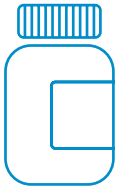
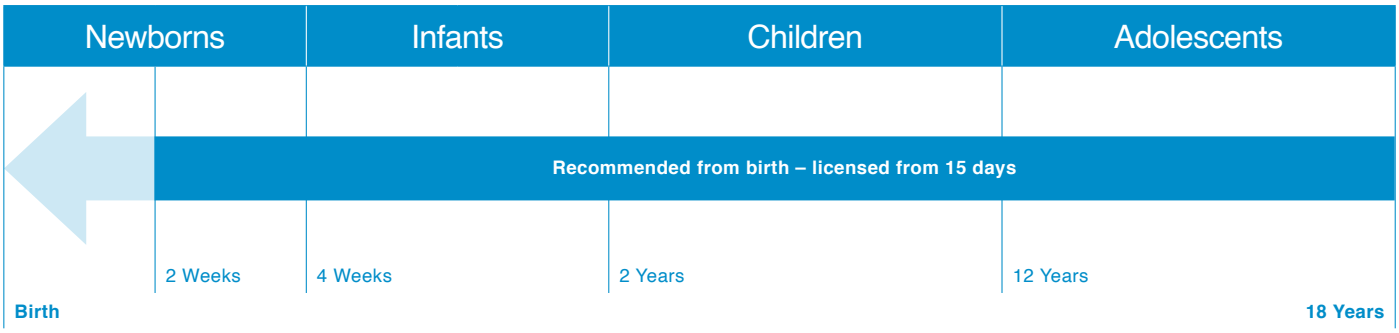
Nevirapine (NVP)

Available Formulations

Single-drug formulations	
	
Liquid formulation	Dispersible tablet (scored)
NVP 10 mg/mL	NVP 50 mg

Formulations for adults
NVP 200-mg immediate-release tablet NVP 400-mg extended-release tablet

WHO dose recommendation - age



Although the United States Food and Drug Administration and European Medicines Agency license NVP for children 15 days or older, WHO and the United States National Institutes of Health guidelines recommend using NVP from birth, including children born prematurely and children born with a low birth weight (Bekker 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
NVP	10 mg/mL	1.5 mL	1.5 mL	2 mL	2 mL	3 mL	3 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).

World Health Organization

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Child-friendly fixed-dose solid formulations for twice-daily dosing for infants and children four weeks and older

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
NVP	Tablet (dispersible) 50 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	200 mg	1	1
	Liquid 10 mg/mL	0.5	0.5	0.5	1	1	1	1	1.5	1.5	1.5	–	–	–

Rationale WHO dose selection

In the presence of replicating virus, a single mutation can select for high-level resistant virus to NVP, and several studies have found associations between low NVP concentrations and virological failure; therefore, achieving and maintaining therapeutic drug levels of NVP is crucial (Gopalan et al.). To unify dosing of all ARV drugs for children, initial WHO dosing guidance on NVP for children was changed from using body surface area to weight-band dosing. A modelling study based on combined NVP pharmacokinetic data from a range of studies involving children, demonstrated that WHO weight-band dosing would maintain adequate drug levels for most children, similar to the United States Food and Drug Administration dosing schedule based on body surface area (Nikanjam et al.).

Newborns and premature infants

NVP is recommended as prophylaxis to reduce the risk of acquiring HIV among newborns without documented HIV infection; as presumptive treatment for newborns who are at high risk of acquiring HIV; and as treatment for newborns with confirmed HIV infection. The target minimal plasma NVP concentration proposed for HIV prophylaxis is >0.1 mg/mL, whereas the pharmacokinetic target for HIV (presumptive) treatment is considered to be >3.0 mg/mL. Therefore, NVP dosages for prophylaxis are lower than HIV treatment dosages for Neonates (Mirochnick et al. and de Vries-Sluijs et al.).

The IMPAACT P1115 research group found that NVP presumptive treatment among newborns was safe and achieved therapeutic pharmacokinetic levels using the following dosing scheme: 6 mg/kg NVP twice daily for infants ≥37 weeks gestational age (GA) and 4 mg/kg twice daily for one week and 6 mg/kg twice daily thereafter for infants 34 to <37 weeks gestational age (Ruel et al.). No lead-in is required for newborns.

Important information

Lead-in requirement

Adults require a two-week lead-in dose of 50% of the therapeutic dose to avoid toxicity from high initial NVP levels, as is recommended for children. However, multiple studies found subtherapeutic NVP concentrations in a high proportion of children during the lead-in period (Gopalan et al. and Fillekes et al.). In addition, starting with the full dose did not translate to increased adverse events in these studies.

World Health Organization

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Phased out

In general, WHO recommends moving away from NVP-based ART and using more robust regimens for children.

Current ongoing trials involving children

Clinical trials on ClinicalTrials.gov

Knowledge gaps

None

Research priorities according to PADO4

None

Drug–drug interactions

NVP should not be used in combination with rifampicin-based TB treatment.

World Health Organization