

Zidovudine

Newborn use only

2020

Alert	Also known as azidothymidine (AZT). No Australian registered intravenous (IV) products are currently available. Retrovir IV ampoules are only available via the Special Access Scheme (SAS) in Australia.												
Indication	Monotherapy or part of a combination therapy for prevention of maternal-foetal HIV transmission.												
Action	Nucleoside analogue that inhibits HIV replication by interfering with viral reverse transcriptase.												
Drug type	Antiretroviral medication												
Trade name	Retrovir												
Presentation	Oral: syrup 10 mg/mL IV: 10 mg/mL in a 20mL single-use vial (SAS) Note: Retrovir is also available in oral capsules, however only the syrup is used in neonates.												
Dose	<p>Oral Start therapy within 4 hours of birth.</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: left;">Gestation at birth</th> <th style="text-align: left;">Dose</th> <th style="text-align: left;">Interval</th> </tr> </thead> <tbody> <tr> <td><30 weeks</td> <td>2 mg/kg</td> <td>12 hourly</td> </tr> <tr> <td>30⁺-33⁺6 weeks</td> <td>2 mg/kg</td> <td>12 hourly for 2 weeks and then 8 hourly</td> </tr> <tr> <td>≥34 weeks</td> <td>4 mg/kg</td> <td>12 hourly*</td> </tr> </tbody> </table> <p>*Dose can be rounded up to the nearest 0.5 mg to assist administration.</p> <p>Intravenous (If neonates are unable to take oral zidovudine) ≥34 weeks gestation – 1.5 mg/kg/dose 6 hourly <34 weeks gestation – 1.5 mg/kg/dose 12 hourly, change to 6 hourly at 34 weeks gestation. Switch to oral once the neonate is tolerating oral feeds.</p> <p>Total duration IV and / or oral dosing</p> <ul style="list-style-type: none"> • Very low risk monotherapy – 2 weeks • Low risk monotherapy – 4 weeks • High risk / combination therapy – 4 weeks 	Gestation at birth	Dose	Interval	<30 weeks	2 mg/kg	12 hourly	30 ⁺ -33 ⁺ 6 weeks	2 mg/kg	12 hourly for 2 weeks and then 8 hourly	≥34 weeks	4 mg/kg	12 hourly*
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Dose adjustment	Therapeutic hypothermia: no information. ECMO: no information. Renal: see monitoring and interactions. Hepatic: see monitoring and adverse reactions.												
Maximum dose													
Total cumulative dose													
Route	PO and IV												
Preparation	Oral: Syrup IV: Dilute in 5% glucose before IV administration to a concentration not exceeding 4 mg/mL. [1] A dilution of 4 mg/mL may be prepared by adding 4 mL of the 10 mg/mL concentration to 6 mL of 5% glucose.												
Administration	PO: Can be given without regard to food. IV: Administer IV infusion over 30 minutes - 1 hour.												
Monitoring	At base line and with modification of therapy full blood count, blood sugar level, liver function, renal function tests, viral load, CD4 counts should be obtained. The panel should be repeated within 2-4 weeks of commencement of therapy and then every 3-4 months. [2-4]												
Contraindications	Life-threatening hypersensitivity reactions (e.g., anaphylaxis, Stevens-Johnson syndrome) to zidovudine or any components of the formulations. [5] Zidovudine infusions should not be given to patients with abnormally low neutrophils or haemoglobin levels. [5]												
Precautions	Zidovudine injection vial stopper contains rubber latex which could cause hypersensitivity reaction in latex-allergic patients. There have been reports of pancytopenia associated with the use of zidovudine, which was reversible in most instances after discontinuance of the drug.												

Drug interactions	<p>Stavudine - zidovudine should not be administered in combination with stavudine because of in vitro virologic antagonism.</p> <p>Co-administration of zidovudine with drugs that are nephrotoxic, cytotoxic, or which interfere with red blood cell and white blood cell number or function (e.g. ganciclovir, amphotericin B or interferon) may increase the risk of toxicity. If concomitant therapy with any of these drugs is necessary then extra care should be taken in monitoring renal function and haematological parameters.</p> <p>Ribavirin antagonizes in vitro antiviral activity of zidovudine and so concomitant use should be avoided.</p> <p>Doxorubicin - simultaneous use of doxorubicin and zidovudine should be avoided. Doxorubicin may inhibit the phosphorylation of zidovudine to its active form.</p> <p>Phenytoin - phenytoin blood levels have been reported to be low in some patients receiving zidovudine. Monitor phenytoin levels if neonate is receiving both medications. [5]</p> <p>Clarithromycin - oral clarithromycin reduces the absorption of zidovudine. This can be avoided by separating the doses by at least 2 hours. [5]</p>
Adverse reactions	<p>Anaemia and neutropenia are common. Transient lactic acidemia, vomiting, headache, insomnia, hepatomegaly with hepatic steatosis, lipodystrophy, lipoatrophy, myopathy, cardiomyopathy and myositis. [6, 7] In most cases the adverse events are mild and self-limiting. Prolonged use increases the risk of adverse events.</p>
Compatibility	<p>Fluids: glucose 5%, sodium chloride 0.9%</p> <p>Y site: aciclovir, amikacin, amphotericin B, aztreonam, cefepime, ceftazidime, ceftriaxone, cimetidine, clindamycin, dexamethasone, dobutamine, dopamine, erythromycin lactobionate, fluconazole, gentamicin, heparin, imipenem, linezolid, lorazepam, metoclopramide, morphine, nafcillin, oxacillin, piperacillin, piperacillin-tazobactam, potassium chloride, ranitidine, remifentanyl, rocuronium, tobramycin, trimethoprim-sulfamethoxazole, and vancomycin.</p> <p>Note: This is not an exhaustive list. Please refer to the relevant resources eg. Micromedex, Australian Injectable Drugs Handbook for detailed information.</p>
Incompatibility	<p>Fluids: no information</p> <p>Y site: lansoprazole, meropenem</p>
Stability	<p>Vial: store below 30°C</p> <p>After dilution, the drug solution is stable for 24 hours if stored below 25°C or in refrigerator. Protect from light. [5]</p>
Storage	<p>Oral syrup and any unused vials are to be stored at room temperature and protected from light. Any remaining unused infusion preparations should be discarded. [5]</p>
Excipients	<p>Retrovir Oral Syrup: Each 5 mL contains zidovudine 50 mg, and glycerol, citric acid, sodium benzoate, saccharin sodium, maltitol solution, Flavour Strawberry 500286E, Flavour White Sugar 3112044, and water-purified.</p> <p>Retrovir IV vials: hydrochloric acid, sodium hydroxide, water for injection.</p>
Special comments	<p>Dosage adjustment is required in renal and hepatic impairment. Fixed drug combinations should be avoided in infants with renal and hepatic insufficiency.</p>
Evidence	<p>Refer to full version.</p>
Practice points	<p>Zidovudine is the recommended antiretroviral agent as either monotherapy or combination therapy for prevention of perinatal HIV transmission to neonates. The ANMF has adapted the 2018 British HIV Association guidelines for the management of HIV in pregnancy and postpartum 2018 and the categories used to determine the duration of therapy are defined as follows. [18, 19]</p> <p>Very low risk: 2 weeks of zidovudine monotherapy is recommended if (1) the woman has been on cART for longer than 10 weeks, AND (2) two documented maternal HIV viral loads <50 HIV RNA copies/mL during pregnancy at least 4 weeks apart, AND (3) Maternal HIV viral load <50 HIV RNA copies/mL at or after 36 weeks.</p> <p>Low risk: 4 weeks of zidovudine monotherapy if (1) the “very low risk criteria” are not all fulfilled but maternal HIV viral load is <50 HIV RNA copies/mL at or after 36 weeks, (2) if the infant is born prematurely (<34 weeks) but most recent maternal HIV viral load is <50 HIV RNA copies/mL.</p>

	High risk: Combination therapy if maternal birth HIV viral load is known to be or likely to be >50 HIV RNA copies/mL on day of birth, if uncertainty about recent maternal adherence or if viral load is not known.
References	Refer to full version.

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Authors Contribution

Original author/s	Dr Nilkant Phad, Dr Srinivas Bolisetty
Evidence Review	Assoc Prof David Osborn
Expert review	Dr Pamela Palasanthiran
Nursing Review	Ms Eszter Jozsa
Pharmacy Review	Ms Carmen Burman, Ms Cindy Chen, Ms Michelle Jenkins
ANMF Group contributors	Dr Himanshu Papat, Ms Carmen Burman, Ms Thao Tran, Dr John Sinn, Ms Emily Do, Ms Wendy Huynh
Final editing and review of the original	Assoc Prof David Osborn, Ms Michelle Jenkins, Dr Srinivas Bolisetty
Electronic version	Dr Ian Callander, Ms Cindy Chen
Facilitator	Dr Srinivas Bolisetty