 1 to 2 months that together are an alternative to daily oral ARV regimens. Must consider prior history of treatment failure and known or suspected drug resistance to individual drugs. Injection site reactions are common but do not often result in discontinuation of the regimen. See Cabotegravir.
	Aged ≥12 years Weighing ≥35 kg	DTG/RPV (Juluca)	NRTI-sparing FDC that is a complete regimen. In addition to age and weight criteria (based on RPV component since DTG approved to younger age/lower weight), must be virologically suppressed (HIV RNA <50 copies/mL) on a stable ARV regimen for at least 6 months and without history of treatment failure. Should be taken with food. No pediatric data.
NNRTIs			
NVP or EFV	Any age (starting at full-term birth) Weighing ≥2 kg	RAL[d]	RAL is preferred over NVP in infants from birth to age 4 weeks who weigh ≥2 kg. Both are dosed twice daily in children. Note that DTG and BIC have a higher barrier to resistance than RAL. In a child >1 month of age, DTG is preferred. See DTG below.
	Age ≥4 weeks Weighing ≥3 kg	DTG	DTG is available as a single drug in dispersible and film-coated tablet formulations, or as part of an FDC tablet, all of which can be dosed once daily if no documented resistance or history of failure with INSTI agents exists. DTG plus FTC/TAF (Descovy) in patients weighing at least 14 kg or the weight-appropriate dose of FTC/TDF (Truvada) can be used in children weighing 20 kg to <25 kg. DTG is available as a component of the FDC ABC/DTG/3TC, which is a complete ARV regimen that can be given to children weighing ≥10 to <25 kg in dispersible tablets (Triumeq PD) and to children and adolescents weighing ≥25 kg in a single tablet to be swallowed (Triumeq). Higher barrier to resistance, which makes it a good choice for patients who have poor adherence. May improve lipid levels. See the Dolutegravir section for more information.

Current ARV Drug(s)	Age, Weight, and Sexual Maturity Rating Requirements	Potential ARV Drug Switch[a]	Comment
	Aged ≥3 months Weighing ≥5 kg	ATV/r	ATV/r has a potentially greater barrier to resistance; however, taking ATV/r may be difficult for some patients, as ATV oral powder must be mixed with food or a beverage before administration, and the palatability of the RTV oral solution is poor.
	Aged ≥3 years Weighing ≥10 kg	DRV/r	DRV/r has a potentially greater barrier to resistance. DRV/r is administered twice daily to patients aged <12 years but may be administered once daily in children aged ≥12 years who do not have any DRV resistance mutations. Note that the palatability of the RTV oral solution is poor when considering administering to children not able to swallow tablets.
	Weighing ≥14 kg	BIC as Biktarvy	Once-daily dosing. BIC is available as a component of the FDC tablet BIC/FTC/TAF (Biktarvy) in two weight-based dose formulations—one formulation for those ≥14 to <25 kg and another for those ≥25 kg. This is a complete ARV regimen that can be taken with or without food.
	Weighing ≥25 kg	EVG as Genvoya	EVG is available as a component of the FDC tablet EVG/c/FTC/TAF (Genvoya), which is a complete ARV regimen that must be taken with food.
	Weighing ≥35 kg	DOR	DOR is available in a once-daily FDC tablet DOR/3TC/TDF (Delstrigo). Fewer side effects than reported with EFV. It has continued activity in the setting of some NNRTI mutations.
	Aged ≥12 years Weighing ≥35 kg	CAB and RPV co-packaged regimen as Cabenuva	Long-acting injectable, complete ARV regimen requiring two IM injections every 1 to 2 months that together are an alternative to daily oral ARV regimens. Must consider prior history of treatment failure and known or suspected drug resistance to individual drugs. Injection site reactions are common but do not often result in discontinuation of the regimen. See Cabotegravir.
	Aged ≥12 years Weighing ≥35 kg	RPV	Lower incidence of adverse lipid effects. May have fewer sleep disturbances and neuropsychiatric symptoms compared to EFV. RPV has continued activity in the setting of some NNRTI mutations.
PIs			

Current ARV Drug(s)	Age, Weight, and Sexual Maturity Rating Requirements	Potential ARV Drug Switch[a]	Comment
LPV/r Twice Daily	Any age (starting at full-term birth) Weighing ≥2 kg	RAL[d]	Better palatability. RAL HD can only be given once daily in those weighing ≥40 kg. Unlike LPV/r, the use of RAL is not restricted to infants with a corrected gestational age of ≥42 weeks and a postnatal age of ≥14 days. RAL granules may be difficult to dose for some caregivers.
	Age ≥4 weeks Weighing ≥3 kg	DTG	Once-daily dosing if no documented resistance or history of failure with INSTI agents exists. May be better tolerated, and it can be given as a dispersible tablet in young children. DTG is available as a component of the FDC ABC/DTG/3TC, which is a complete ARV regimen that can be given to children weighing ≥10 kg to <25 kg in dispersible tablets (Triumeq PD) and to children and adolescents weighing ≥25 kg in a single tablet to be swallowed (Triumeq). DTG plus FTC/TAF (Descovy) in those weighing at least 14 kg or the weight-appropriate dose of FTC/TDF (Truvada) can be used in children weighing 20 kg to <25 kg. May improve lipid levels. See the Dolutegravir section for more information.
	Aged ≥3 years Weighing ≥10 kg	EFV	Once-daily dosing. Better palatability. Lower incidence of adverse lipid effects. Review NNRTI mutations before use. See the Efavirenz section for concerns about EFV dosing for children aged <3 years.
	Aged ≥3 months Weighing ≥5 kg	ATV/r	Once-daily dosing. ATV/r may have a lower incidence of adverse lipid effects; however, taking ATV/r may be difficult for some patients, as ATV oral powder must be mixed with food or a beverage before administration, and the palatability of the RTV oral solution is poor.
	Aged ≥3 years Weighing ≥10 kg	DRV/r	DRV/r may have a lower incidence of adverse lipid effects. DRV/r is administered twice daily to patients aged <12 years, but it may be administered once daily in children aged ≥12 years who do not have DRV resistance mutations. Note that palatability of the RTV oral solution is poor when considering administering to children not able to swallow tablets.
	Weighing ≥14 kg	BIC as Biktarvy	Once-daily dosing. BIC is available as a component of the FDC tablet BIC/FTC/TAF (Biktarvy) in two weight-based dose formulations—one for those ≥14 to <25 kg and another for those ≥25 kg. This is a complete ARV regimen that can be taken with or without food.

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

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

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

Current ARV Drug(s)	Age, Weight, and Sexual Maturity Rating Requirements	Potential ARV Drug Switch[a]	Comment
	Aged ≥12 years Weighing ≥35 kg	FTC/RPV/TAF (Odefsey)	Once-daily dosing. Single pill. Aligns a child's regimen with an efficacious regimen that is used in adults. Review NNRTI mutations and check for drug–drug interactions before use. Must be taken with food at a consistent time daily.
	Aged ≥12 years Weighing ≥35 kg SMR 4 or 5	FTC/RPV/TDF (Complera)	Once-daily dosing. Single pill. Aligns a child's regimen with an efficacious regimen that is used in adults. Review NNRTI mutations and check for drug–drug interactions before use. Must be taken with food at a consistent time daily. Renal and bone toxicity of TDF limit its use.
	Aged ≥12 years Weighing ≥35 kg	DTG/RPV (Juluca)	NRTI-sparing FDC that is a complete regimen. In addition to age and weight criteria (based on RPV component since DTG approved to younger age/lower weight), must be virologically suppressed (HIV RNA <50 copies/mL) on a stable ARV regimen for at least 6 months and without history of treatment failure. Should be taken with food. No pediatric data.

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

[b] For infants and young children who are being treated with liquid formulations of ABC, initiation with once-daily ABC is not generally recommended. In clinically stable patients with undetectable viral loads who have had stable CD4 T lymphocyte cell counts on twice-daily ABC, the dose can be changed from twice daily to once daily. ABC is not approved by the U.S. Food and Drug Administration for use in neonates and infants aged <3 months. Recent data from the IMPAACT P1106 trial and two observational cohorts provide reassuring evidence of the safety of ABC in infants aged <3 months. Based on these data, clinicians may consider the use of ABC in infants aged ≥1 month to <3 months, in consultation with a pediatric HIV specialist (see Abacavir).

[c] For children and adolescents weighing ≥14 kg to <35 kg, TAF can be used in combination with an INSTI or an NNRTI, but **not** a boosted PI. For children and adolescents weighing ≥35 kg, TAF can be used in combination with an INSTI, an NNRTI, or a boosted PI.

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

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAB = cabotegravir; DOR = doravirine; DRV = darunavir; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FTC = emtricitabine; HD = high dose; HLA = human leukocyte antigen; IM = intramuscular; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SMR = sexual maturity rating; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

Table 19. Discordance Among Virologic, Immunologic, and Clinical Responses

Differential Diagnosis of Poor Immunologic Response Despite Virologic Suppression
Poor Immunologic Response Despite Virologic Suppression and Good Clinical Response • Laboratory error (in CD4 value or viral load measurement) • Misinterpretation of normal, age-related CD4 count decline (i.e., the immunologic response is not actually poor) • Low pre-treatment CD4 count or percentage • AEs that are associated with the use of certain drugs (e.g., ZDV, TMP-SMX, systemic corticosteroids) • Use of systemic corticosteroids or chemotherapeutic agents • Conditions that can cause low CD4 values (e.g., HCV, acute viral infections, TB, malnutrition, Sjogren's syndrome, sarcoidosis, syphilis)
Poor Immunologic and Clinical Responses Despite Virologic Suppression • Laboratory error (in CD4 value or viral load measurement) • Falsely low viral load result for an HIV strain/type that is not detected by viral load assay (i.e., HIV-1 non-M groups, HIV-1 non-B subtypes, HIV-2 [although this is unusual with newer viral load assays]) • Persistent immunodeficiency that occurs soon after initiating 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
• 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, worsening neurodevelopmental delay), lungs (e.g., bronchiectasis), cardiac (i.e., cardiomyopathy), renal (i.e., HIV-related kidney disease) • A new clinical event due to a non-HIV illness or condition • A new, or otherwise unexplained, HIV-related clinical event (e.g., treatment failure)

Key: AEs = adverse effects; ART = antiretroviral therapy; CD4 = CD4 T lymphocyte; HCV = hepatitis C virus; IRIS = immune reconstitution inflammatory syndrome; TB = tuberculosis; TMP-SMX = trimethoprim-sulfamethoxazole; ZDV = zidovudine

Table 20. Options for Regimens With at Least Two Fully Active Agents to Achieve Virologic Suppression in Patients With Virologic Failure and Evidence of Viral Resistance

To optimize antiretroviral (ARV) drug effectiveness, clinicians should evaluate a patient's treatment history and drug-resistance test results when choosing a new ARV regimen. Doing so is particularly important when selecting the nucleoside reverse transcriptase inhibitor (NRTI) components of a non-nucleoside reverse transcriptase inhibitor (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, tenofovir alafenamide, or ZDV. The presence of this mutation may increase susceptibility to these NRTIs.

Please see individual drug profiles for information about weight and age limitations (e.g., do not use darunavir in children aged <3 years), drug interactions, and dose adjustments when devising a regimen for children with multiclass drug resistance (see Appendix A: Pediatric Antiretroviral Drug Information). 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.

Prior Regimen	New Regimen Options[a]
Two NRTIs plus an NNRTI	Two NRTIs plus an INSTI[b] Two NRTIs plus a boosted PI
Two NRTIs plus a PI	Two NRTIs plus a second-generation INSTI[b] Two NRTIs plus a different boosted PI INSTI plus a different boosted PI and with or without NRTI(s) Two NRTIs plus an NNRTI[c]
Two NRTIs plus an INSTI	Two NRTIs plus a boosted PI DTG[a,b] or BIC[a,b] (if not used in the prior regimen) with a boosted PI with or without 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). Two NRTIs plus an NNRTI[c]
Failed regimen(s) that included NRTI(s), NNRTI(s), and PI(s)	If NRTIs Are Fully Active • INSTI plus two NRTIs If NRTIs Are Not Fully Active • INSTI plus two NRTIs with or without an RTV-boosted PI If There Is Minimal NRTI Activity* • INSTI with or without an RTV-boosted PI with or without ETR, or RPV with or without NRTI(s) • Consider adding T-20 and/or MVC if additional active drug(s) are needed. • Consider off-label use of approved agents or enrollment in clinical trials for novel antiretroviral treatments.

	• Hepatitis B co-infection[d]

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

[b] Raltegravir has a low barrier to resistance and requires twice-daily dosing in children and adolescents; BIC and DTG have a higher barrier to resistance and only require once-daily dosing. Many Panel members would use bictegravir/emtricitabine/tenofovir alafenamide (Biktarvy) in patients with prior treatment failure who have virus with the M184 mutation (see the Bictegravir section).

[c] NNRTIs could be an option in younger patients with no exposure to NNRTIs and with taste aversion to boosted PIs.

[d] When modifying ARV regimens in children with chronic Hepatitis B/HIV co-infection, the new regimen must contain agents active against Hepatitis B.

Key: BIC = bictegravir; DTG = dolutegravir; ETR = etravirine; 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

Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets or as a Co-packaged Formulation, by Drug Class

Updated: April 11, 2023
Reviewed: April 11, 2023

Brand Name	NRTIs						NNRTIs			INSTIs				PIs			PK Enhancers	
	ABC	3TC	ZDV	FTC	TDF	TAF[a]	DOR	EFV	RPV[b]	BIC[a]	CAB[b]	DTG	EVG[a]	ATV	DRV	LPV[c]	COBI	RTV
NRTI																		
Cimduo		X			X													
Combivir		X	X															
Descovy				X		X												
Epzicom	X	X																
Temixys		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						

Brand Name	NRTIs						NNRTIs			INSTIs				PIs			PK Enhancers	
	ABC	3TC	ZDV	FTC	TDF	TAF[a]	DOR	EFV	RPV[b]	BIC[a]	CAB[b]	DTG	EVG[a]	ATV	DRV	LPV[c]	COBI	RTV
Triumeq PD	X	X										X						
NNRTI/INSTI																		
Juluca									X			X						
Cabenuva									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

[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] CAB and RPV for intramuscular injection are available as a co-packaged product (Cabenuva); oral formulations of CAB and RPV for initial lead-in dosing must be prescribed separately; see Cabotegravir and Rilpivirine.

[c] LPV is only available in FDC tablets or solution.

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; BIC = bictegravir; CAB = cabotegravir; COBI = cobicistat; DOR = doravirine; DRV = darunavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; FDA = U.S. Food and Drug Administration; FDC = fixed-dose combination; FTC = emtricitabine; HBV = hepatitis B virus; INSTI = integrase strand transfer inhibitor; LPV = 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 and Co-packaged Formulations: Minimum Body Weights and Considerations for Use in Children and Adolescents

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General Considerations When Using Fixed-Dose Combination Products

Please see the individual drug sections under Pediatric Antiretroviral Drug Information for the recommended dosing of individual fixed-dose combination (FDC) products.
FDC tablets and individual ARV drugs also can be looked up by drug name (brand name and generic) at DailyMed. Size is listed under the Ingredients and Appearance section

For images of most of the FDC tablets 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 FDC tablets and individual ARV drugs (see the ARV Chart at HIV i-BASE). Although most of the drugs listed in the chart are the same as those in the United States, there are several differences: some formulations available in the United States are not included; a few of the brand names are not the same as those listed in Appendix A, Table 2; and the chart includes a formulation that is not available in the United States.

Integrase Strand Transfer Inhibitors (INSTIs)

- Bictegravir (BIC) and dolutegravir (DTG), second-generation INSTIs, have a higher barrier to resistance than the first-generation INSTIs, elvitegravir (EVG) and raltegravir (RAL).
- For children weighing ≥10 kg, dolutegravir is available in once-daily FDC formulations of abacavir/dolutegravir/lamivudine (ABC/DTG/3TC). If ABC/DTG/3TC is not an option, then single-entity DTG can be used in combination with other FDC tablets.
    - ABC/DTG/3TC is available in two different formulations, with the appropriate formulation depending on weight. For children weighing ≥10 kg to <25 kg, ABC/DTG/3TC is available in a dispersible tablet, once-daily regimen (Triumeq PD); the number of tablets per dose depends on the child's weight. For children and adolescents weighing ≥25 kg, ABC/DTG/3TC is available as a once-daily single-tablet regimen (Triumeq).
    - Whether considering DTG in FDC or single-entity form, **the film-coated tablets and dispersible tablets are not bioequivalent and, thus, are not interchangeable on a milligram-per-milligram basis.** Refer to Dolutegravir for dosing information.
- For children weighing ≥14 kg, bictegravir is available as the single-tablet, once-daily regimen bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF; Biktarvy). There are two dosage strengths for pediatric use: one for use in children weighing ≥14 to <25 kg and another for children and adolescents weighing ≥25 kg and adults.
- For children weighing ≥25 kg, elvitegravir is available as the single-tablet, once-daily regimen elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (EVG/c/FTC/TAF; Genvoya). EVG/c/FTC/TAF (Genvoya) has more drug–drug interactions than ABC/DTG/3TC (Triumeq or Triumeq PD) or BIC/FTC/TAF (Biktarvy).
- The two-drug, co-packaged regimen of long-acting cabotegravir and rilpivirine (CAB and RPV; Cabenuva) is approved by the U.S. Food and Drug Administration (FDA) for use in children and adolescents aged ≥12 years and weighing ≥35 kg. CAB and RPV are administered by intramuscular injection on a monthly or every-2-months schedule after an optional oral dose lead-in. See Cabotegravir for instructions about dosing and administration.

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs)

- ABC or TAF in combination with 3TC or FTC are favored over zidovudine/lamivudine (ZDV/3TC) because of the lower risk of NRTI)-associated mitochondrial toxicity.
- Tenofovir disoproxil fumarate (TDF) is more potent than ABC at high viral loads (>100,000 copies/mL) 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 not recommended for children with sexual maturity ratings (SMRs) of 1 to 3 because of TDF-associated bone toxicity.
- For children weighing ≥14 kg who can swallow pills, FTC/TAF (Descovy) offers a once-daily alternative to twice-daily ZDV plus 3TC or ABC plus 3TC.
- For children weighing ≥14 kg and ≤35 kg, FTC/TAF (Descovy) can be used in combination with an INSTI or NNRTI, but not with a protease inhibitor; this restriction does not apply to regimens containing ZDV or ABC.

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

- The FDC tablet doravirine/lamivudine/tenofovir disoproxil fumarate (DOR/3TC/TDF) is approved by the FDA for children and adolescents weighing ≥35 kg who are antiretroviral (ARV) naive or virologically suppressed on a stable ARV regimen (see the Doravirine section).
- RPV has low potency at high viral loads (>100,000 copies/mL) and requires a high-fat meal for optimal absorption, so efavirenz (EFV) or an INSTI are favored over RPV.

Fixed-Dose Combinations Available for Children and Adolescents

FDC by Class Brand name and generic[a] products, when available	FDC Components	Minimum Body Weight or Weight Range (kg) or Age[b]	Pill Size (mm × mm) or Largest Dimension (mm)[c]	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 × 7	Take with or without food.
Descovy	FTC 120 mg/TAF 15 mg	With an INSTI or NNRTI • 14 to < 25 kg	N/A	Take with or without food.
	FTC 200 mg/TAF 25 mg	With an INSTI or NNRTI • 25 kg With a Boosted PI	12.5 × 6.4	Take with or without food.

FDC by Class Brand name and generic[a] products, when available	FDC Components	Minimum Body Weight or Weight Range (kg) or Age[b]	Pill Size (mm × mm) or Largest Dimension (mm)[c]	Food Requirements
		• 35 kg		
Epzicom and Generic ABC/3TC	ABC 600 mg/3TC 300 mg	25 kg	21 × 9	Take with or without food.
Temixys	3TC 300 mg/TDF 300 mg	35 kg	N/A	Take with or without food.
Truvada	FTC 100 mg/TDF 150 mg	17 to <22 kg	14	Take with or without food.
	FTC 133 mg/TDF 200 mg	22 to <28 kg	16	Take with or without food.
	FTC 167 mg/TDF 250 mg	28 to <35 kg	18	Take with or without food.
	FTC 200 mg/TDF 300 mg	35 kg	19 × 8.5	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 with a meal.[d]
Delstrigo	DOR 100 mg/3TC 300 mg/TDF 300 mg	35 kg	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.[d]
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[e]	21	Take on an empty stomach.
NRTI/INSTI				
Biktarvy	BIC 30 mg/FTC 120 mg/TAF 15 mg	14 to <25 kg	N/A	Take with or without food.
	BIC 50 mg/FTC 200 mg/TAF 25 mg	25 kg	15 × 8	Take with or without food.
Dovato	DTG 50 mg/3TC 300 mg	Adults[f]	19	Take with or without food.

FDC by Class Brand name and generic[a] products, when available	FDC Components	Minimum Body Weight or Weight Range (kg) or Age[b]	Pill Size (mm × mm) or Largest Dimension (mm)[c]	Food Requirements
Triumeq	ABC 600 mg/DTG 50 mg/3TC 300 mg	25 kg	22 × 11	Take with or without food.
Triumeq PD	ABC 60 mg/DTG 5 mg/3TC 30 mg	10 to < 25 kg[g]	N/A (dispersible)	Take with or without food.
NNRTI/INSTI				
Cabenuva[h]	Cabenuva 400 mg/600 mg kit contains CAB 400 mg/2 mL vial and RPV 600 mg/2 mL vial	35 kg and aged ≥12 years	N/A	See Cabotegravir for instructions about dosing and administration.
	Cabenuva 600 mg/900 mg kit contains CAB 600 mg/3 mL vial and RPV 900 mg/3 mL vial	35 kg and aged ≥12 years	N/A	See Cabotegravir for instructions about dosing and administration.
Juluca	DTG 50 mg/RPV 25 mg	Adults[f]	14	Take with a meal.[d]
NRTI/INSTI/COBI				
Genvoya	EVG 150 mg/COBI 150 mg/FTC 200 mg/TAF 10 mg	25 kg	19 × 8.5	Take with food.
Stribild	EVG 150 mg/COBI 150 mg/FTC 200 mg/TDF 300 mg	35 kg and SMR of 4 or 5[i]	20	Take with food.
NRTI/PI/COBI				
Symtuza	DRV 800 mg/COBI 150 mg/FTC 200 mg/TAF 10 mg	40 kg	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.

FDC by Class Brand name and generic[a] products, when available	FDC Components	Minimum Body Weight or Weight Range (kg) or Age[b]	Pill Size (mm × mm) or Largest Dimension (mm)[c]	Food Requirements
PI/RTV				
Kaletra	LPV/r Oral Solution • LPV 80 mg/mL and RTV 20 mg/mL Tablets • LPV 200 mg/RTV 50 mg • LPV 100 mg/RTV 25 mg	Post-Menstrual Age of 42 Weeks and a Postnatal Age **of ≥14 Days** • No minimum weight	19	Take with or without food.

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

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

[c] Sizes or largest dimensions 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.

[d] Patients must be able to take oral RPV with a meal of at least 500 calories on a regular schedule (a protein drink alone does not constitute a meal).

[e] Because of pharmacokinetic concerns, the Panel recommends caution when using Symfi Lo in children and adolescents who have SMRs of 1 to 3 and weigh ≥40 kg (see the Efavirenz section).

[f] The Panel does not currently recommend using dolutegravir/lamivudine (DTG/3TC; Dovato) or dolutegravir/rilpivirine (DTG/RPV; Juluca) as a two-drug complete regimen in adolescents and children. These FDC tablets could be used as part of a three-drug regimen in children who meet the minimum body weight requirements for each component drug.

[g] ABC/DTG/3TC is available in dispersible tablets (Triumeq PD) for children weighing ≥10 mg to <25 mg with the dosage and number of tablets based on weight. Refer to the Dolutegravir section for exact dosage and instructions for administration. Dispersible tablets (Triumeq PD) are not recommended for children and adolescents weighing ≥25 kg.

[h] Long-acting CAB and RPV for intramuscular injection are available as a co-packaged product (Cabenuva); oral formulations of CAB and RPV for the optional initial lead-in dosing or bridging between injections >7 days from the target injection window must be prescribed separately (see the Cabotegravir and Rilpivirine sections).

[i] Although Stribild is approved by the FDA for use in children and adolescents weighing ≥35 kg and age ≥12 years, the Panel **does not recommend** its use in children with SMRs of 1 to 3 given the availability of other INSTI-containing FDCs.

Key: 3TC = lamivudine; ABC = abacavir; ATV = atazanavir; BIC = bictegravir; CAB = cabotegravir; COBI = cobicistat; DOR = doravirine; DRV = darunavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; FDA = U.S. Food and Drug Administration; FDC = fixed-dose combination; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; kg = kilogram; LPV = lopinavir; LPV/r = lopinavir/ritonavir; mg = milligram; mL = milliliter; mm = millimeter; N/A = information not available or not applicable; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; the Panel = Panel on Antiretroviral Therapy and Medical Management of Children Living With HIV; PI = protease inhibitor; RPV = rilpivirine; RTV = ritonavir; SMR = sexual maturity rating; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

Appendix C, Table A. HIV Infection Stage Based on Age-Specific CD4 Count or Percentage

Stage[a]	Aged <1 Year		Aged 1 Year to <6 Years		**Aged ≥6** Years	
	Cells/mm^3	%	Cells/mm^3	%	Cells/mm^3	%
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 count; the CD4 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.

Key: CD4 = CD4 T lymphocyte

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.

Appendix C, Table B. HIV-Related Symptoms and Conditions

Mildly Symptomatic
Children with two or more of the following conditions, but none of the conditions listed in the Moderately Symptomatic category, are considered mildly symptomatic: • 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
• Anemia (hemoglobin <8 g/dL [<80 g/L]), neutropenia (white blood cell count <1,000 per µL [<1.0 × 10^9 per L]), and/or thrombocytopenia (platelet count <100 × 10^3 per µL [<100 × 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 • CMV 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

- Bacterial infections, multiple or recurrent[a]
- Candidiasis of bronchi, trachea, or lungs
- Candidiasis of esophagus
- Cervical cancer, invasive
- 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[b]
- 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)
- *Mycobacterium avium* complex or *Mycobacterium kansasii*, disseminated or extrapulmonary
- *Mycobacterium* tuberculosis of any site, pulmonary, disseminated, or extrapulmonary
- *Mycobacterium*, other species or unidentified species, disseminated or extrapulmonary
- Pneumocystis jirovecii (previously known as Pneumocystis carinii) pneumonia
- Pneumonia, recurrent[c]
- Progressive multifocal leukoencephalopathy
- Salmonella septicemia, recurrent
- Toxoplasmosis of brain, onset at age >1 month

- Wasting syndrome attributed to HIV[b]

[a] Only among children aged <6 years.

[b] 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).

[c] Only among adults, adolescents, and children aged ≥6 years.

Key: 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.

Appendix D, Table A. Likelihood of Developing AIDS or Death Within 12 Months, by Age and CD4 T-Cell Percentage or Log_{10} HIV-1 RNA Copy Number in HIV-Infected Children Receiving No Therapy or Zidovudine Monotherapy

CD4 Percentage					Log_{10} HIV RNA Copy Number		
Age	10%	20%	25%	30%	6.0	5.0	4.0
Percent Mortality (95% Confidence Interval)							
6 Months	28.7	12.4	8.5	6.4	9.7	4.1	2.7
1 Year	19.5	6.8	4.5	3.3	8.8	3.1	1.7
2 Years	11.7	3.1	2.0	1.5	8.2	2.5	1.1
5 Years	4.9	0.9	0.6	0.5	7.8	2.1	0.7
10 Years	2.1	0.3	0.2	0.2	7.7	2.0	0.6
Percent Developing AIDS (95% Confidence Interval)							
6 Months	51.4	31.2	24.9	20.5	23.7	13.6	10.9
1 Year	40.5	20.9	15.9	12.8	20.9	10.5	7.8
2 Years	28.6	12.0	8.8	7.2	18.8	8.1	5.3
5 Years	14.7	4.7	3.7	3.1	17.0	6.0	3.2
10 Years	7.4	2.2	1.9	1.8	16.2	5.1	2.2

Note: Table modified from: HIV Paediatric Prognostic Markers Collaborative Study Group. *Lancet*. 2003;362:1605-1611.

Appendix D, Table B. Death and AIDS/Death Rate per 100 Person-Years by Current Absolute CD4 Cell Count andAge in HIV-Infected Children Receiving No Therapy or Zidovudine Monotherapy (HIV Paediatric Prognostic Markers Collaborative Study) and Adult Seroconverters (CASCADE Study)

Age (Years)	Absolute CD4 Cell Count (cells/mm^3)					
	<50	50–99	100–199	200–349	350–499	500+
Rate of Death Per 100 Patient-Years						
0–4	59.3	39.6	25.4	11.1	10.0	3.5
5–14	28.9	11.8	4.3	0.89	0.00	0.00
15–24	34.7	6.1	1.1	0.71	0.58	0.65
25–34	47.7	10.8	3.7	1.1	0.38	0.22
35–44	58.8	15.6	4.5	0.92	0.74	0.85
45–54	66.0	18.8	7.7	1.8	1.3	0.86
55+	91.3	21.4	17.6	3.8	2.5	0.91
Rate of AIDS or Death per 100 Patient-Years						
0–4	82.4	83.2	57.3	21.4	20.7	14.5
5–14	64.3	19.6	16.0	6.1	4.4	3.5

15–24	61.7	30.2	5.9	2.6	1.8	1.2
25–34	93.2	57.6	19.3	6.1	2.3	1.1
35–44	88.1	58.7	25.5	6.6	4.0	1.9
45–54	129.1	56.2	24.7	7.7	3.1	2.7
55+	157.9	42.5	30.0	10.0	5.1	1.8

Note: Table modified from: HIV Paediatric Prognostic Markers Collaborative Study and the CASCADE Collaboration. *J Infect Dis.* 2008;197:398-404.

Appendix D, Table C. Association of Baseline Human Immunodeficiency Virus (HIV) RNA Copy Number and CD4T-Cell Percentage with Long-Term Risk of Death in HIV-Infected Children[a]

Baseline HIV RNA[c] (Copies/mL) Baseline CD4 Percentage	No. Patients[d]	Deaths[b]	
		Number	Percentage
≤100,000			
≥15%	103	15	(15%)
<15%	24	15	(63%)
>100,000			
≥15%	89	32	(36%)
<15%	36	29	(81%)

[a] Data from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Intravenous Immunoglobulin Clinical Trial.

[b] Mean follow-up: 5.1 years.

[c] Tested by NASBA® assay (manufactured by Organon Teknika, Durham, North Carolina) on frozen stored serum.

[d] Mean age: 3.4 years.

Source: Mofenson LM, Korelitz J, Meyer WA, et al. The relationship between serum human immunodeficiency virus type 1 (HIV-1) RNA level, CD4 lymphocyte percent, and long-term mortality risk in HIV-1-infected children. J Infect Dis. 1997;175(5):1029–1038.