

## The need for new formulations and new research

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Although a number of child-friendly formulations, particularly paediatric FDC tablets and paediatric single drugs in solid forms, are available, it is clear that additional formulations will be needed to facilitate the scale-up of treatment for infants and children, and to keep pace with new recommendations and guidance.

Additional research is necessary to better understand the best dosing formulations for children. Dispersible tablets are easier to dose in children, but require access to clean water, and have not been studied in breast milk, which is important for administration to infants. Breast milk dispersibility is especially important for formulations that will be used for infant prophylaxis to prevent mother-to-child transmission (MTCT) of HIV infection. One option for prevention of mother-to-child transmission (PMTCT) in the new WHO recommendations calls for long-term infant prophylaxis with NVP. In the first few weeks of life, this is best accomplished by using NVP liquid, but beyond 6 weeks, infant dosing would be made easier if there was a dispersible scored 20 mg NVP tablet.

Darunavir (DRV) will be an important drug for paediatric treatment in the future, especially as increasing numbers of children require third-line therapy. DRV is usually boosted with low-dose ritonavir (RTV). At present, although there are several capsule strengths of DRV available, including strengths that are suitable for paediatric dosing, no DRV/RTV co-formulation is available.

Once-daily FDCs containing tenofovir (TDF), efavirenz (EFV) and emtricitabine (FTC) or 3TC have become the mainstays of adult treatment. Currently, TDF is not approved for use in children less than 12 years, but a number of paediatric studies are in progress and a paediatric approval is expected. An FDC containing TDF 75 mg and 3TC 75 mg together with a scored adult tablet containing TDF 300 mg and 3TC 300 mg would align well with the harmonized schedule.

For countries that choose to use ABC as a first-line drug in children, it is critical to have access to a triple-drug FDC containing ABC, 3TC and NVP. This would complement the dual FDC of ABC/3TC.

A number of additional high-priority formulations have been identified by the Paediatric ARV Working Group and these are listed below.

**Urgently needed dosing strengths of drugs not yet available in child-friendly formulations**

Drug	Formulation (mg)	Comments
<b>DRUGS NEEDED FOR PMTCT</b>		
NVP	20 mg scored tablet	Used for infant prophylaxis from 6 weeks onwards
<b>DRUGS NEEDED FOR PAEDIATRIC ART</b>		
LPV/RTV	40/10 mg sprinkle	Heat-stable formulation that will be equivalent to 0.5 ml of liquid and used to treat infants and children who are unable to take the paediatric tablet
ABC/3TC	Scored adult 300/150 mg tablet	Used in children >25 kg
ABC/3TC/NVP	60/30/50 mg	Triple FDC to align with the dual FDC
RTV	50 mg heat-stable sprinkle or tablet	Useful for co-administration with unboosted PIs and for super boosting when PIs need to be dosed with rifampicin
TDF/3TC	75/75 mg tab	
	Scored 300/300 mg tab	
DRV/RTV	Unclear	Current labelling calls for different ratios of DRV to RTV for different age brackets. It is unclear what the correct ratio should be to produce a co-formulated FDC, but this is a priority formulation
Raltegravir	Unclear	Raltegravir is not yet approved for paediatric use but this is high-priority formulation

See updated guidance on required paediatric formulations at <http://www.who.int/hiv/topics/paediatric/technical/en/index>.