Table 4.3 Preferred and alternative first-line ART regimens for adults, adolescents, children and neonates

Populations	Preferred first-line regimen	Alternative first-line regimen	Special circumstances
Adults and adolescents	TDF + 3TC (or FTC) + DTG[a,b]	TDF + 3TC + EFV 400 mg[b]	TDF + 3TC (or FTC) + EFV 600 mg[b] AZT + 3TC + EFV 600 mg[b] TDF + 3TC (or FTC) + PI/r[b] TDF + 3TC (or FTC) + RAL TAF[c] + 3TC (or FTC) + DTG ABC + 3TC + DTG[a] TDF + 3TC (or FTC) + PI/r[b]
Children	ABC + 3TC + DTG[d]	ABC + 3TC + LPV/r TAF[e] + 3TC (or FTC) + DTG	ABC + 3TC + EFV (or NVP) ABC + 3TC + RAL[f] AZT + 3TC + EFV[g] (or NVP) AZT + 3TC + LPV/r (or RAL)
Neonates	AZT (or ABC) + 3TC + RAL[h]	AZT + 3TC + NVP	AZT + 3TC + LPV/r[i]

[a] Section 4.8 discusses toxicity considerations for pregnant and breastfeeding women.

[b] EFV-based ART should not be used in settings with national estimates of pretreatment resistance to EFV of 10% or higher. In settings with high HIV drug resistance prevalence and where DTG is unavailable or unsuitable due to toxicity, a boosted PI-based regimen should be used. The choice of PI/r will depend on programmatic characteristics. Alternatively, HIV drug resistance testing should be considered, where feasible, to guide first-line regimen selection (see section 4.9).

[c] TAF may be considered for people with established osteoporosis and/or impaired kidney function.

[d] For age and weight groups with approved DTG dosing, from four weeks and 3 kg.

[e] For age and weight groups with approved TAF dosing.

[f] RAL can be used as an alternative regimen only if LPV/r solid formulations are not available.

[g] EFV should not be used for children younger than three years of age.

[h] Neonates starting ART with a RAL-based regimen should transition to DTG as soon as possible. This guideline provides new dosing guidance (see the annexes for dosing) for ABC for neonates. However, due to limited availability of ABC syrup, AZT syrup remains an effective option to combine with 3TC for the first four weeks of life.

[i] LPV/r syrup or granules can be used if starting after two weeks of age.

Cost and cost–effectiveness, equity, acceptability and feasibility

In 2019, the Guideline Development Group examined the costs, cost–effectiveness, equity, acceptability and feasibility. The conclusions drawn from the Guideline Development Group meeting were that a DTG-based regimen was a highly cost-effective option, feasible, acceptable and equitable. Since this recommendation was developed, DTG uptake has greatly expanded, and further formulations such as dispersible tablets for children have been approved and are expected to become increasingly available.

Clinical and implementation considerations

Despite a lower risk of drug–drug interactions compared with NNRTIs and boosted PIs, DTG cannot be used with some anticonvulsant drugs (such as phenytoin) and antiarrhythmic drugs (such as dofetilide). DTG cannot be simultaneously administered with cation-

In this 2021 update, we confirm dosing information for children for tenofovir alafenamide (TAF), fixed-dose combinations containing TAF were included for children weighing 25 kg or more with a 25-mg dose when used with unboosted regimens. This aligns with dosing approved by United States Food and Drug Administration *(9)*. Studies to investigate dosing for children weighing less than 25 kg are ongoing, and more information will be made available as soon as approval is extended.

This dosing annex and the simplified dosing schedule will be regularly reviewed and updated as additional data and new formulations become available. Updated information on ARV drug dosing in children and rationale for dose simplification is available on the newly developed paediatric ARV dosing dashboard *(10)*.

ARV drugs and formulations are available from several manufacturers, and the available dosage strengths of tablets, capsules and liquid formulations may vary from the information provided here. Several optimal dosage forms for children are currently being developed but have not yet received regulatory approval at the time these updated guidelines were published. National programme managers should ensure that products planned for use have received stringent regulatory approval and are of appropriate quality and stability. The current list of WHO prequalified drugs is available *(11)*. The United States Food and Drug Administration has a current list of approved and tentatively approved ARV drugs *(12)*. The policy of the Global Fund to Fight AIDS, Tuberculosis and Malaria on procurement and quality assurance is available *(13)*.

General principles

WHO followed the following principles in developing the simplified tables.

- Using an age-appropriate fixed-dose combination is preferred for any regimen if such a formulation is available.
- Oral liquid or syrup formulations should be avoided if possible (except for neonatal treatment and prevention). Dispersible tablets (or granules) are the preferred solid oral dosage forms, since these formulations can be made into liquid at the point of use.
- If suitable dispersible fixed-dose combinations are not available and oral liquids must be used, children should be switched to a solid oral dosage form as soon as possible.
- Although dosing newborns generally requires using oral liquid formulations for administrating precise dosing, switching to solid oral dosage form as soon as possible is recommended.
- If children have to use adult formulations, care must be taken to avoid underdosing and overdosing. Using scored tablets is preferred to ensure accurate dosing, especially if adult dosage forms are used. Splitting unscored tablets should be avoided since the uniform distribution of active drug product cannot be assured in tablet fragments.
- Some tablets such as LPV/r or ATV/r heat-stable tablets are made in a special embedded matrix formulation (a proprietary melt extrusion technology that stabilizes drug molecules that are normally heat labile) and should not be cut, split, dissolved, chewed or crushed, since bioavailability is significantly reduced when they are not swallowed whole.
- Among children for whom an LPV/r-based regimen remains the appropriate treatment choice, LPV/r is available in a 40 mg/10 mg pellet or granule formulation for infants and young children. However, children weighing 10 kg or more should be transitioned to LPV/r heat-stable tablets as soon as they are able to swallow tablets whole to ease administration and improve palatability and to reduce pill burden.
- After the first four weeks of life, at each clinic visit, infants and children should be weighed and doses should be adjusted based on observed growth and change in body weight.
- Country programmes should consider the national regulatory status and local availability status of specific dosage forms when developing national recommendations for treating children.
- Research is ongoing for several ARV medications to establish dosing guidance for neonates, infants and young children. The age indications for each drug mentioned in the drug pages are based on current evidence and will be updated as new recommendations become available.

Table A1.1 Simplified dosing of child-friendly fixed-dose solid formulations for twice-daily dosing for infants and children four weeks and older[a]

Drug	Strength of paediatric tablets	Number of tablets by weight band morning and evening										Strength of adult tablet	Number of tablets by weight band	
		3–<6 kg		6–<10 kg		10–<14 kg		14–<20 kg		20–<25 kg			25–<35 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
AZT/3TC	Tablet (dispersible) 60 mg/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300 mg/150 mg	1	1
ABC/3TC	Tablet (dispersible) 60 mg/30 mg[b]	1	1	1.5	1.5	2	2	2.5	2.5	3	3	600 mg/300 mg	0.5	0.5
	Tablet (dispersible) 120 mg/60 mg	0.5	0.5	0.5	1	1	1	1	1.5	1.5	1.5	600 mg/300 mg	0.5	0.5

[a] For infants younger than four weeks old, see Table A1.4 for more accurate dosing, which is reduced because of the decreased ability to excrete and metabolize medications. For infants who are at least four weeks old but weigh less than 3 kg, the immaturity of renal and hepatic pathways of elimination are less of a concern, but uncertainty still exists on the appropriate dosing of ARV drugs for preterm and low-birth-weight infants.

[b] This formulation will be phased out of use over time, and programmes should transition to using the 120 mg/60 mg dispersible scored tablets.

Table A1.2 Simplified dosing of child-friendly solid formulations for once-daily dosing for infants and children four weeks and older[a]

Drug	Strength of paediatric tablet	Number of tablets or capsules by weight band once daily					Strength of adult tablet	Number of tablets or capsules by weight band once daily
		3–<6 kg	6–<10 kg	10–<14 kg	14–<20 kg	20–<25 kg		25–<35 kg
EFV[b]	Tablet (scored) 200 mg	–	–	1	1.5	1.5	-	2
ABC/3TC	Tablet (dispersible) 60 mg/30 mg	2	3	4	5	6	600 mg/300 mg	1
	Tablet (dispersible) 120 mg/60 mg	1	1.5	2	2.5	3		
TAF/FTC[c]	Tablet 25 mg/ 200 mg	–	–	–	–	–	25 mg/200 mg	1
ATV[d]	Capsules 100 mg	–	–	2	2	2	300 mg	1[e]
	Capsules 200 mg	–	–	1	1	1		
DRV[f]	Tablet 600 mg	–	–	–	1	1	600 mg	1
	Tablet 150 mg	–	–	–	4	4		
RTV[g]	Tablet 25 mg	–	–	–	4	4	100 mg	1
	Tablet 50 mg	–	–	–	2	2		

Table A1.2 Simplified dosing of child-friendly solid formulations for once-daily dosing for infants and children four weeks and older[a] (continued)

Drug	Strength of paediatric tablet	Number of tablets or capsules by weight band once daily					Strength of adult tablet	Number of tablets or capsules by weight band once daily
		3–<6 kg	6–<10 kg	10–<14 kg	14–<20 kg	20–<25 kg		25–<35 kg
DTG[h]	Film-coated tablet 50 mg	–	–	–	–	1	50 mg	1
	Dispersible tablet 5 mg	1	3	4	5	6		
	Dispersible scored tablet 10 mg	0.5	1.5	2	2.5	3		

[a] See Table A1.4 for dosing recommendations for infants younger than four weeks old. Doses for this age group are reduced to account for the decreased ability to excrete and metabolize medications. For infants who are at least four weeks old but weigh less than 3 kg, immaturity of renal and hepatic pathways of elimination are less of a concern, but uncertainty still exists on the appropriate dosing of ARV drugs for preterm and low-birth-weight infants.

[b] EFV is not recommended for children younger than three years and weighing less than 10 kg.

[c] At the time of this update, the United States Food and Drug Administration approved TAF film-coated tablets for children older than six years for use in unboosted regimens such as with DTG. The United States Food and Drug Administration tentatively approved a fixed-dose combination containing TAF/FTC/DTG (TAF 25 mg, FTC 200 mg, DTG 50 mg) that can be used once daily for children and adolescents living with HIV weighing at least 25 kg.

[d] ATV is only approved for children three months and older. ATV single-strength capsules should be administered with RTV 100 mg for all weight bands 10 kg and above. ATV powder formulation has limited availability in low- and middle-income countries but enables ATV to be administered to infants and children as young as three months. Infants and children weighing 5–<15 kg should be administered 200 mg of ATV powder (four packets, 50 mg per packet) with 80 mg of RTV oral solution (1 mL) *(14)*.

[e] ATV 300 mg with RTV 100 mg for 25–<30 kg is recommended based on the findings from the PRINCE-2 study *(15)*.

[f] DRV in combination with RTV should be used for children older than three years, once daily when this is used without previous exposure to PIs. Although the approved dosing for 30–<35 kg is 675 mg, preliminary data from adult studies suggest that even lower DRV doses may be effective, and the 600 mg dose was therefore extended to the entire 25- to <35 kg weight band.

[g] RTV should only be use as a boosting agent in combination with ATV or DRV or to super-boost LPV/r when given with concomitant rifampicin for TB (see Table A1.5).

[h] At the time of this update, the United States Food and Drug Administration approved 5 mg dispersible tablets and tentatively approved 10-mg scored dispersible tablets for treatment-naive or treatment-experienced INSTI-naive children at least four weeks old and weighing at least 3 kg, based on data from the IMPAACT 1093 trial *(4)* and ODYSSEY *(16)*. The United States Food and Drug Administration and European Medicines Agency approved simplified dosing of the DTG 50 mg film-coated tablets for all children weighing ≥20 kg. DTG dispersible tablets and DTG film-coated tablets are not bioequivalent; 30 mg of DTG dispersible tablet corresponds to 50 mg of DTG film-coated tablets. DTG 50 mg film-coated tablets are preferred for children who have reached 20 kg (unless they cannot swallow tablets). Safety monitoring remains important given the current limited experience with this dosing. For adolescents living with HIV weighing more than 30 kg, a fixed-dose formulation of TDF 300 mg, 3TC 300 mg and DTG 50 mg (TLD) can be used and is preferred.

Table A1.3 Simplified dosing of child-friendly solid and oral liquid formulations for twice-daily dosing for infants and children four weeks of age and older[a]

Drug	Strength of paediatric tablets	Number of tablets or mL by weight-band morning (AM) and evening (PM)										Strength of adult tablet	Number of tablets by weight band	
		3–<6 kg		6–<10 kg		10–<14 kg		14–<20 kg		20–<25 kg			25–<35 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
Solid formulations														
AZT	Tablet (dispersible) 60 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300 mg	1	1
ABC	Tablet (dispersible) 60 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300 mg	1	1
LPV/r[b]	Tablet 100 mg/25 mg	–	–	–	–	2	1	2	2	2	2	–	3	3
	Pellets 40 mg/10 mg	2	2	3	3	4	4	5	5	6	6		–	–
	Granules 40 mg/10 mg sachet	2	2	3	3	4	4	5	5	6	6		–	–
DRV[c]	Tablet 75 mg	–	–	–	–	–	–	5	5	5	5	400 mg	1	1
RTV[d]	Tablet 25 mg	–	–	–	–	–	–	2	2	2	2	100 mg	1	1
	Tablet 50 mg	–	–	–	–	–	–	1	1	1	1			
RAL[e]	Chewable tablets 25 mg	1	1	2	2	3	3	4	4	6	6	400 mg	1	1
	Chewable tablets 100 mg	–	–	–	–	–	–	1	1	1.5	1.5			

Table A1.3 Simplified dosing of child-friendly solid and oral liquid formulations for twice-daily dosing for infants and children four weeks of age and older[a] (continued)

Drug	Strength of oral liquid	Number of tablets or mL by weight-band morning (AM) and evening (PM)										Strength of adult tablet	Number of tablets by weight band	
		3–<6 kg		6–<10 kg		10–<14 kg		14–<20 kg		20–<25 kg			25–<35 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
Liquid formulations														
AZT	10 mg/mL	6 mL	6 mL	9 mL	9 mL	12 mL	12 mL	–	–	–	–	–	–	–
ABC[f]	20 mg/mL	3 mL	3 mL	4 mL	4 mL	6 mL	6 mL	–	–	–	–	–	–	–
3TC	10 mg/mL	3 mL	3 mL	4 mL	4 mL	6 mL	6 mL	–	–	–	–	–	–	–
LPV/r[b]	80 mg/20 mg/mL	1 mL	1 mL	1.5 mL	1.5 mL	2 mL	2 mL	2.5 mL	2.5 mL	3 mL	3 mL	–	–	–
DRV[c]	100 mg/mL	–	–	–	–	2.5 mL	2.5 mL	3.5 mL	3.5 mL	–	–	–	–	–
RTV[d]	80 mg/mL	–	–	–	–	0.5 mL	0.5 mL	0.6 mL	0.6 mL	–	–	–	–	–
RAL[e]	10 mg/mL (Oral granules for suspension: 100 mg/ sachet)	3 mL	3 mL	5 mL	5 mL	8 mL	8 mL	10 mL	10 mL	–	–	–	–	–

[a] See Table A1.4 for dosing recommendations for infants younger than four weeks. Doses for this age group are reduced to account for the decreased ability to excrete and metabolize medications. For infants who are at least four weeks old but weigh less than 3 kg, immaturity of renal and hepatic pathways of elimination are less of a concern, but uncertainty still exists on the dosing of ARV drugs for preterm and low-birth-weight infants.

[b] Although ABC dose represents a significant increase compared with the neonatal dose, this dose was designed to match the recommended dose for the solid formulation above.

[c] LPV/r liquid requires a cold chain during transport and storage. The LPV/r heat-stable tablet formulation must be swallowed whole and should not be split, chewed, dissolved or crushed. Adult 200/50 mg tablets could be used for children weighing 14–<25 kg (one tablet in the morning and one in the evening) and for children weighing 25–<35 kg (two tablets in the morning and one in the evening). The LPV/r pellet formulation should not be used for infants younger than three months. More details on the administration of LPV/r pellets are available *(17)*. This dosing schedule applies to equivalent solid dosage forms such as LPV/r granules, which can be used from two weeks of age. Since the supply is currently constrained, both pellets and granules should be discouraged for children weighing more than 14 kg, who should receive LPV/r 100/25 mg tablets instead. Information on LPV/r formulations for children is available *(18)*.

[d] DRV to be used for children older than three years must be administered with 0.5 mL of RTV 80 mg/mL oral suspension if they weigh less than 15 kg and with RTV 50 mg (using 25 mg or 50 mg solid formulation) for children weighing 15–<30 kg. RTV 100-mg tablets can be used as a booster if lower-strength RTV tablets are not available, based on limited experience suggesting good acceptability and tolerability.

[e] RTV should only be used at this dose as a boosting agent in combination with ATV or DRV.

[f] RAL granules are approved from birth. The feasibility and acceptability of such formulations have not been widely investigated, and concerns have been raised about administration in resource-limited settings. Because of the administration challenges presented by the granule formulation, the Paediatric Antiretroviral Working Group endorsed the use of the 25 mg chewable tablets as dispersible for infants and children older than four weeks and weighing at least 3 kg. This was largely based on in vitro data on solubility and bioequivalence between tablets and granules *(19)* and on considering the limited availability of adequate alternatives for this age group. However, the findings from a feasibility and acceptability assessment conducted in South Africa demonstrate that administering RAL granules in rural settings is feasible as long as it is supported by adequate training and counselling.

Table A1.6 Simplified dosing of isoniazid and co-trimoxazole prophylaxis for infants and children at least four weeks old

Drug	Strength of paediatric tablet or oral liquid	Number of tablets or mL by weight band once daily					Strength of adult tablet	Number of tablets by weight band
		3–<6 kg	6–<10 kg	10–<14 kg	14–<20 kg	20–<25 kg		25–<35 kg
Isoniazid	100 mg	0.5	1	1.5	2	2.5	300 mg	1
Co-trimoxazole (sulfamethoxazole and trimethoprim)	Suspension 200 mg/ 40 per 5 mL	2.5 mL	5 mL	5 mL	10 mL	10 mL	–	–
	Tablets (dispersible) 100 mg/20 mg	1	2	2	4	4	–	–
	Tablets (scored) 400 mg/80 mg	–	0.5	0.5	1	1	400 mg/80 mg	2
	Tablets (scored) 800 mg/160 mg	–	–	–	0.5	0.5	800 mg/160 mg	1
Isoniazid/ (sulfamethoxazole and trimethoprim)/ B6	Tablets (scored) 300 mg/(800 mg/ 160 mg) /25 mg	–	–	–	0.5	0.5	300 mg/ (800 mg/ 160 mg)/ 25 mg	1