ZIDOVUDINE - Azidothymidine

<table>
<tr><td>Trade Name</td><td>Retrovir (GlaxoSmithKlyne)</td></tr>
<tr><td>Class</td><td>Antiretroviral agent; reverse transcriptase inhibitor</td></tr>
<tr><td>Mechanism of Action</td><td>Active metabolite zidovudine triphosphate halts DNA synthesis of retroviruses including HIV, through competitive inhibition of reverse transcriptase and incorporation into viral DNA. Also active against Epstein-Barr virus and G-ve bacteria in vitro.</td></tr>
<tr><td>Indications</td><td>One of several measures to prevent transmission of HIV from mother to baby. Additional antiretrovirals may be required depending sensitivity of mother’s HIV, or if HIV is active. Cotrimoxazole also required – see comments.</td></tr>
<tr><td>Contraindications</td><td>Hypersensitivity</td></tr>
<tr><td>Supplied As</td><td>Oral syrup: 10mg/mL
Injection: 200mg/20mL (10mg/mL)</td></tr>
<tr><td>Dilution</td><td>IV:
<table>
<tr><th>Drug</th><th>0.9% Saline</th><th>Final Volume</th><th>Concentration</th></tr>
<tr><td>10mg (1mL)</td><td>9mL</td><td>10mL</td><td>1mg/mL</td></tr>
</table>
If the dose volume is <0.5mLthen will need to further dilute before infusing via the T34 pump (see T34 protocol)
Oral: Not required</td></tr>
<tr><td>Dosage</td><td>≥ 35 weeks: Oral: 4mg/kg/dose
IV: 1.5mg/kg/dose
< 35weeks: Oral: 2mg/kg/dose for 2 wks, then,
3mg/kg/dose for 2 wks
IV: 1.5mg/kg/dose
Started within 6 -12 hours of birth (choose 0800 and 2000 if possible)</td></tr>
<tr><td>Interval</td><td>Give oral and IV strictly to time:
Treat for a total of 2 - 4 weeks depending on risk profile as determined by the Neonatologist / Infectious Diseases Team
≥ 35 weeks: Oral: 12 hourly
IV: 6 hourly
< 35 weeks: Oral: 12 hourly
IV: 12 hourly</td></tr>
<tr><td>Administration</td><td>Oral: dose on empty stomach if possible
IV: infuse dose over 30 minutes</td></tr>
</table>

Compatible With	**Solution:** dextrose 5%, sodium chloride 0.9% (other strengths of dextrose and sodium chloride have not been tested) **Terminal Y-site:** aciclovir, amikacin, amiodarone, amphotericin, ceftazidime, ceftriaxone, clindamycin, dexamethasone, dexmedetomidine, dobutamine, dopamine, erythromycin, fluconazole, gentamicin, heparin, imipenem, metronidazole, milrinone, morphine sulphate, octreotide, pancuronium, phenylephrine, piperacillin, potassium chloride, ranitidine, tobramycin sulfamethoxazole+trimethoprim, vancomycin vasopressin, voriconazole
Incompatible With	Meropenem, blood, protein. There is no information available on compatibility of zidovudine with Smoflipid or Primene based TPN so recommend using separate line
Monitoring	Day 2 – FBC and differential and HIV Viral load RNA (see comments for lab information) 4 - 6 weeks – FBC and differential and HIV Viral load RNA 3 - 4 months – FBC and differential and HIV Viral Load RNA
Stability	Single use vial only Discard vial immediately after using
Storage	Room temperature. (Stock for expected cases is held in Birthing Suite)
Adverse Reactions	Anaemia and neutropenia are most common, early in treatment, discuss with paediatric infectious diseases specialist. Uncommon side effects include: weakness, fever, malaise, dizziness, headache, insomnia, myopathy, paraesthesia, stomach upset, rash, lactic acidosis, hepatomegaly, pancreatitis, convulsions, pigmentation of nails, skin and oral mucosa.
Metabolism	High first pass metabolism for oral zidovudine with bioavailability of ~70%. Primarily metabolised by hepatic glucuronidation/urinary excretion of the inactive metabolites; 14-29% excreted unchanged in urine.
Comments…	Course is for 2 to 4 weeks, after birth, for prevention of HIV in baby. Future treatment determined by clinical status, no breast-feeding and results of PCR. **HIV Viral load RNA** is taken from baby at 2 days, 4 - 6 weeks and 3 - 4 months. Fill 2 but preferably 3 full EDTA tubes. This test is done in Christchurch. The second one is at least 2 weeks after finishing the treatment If a decision is made to do **HIV Proviral DNA** tests – these are sent to Auckland. Take the blood on Mon-Wed before 1200 and put the 2 full EDTA tubes in a separate bag with a separate form.

… Comments	Some babies will require sulphamethoxazole+trimethoprim (cotrimoxazole) 120mg (0.5mL) three times a week for prophylaxis against PCP from 4-6 weeks of age, on recommendation of the ID specialist.(If HIV DNA positive in first week of life or the mother is immunosuppressed.) **Supply of Zidovudine Liquid** In most cases the supply of zidovudine liquid dispensed by the hospital pharmacy for treatment of the baby from birth will be sufficient to last the 4 weeks of treatment The following hyperlink provides access to the application form for special authority funding for funded supply of zidovudine liquid in the community if the supply dispensed from hospital needs to be replaced or the course is for some reason extended. https://schedule.pharmac.govt.nz/latest/SA1651.pdf
References	1. Parfitt K (Ed), Martindale The Extra Pharmacopoeia, 32nd edition, 1999 2. Amer Hosp Formulary Service Drug Information text, 1999 3. WHD protocol Management of Pregnant, HIV positive, women, 2002 4. Trissel LA, Handbook on Injectable Drugs, 11th Ed, 2001 and in www.micromedexsolutions.com 5. Neofax 13th Ed, 2000 and in www.micromedexsolutions.com 6. Benjamin DK, Miller WC et al. Rational testing of the HIV-exposed infant. Pediatrics 108(1):e3 7. Watts DH. Management of HIV infection in pregnancy. NEJM 2002, 346(24):1879-91 8. BHIVA Pregnancy management Guideline. HIV Medicine 2014;15(Suppl 4),1-77. 9. Fergusson, Goode et al. Evaluation of 4 week Neonatal Antiretroviral Prophylaxis. Paediatr infections Dis 3015: 408-12 May 2011 www.nzf.org 10. BHIVA-Pregnancy-guidelines-2020-3rd-i 11. QCH guideline HIV in pregnancy.pdf 12. Table of maternal risk profile and leng
Updated By	K Simonsen, N Austin A Lynn, B Robertshawe, F Robertson May 2009 (new pumps) A Lynn, B Robertshawe, N Austin June 2011 A Lynn, B Robertshawe Dec 2012 (re-order profile) A Lynn, B Robertshawe, N Austin, T Walls Oct 2017 (dosing, blood monitoring) A Lynn, B Robertshawe, N Austin, T Walls May 2022 (compatibility, monitoring, accessibility) A Lynn, B Robertshawe, N Austin, T Walls July 2022 (modification of duration of treatment)