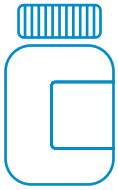
Lamivudine (3TC)

Available Formulations

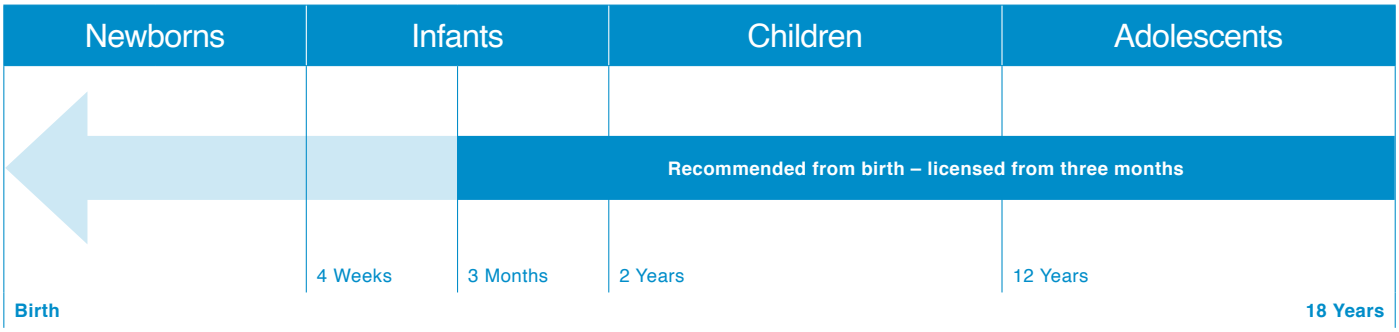
Single-drug formulations	Fixed-dose combinations	
		
Liquid formulation	Dispersible tablet (scored)	Dispersible tablet (scored)
3TC 10 mg/mL	AZT + 3TC 60/30 mg	ABC + 3TC 60/30 mg ABC + 3TC 120/60 mg

Formulations for adults
ABC + 3TC + AZT 300/150/300 mg AZT + 3TC 300/150 mg ABC + 3TC 600/300 mg DTG + ABC + 3TC 50/600/300 mg DTG + 3TC 50/300 mg DOR + 3TC + TDF 100/300/245 mg

The relative bioavailability of 3TC oral solution for children is about 40% lower than for tablets containing 3TC, whereas these two formulations have comparable bioavailability for adults. This difference has been linked to reduced absorption because of sorbitol, which is a component of the oral solution (Adkison et al.).

The fixed-dose combinations for children were registered through the WHO prequalification programme and do therefore not have a label from the United States Food and Drug Administration in place. For adults, 3TC + AZT dispersible tablets are bioequivalent to the oral solutions of 3TC and AZT (WHOPAR 3TC + AZT dispersible tablets) and 3TC + ABC dispersible tablets are bioequivalent to the film-coated adult fixed-dose combination (WHOPAR 3TC + ABC dispersible tablets).

WHO dose recommendation - age



Although 3TC is licensed by the United States Food and Drug Administration and European Medicines Agency for children three months and older, WHO as well as United States National Institutes of Health guidelines recommend administering it from birth (Moodley et al.; Bouazza et al.).

World Health Organization

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WHO dose recommendations – weight bands

Oral liquid from birth to four weeks of age[a]

Drug	Strength of formulation	2 – <3 kg		3 – <4 kg		4 – <5 kg	
		AM	PM	AM	PM	AM	PM
3TC	10 mg/mL	0.5 mL	0.5 mL	0.8 mL	0.8 mL	1 mL	1 mL

[a]To avoid dose changes over a short period of time and to minimize the likelihood of errors, all ARV drugs except for RAL should be dosed based on weight when treatment starts and maintained until four weeks of age (weight gain is limited during the first four weeks of life).

Child-friendly fixed-dose solid formulations for twice-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	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
3TC	Liquid 10 mg/mL	3 ml	3 ml	4 ml	4 ml	6 ml	6 ml	–	–	–	–	–	–	–
AZT/3TC	Tablet (dispersible) 60/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300/150 mg	1	1
ABC/3TC[a]	Tablet (dispersible) 60/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	600 / 300 mg	0.5	0.5
ABC/3TC	Tablet (dispersible) 120/60 mg	0.5	0.5	0.5	1	1	1	1	1.5	1.5	1.5			

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

Simplified dosing of child-friendly solid formulations for once-daily dosing for infants and children four weeks of age 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 by weight band once daily
		3 – <6 kg	6 – <10 kg	10 – <14 kg	14 – <20 kg	20 – <25 kg		25 – <35 kg
ABC/3TC	Tablet (dispersible) 60/30 mg[a]	2	3	4	5	6	600 mg / 300 mg	1
	Tablet (dispersible) 120/60 mg	1	1.5	2	2.5	3		

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

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Rationale for WHO dose selection

To simplify drug dosing in resource-limited settings and enable the administration of fixed-dose combination 3TC formulations for children, WHO weight band dosing has been introduced for 3TC. Some children in the low weight bands receive significantly higher 3TC doses than the does approved by the United States Food and Drug Administration of 5 mg/kg 3TC twice daily or 10 mg/kg once daily for children older than three months, and the United States National Institutes of Health guidelines recommendation of 4 mg/kg twice daily of the oral solution for children between four and 13 weeks of age. Nevertheless, the United States National Institutes of Health guidelines also included the WHO weight band dosing as part of their 3TC dosing recommendations. Various studies found 3TC drug concentrations among children comparable to those of adults when 3TC is administered using WHO weight band dosing recommendations (L'Homme et al.; Bouazza et al.).

Neonates

During the first four weeks of life, the recommended dose of 3TC is lower than that for older children, because renal function is immature after birth. Various studies have confirmed adequate exposure when administering 2 mg/kg 3TC twice daily to newborns (Moodley et al.; Mirochnick et al.). WHO dose recommendations are comparable with the United States National Institutes of Health guidelines.

Important information

Once-daily versus twice-daily dosing

Once-daily dosing has been tested among children aged three months to 13 years. All children received 8 mg/kg once-daily 3TC tablets instead of 4 mg/kg twice daily and achieved comparable 3TC exposure (Bergshoeff et al. and a PENTA study). These findings were later confirmed in a large clinical trial showing non-inferiority between children using 3TC once daily instead of twice daily (Musiime et al.).

Current ongoing trials involving children

Clinical trials on ClinicalTrials.gov

Knowledge gaps

The use of 3TC fixed-dose combination formulations for children to be used for newborns, including preterm and low-birth-weight infants.

Dosing 3TC for children with reduced renal function.

Research priorities according to PADO4

New dispersible fixed-dose combinations are needed that include 3TC as part of the NRTI backbone.

Drug–drug interactions

The dose of 3TC does not need to be adjusted when given together with rifampicin-based TB treatment.

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