



WHO / Christine McNab

## POLICY BRIEF

# THE 2021 OPTIMAL FORMULARY AND LIMITED-USE LIST FOR ANTIRETROVIRAL DRUGS FOR CHILDREN



## The 2021 optimal formulary and limited-use list for antiretroviral drugs for children: policy brief

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# 1. BACKGROUND

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Since 2011, the publication of the Optimal Formulary and Limited-use List has provided clear guidance to country programmes, procurement entities and funding agencies on the essential antiretroviral therapy (ART) dosage forms for children needed to deliver WHO-recommended ART regimens to neonates (0- <4 weeks of age), and children for all lines of treatment. The products included on the list are regularly reviewed against a specific list of criteria (see Table 3) that considers current WHO recommendations,

supply constraints and programmatic realities to support programmes in taking a pragmatic approach to implementing updated WHO-recommended regimens in a rapidly changing antiretroviral (ARV) drug landscape.

This sixth edition of the Optimal Formulary and Limited-use List is intended to support the transition and implementation of preferred and alternative ART regimens recommended for infants and children in the 2019 WHO guidelines across all lines of treatment.



WHO/Ilyas Ahmed

## 2. CURRENT WHO GUIDELINES

**Table 1.** Summary of preferred and alternative first-line ART for neonates and children

	Neonates	Children
Preferred	AZT+3TC+RAL <sup>a</sup>	ABC + 3TC + DTG
Alternatives	AZT+3TC+NVP	ABC + 3TC + LPVr TAF <sup>c</sup> + 3TC (or FTC) + DTG ABC + 3TC + RAL <sup>d</sup>
Special circumstances <sup>d</sup>	AZT+3TC+LPVr <sup>b</sup>	ABC + 3TC + EFV <sup>e</sup> (or NVP <sup>f</sup> ) AZT + 3TC + EFV <sup>e</sup> (or NVP <sup>f</sup> ) AZT + 3TC + LPVr (or RAL)

<sup>a</sup> For the shortest time possible, until a solid formulation of LPVr or DTG can be safely administered.

<sup>b</sup> From two weeks of age if oral solution or granule formulations can be used. Although LPVr pellets cannot be used for neonates, they can be used from three months of age.

<sup>c</sup> For age and weight groups with approved TAF dosing (since January 2020, TAF has been approved from 25 kg).

<sup>d</sup> For special circumstances when preferred and alternative regimens are not available or cannot be used.

<sup>e</sup> From three years of age.

<sup>f</sup> Only in cases where no other alternatives are available.

**Table 2.** Summary of sequencing options for ART for children

First-line ART	Second-line ART <sup>a</sup>	Third-line ART
Two NRTIs + LPVr	Two NRTIs + DTG	DRV/r + DTG <sup>b</sup> with or without one or two NRTIs. Where possible, consider optimization using genotyping
Two NRTIs + EFV or NVP	Two NRTIs + DTG	
Two NRTIs + DTG or RAL	Two NRTIs + LPVr or ATVr	

<sup>a</sup> An optimized NRTI backbone should be used: AZT following TDF or ABC failure and vice versa.

<sup>b</sup> DTG-based third-line ART following the use of an integrase inhibitor must be administered with DTG twice daily.

In March 2021, the WHO-convened Paediatric ARV Working Group (PAWG) carefully considered the benefits and risks related to a programmatic transition to DTG-based regimens for children established on first- and second-line and encourages rapid programmatic transition to DTG-based regimens for ALL children established on first- and second-line ART irrespective of their current regimen. Transition to DTG should take into account:

- Availability and anticipated supply of DTG 10 mg score tablets and, in case of inadequate

supplies to provide DTG to all children, the need to prioritize children who most need DTG beyond those starting ART:

- Children on NNRTI-based regimens
- Children who need to start rifampicin-based TB treatment
- Children on LPVr liquid and solid formulations, particularly where those continue to present challenges in administration and/or challenges with attaining optimal viral load suppression



- While viral load monitoring remains a good practice to deliver appropriate care to children living with HIV, viral load (VL) should not be considered a precondition to undertaking a programmatic or individual transition and children should not have their transition to DTG delayed due to lack of documented viral load.

The group also agreed that DTG dosing recommendations during TB treatment should align with US FDA approval and support the use of DTG twice daily across age groups and weight bands (as currently recommended for adults).

Finally, the group reviewed administration guidance and agreed that DTG dispersible tablets should be ideally dispersed in water or swallowed whole. Crushing, chewing or mixing with other foods or liquids can be considered as long as the child can consume the entire amount of liquid or food.



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### 3. CRITERIA USED TO EVALUATE PRODUCTS FOR INCLUSION

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Although drug availability is a critical consideration for implementation planning, it is not a criterion for selecting products for the Optimal Formulary and Limited-use List since availability is country-specific and subject to change. Funding agencies, procurement entities, manufacturers, national medicine regulatory authorities and national governments all have a critical role to play in working together to ensure the availability of products on the

Optimal Formulary and Limited-use List, which can be achieved by fast-tracking in-country registration, maintaining procurement and supply-chain planning, facilitating commercialization and ensuring manufacturing capacity and filing applications for registration in other countries. Having one or more quality-assured suppliers available at the national level is, however, a criterion for selection of products.

**Table 3.** 2018 criteria to define optimal paediatric ARV dosage forms

Criterion	Description
Meets WHO requirements	Included in the latest WHO guidelines for treatment for children
Dosing flexibility	Allows for the widest range of dosing options
Approved by WHO Listed Authorities (WLA)	One or more quality-assured products available
User friendly	Easy for health-care workers to prescribe Easy for caregivers to administer Supports adherence in children
Optimizes supply chain	Easy to transport Easy to store Easy to distribute
Comparative cost	Cost should not be the deciding factor in selecting a drug, but the comparative cost of similar drugs or drug formulations should be considered

## 4. OPTIMAL FORMULARY

The Optimal Formulary is designed to include the minimum number of ARV drug formulations needed to deliver WHO-recommended (preferred and alternative) first- and second-line ART regimens for infants and children.

Appropriate dosage forms for postnatal prophylaxis for preventing the vertical transmission of HIV to HIV-exposed infants are also included given the critical need for these products.

**Optimal Formulary:** Minimum number of ARV drug formulations needed to provide all currently WHO-recommended preferred and alternative first- and second-line ART options for infants and children and infant prophylaxis for preventing vertical transmission of HIV.

Drug	Dosage form	Strength	Rationale for use	Pack size
DTG <sup>a</sup>	Tablet (dispersible, scored)	10 mg	For first-line or second-line ART for infants and children who are $\geq 4$ weeks of age and weighing 3- $<20$ kg	90 count
ABC + 3TC	Tablet (dispersible, scored)	120 mg/60 mg	For preferred first-line or second-line ART for infants and children weighing 3-25 kg	30 and 60 count packs
AZT <sup>b</sup>	Oral solution	50 mg/5 mL	For postnatal prophylaxis and treatment of neonates (first four weeks of life)	240 mL bottle
NVP	Oral solution	50 mg/5 mL	For postnatal prophylaxis and neonatal treatment only	100 mL bottle
LPVr	Tablet (heat stable)	100 mg/25 mg	For alternative first-line or second-line ART for children weighing $\geq 10$ kg and who are able to swallow tablets whole	60 count pack
LPVr	Oral granules	40 mg/10 mg	For alternative first-line or second-line ART for infants and children weighing $\leq 10$ kg or unable to swallow 100 mg/25 mg tablets whole	120 count pack
AZT + 3TC	Tablet	60 mg/	For second-line ART for infants and children	60 count

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