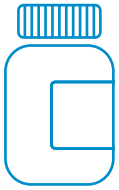
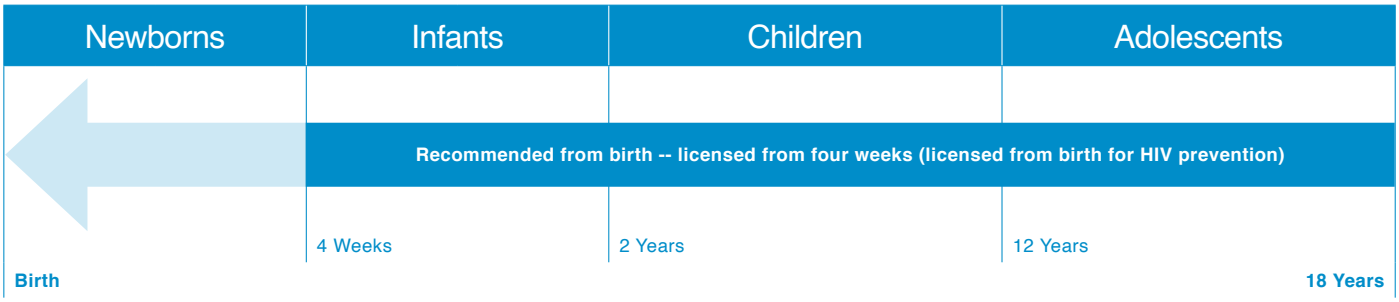
Zidovudine (AZT)

Available Formulations

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

Formulations for adults
AZT 300 mg AZT + 3TC 300/150 mg AZT + 3TC + NVP 300/150/200 mg

WHO dose recommendation - age



Although the United States Food and Drug Administration and European Medicines Agency license AZT for children living with HIV four weeks and older, AZT is licensed for preventing mother-to-child HIV-1 transmission from birth (8 mg/kg per day for oral dosing). WHO recommends using it from birth, as do the guidelines of the United States National Institutes of Health. Moreover, AZT can be used for premature or low-birth-weight children (Capparelli et al.).

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
AZT	10 mg/mL	1 mL	1 mL	1.5 mL	1.5 mL	2 mL	2 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).

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Child-friendly fixed-dose solid formulations for twice-daily dosing in infants and children 4 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 or capsules by weight band once daily	
		3 – <6 kg		6 – <10 kg		10 – <14 kg		14 – <20 kg		20 – <25 kg			25 – 34.9 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
AZT	Tablet (dispersible) 60 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300 mg	1	1
	Liquid 10 mg/mL	6 mL	6 mL	9 mL	9 mL	12 mL	12 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

Rationale WHO dose selection

To unify dosing of all ARV drugs for children, WHO AZT dosing guidance for children was changed from using body surface area dosing to weight-band mg/kg dosing. A pharmacokinetic study demonstrated that following WHO weight-band dosing resulted in adequate drug levels for most children. However, exposure among younger children and those with low weight for age was substantially higher than exposure for adults. Such children might therefore have a higher risk of developing dose-related toxicity (Fillekes et al.).

Newborns and Premature Infants

The WHO and United States National Institutes of Health guidelines recommend using the same AZT dose for both HIV prevention and HIV treatment of newborns. In the United States Food and Drug Administration label, however, AZT is advised only for newborns as HIV preventive therapy. The dose recommendations for newborns by the United States Food and Drug Administration label differ considerably from the dosing recommendations by WHO and United States National Institutes of Health for HIV prevention and treatment, which are aligned with those used in clinical trials (Capparelli et al.). Various studies have reported on the pharmacokinetics of AZT among newborns and premature infants. The enzymes responsible for glucuronidating AZT have low activity after birth but rapidly mature in the first 4–6 weeks, resulting in increased clearance of AZT. Therefore, the recommended initial dose of AZT after birth is low and increases after four weeks of therapy among full-term newborns. Dosing recommendations for preterm newborns are complex; the United States National Institutes of Health guidelines describe detailed dose recommendations.

For newborns who are unable to tolerate oral agents, the intervenous dose is 75% of the oral dose while maintaining the same dosing interval.

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Important information

Toxicity

Toxicity to the blood and blood-forming organs, including neutropaenia and severe anemia, is associated with AZT and is believed to be AZT concentration-dependent (Fillekes et al.). Using AZT also has a greater risk of developing mitochondrial toxicity compared with other NRTI drugs (Moyle et al.).

Research priorities according to PADO4

Current ongoing trials involving children

Knowledge gaps

None

Research priorities according to PADO4

None

Drug–drug interactions

Limited data for adults suggest that AZT plasma concentrations decrease when used concomitantly with rifampicin. Therefore, AZT should preferably not be used with rifampicin to avoid risk of treatment failure.

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