

PARACETAMOL – For Patent Ductus Arteriosus

Trade Name	Paracetamol Kabi (Fresenius Kabi NZ)
Class	Antipyretic and analgesic.
Mechanism of Action	Patent ductus arteriosus: Potential mechanisms include inhibition of central prostaglandin synthesis and inhibition of the cyclooxygenase (COX) isoenzyme, particularly the COX-2 isoform.
Indications	<p>Haemodynamically significant patent ductus arteriosus</p> <ol style="list-style-type: none"> 1. Firstline management if there are contraindications to using indomethacin (the standard firstline treatment) 2. Secondline management after an indomethacin course if more indomethacin is undesirable 3. Use before 28 days of age 4. Limit to one course only ie: max of 6 days treatment
Contraindications	Hypersensitivity to paracetamol Hepatic failure G6PD deficiency can lead to haemolytic anaemia
Precautions	Caution in renal failure Caution with hepatocellular insufficiency Dehydration Clearance falls with unconjugated hyperbilirubinaemia
Supplied As	IV: 10 mg/mL in 100mL glass vials Oral: 120 mg/ 5 mL
Dilution	IV: Can be diluted in 0.9% saline and 5% dextrose if needed Oral: Nil
Dosage/Interval	15mg/kg/dose 6 hourly for 3-6 days Oral or IV but preference to give iv if access is possible
Administration	IV: Infusion over 15 minutes Oral: can be given anytime in regards to feeds
Intravenous Dose Compatible With ...	<p>Solution: Sodium chloride 0.9% and 5% & 10% dextrose</p> <p>Terminal Y-site:</p> <p>Cefazolin, cefoxitin, dexamethasone 10 mg/mL, dexmedetomidine, diphenhydramine 50 mg/mL, fentanyl 50 mcg/mL, gentamicin, heparin 100 units/mL, hydrocortisone 50 mg/mL, hydromorphone 4 mg/mL, ketorolac 15 mg/mL, labetalol, lactated Ringer solution, lidocaine 20 mg/mL, lorazepam 0.5 mg/mL, magnesium sulphate, mannitol 150 mg/mL (15%), methylprednisolone 125 mg/mL, methylprednisolone, metoclopramide 5 mg/mL, midazolam 5 mg/mL, morphine 15 mg/mL, nalbuphine 20 mg/mL, ondansetron 2 mg/mL, pentoxifylline, piperacillin/tazobactam, potassium chloride 0.1 mEq/mL, TPN, vancomycin.</p>

<p>... Intravenous Dose Incompatible With</p>	<p>Aciclovir, atropine, chlorpromazine, diazepam, metronidazole, phenobarbital, phenytoin, propofol.</p> <p>Information on compatibility of IV paracetamol with other medicines is relatively limited.</p> <p>There is no information on compatibility of paracetamol with alprostadil, amoxicillin, cefotaxime, dopamine, dobutamine, flucloxacillin, erythromycin, lipid or sildenafil. If any of these medicines are prescribed in combination with paracetamol it is recommended to use a separate line and consult pharmacist for further advice.</p>
<p>Interactions</p>	<p>Increased rate of metabolism of paracetamol when given in combination with carbamazepine, phenobarbital, phenytoin, rifampicin.</p> <p>Flucloxacillin + paracetamol may predispose to metabolic acidosis especially if patient has renal impairment</p> <p>Isoniazid + paracetamol may increase risk of formation of toxic paracetamol metabolites</p> <p>Zidovudine + paracetamol may increase risk of bone marrow suppression</p>
<p>Monitoring</p>	<p>Heart scan after 3 days to assess the PDA:</p> <ul style="list-style-type: none"> - If PDA is closed then stop the course - If PDA is open and needs ongoing treatment check LFT to ensure it is safe to continue with a 6 day course - No studies have measured trough levels so no routine levels are not required.
<p>Stability</p>	<p>IV: If diluted, administer within 30 minutes.</p> <p>Vials are preservative free and are for single use only.</p>
<p>Storage</p>	<p>IV: Do not store in the fridge Single use only</p> <p>Complete infusion within 1 hour of opening the vial</p>
<p>Adverse Reactions</p>	<p>Pain at injection site</p> <p>Rash, fever, bone marrow depression</p> <p>Beware of accumulation if used regularly</p> <p>Hepatotoxicity in neonates rare.</p> <p>Use with caution in hepatic or renal failure</p> <p>Overdose: hepatotoxicity, renal tubular acidosis, metabolic acidosis, encephalopathy. Monitor LFT and coag profile and treat with n-acetylcysteine</p>
<p>Metabolism</p>	<p>100% bioavailability.</p> <p>Metabolised in the liver by conjugation and metabolism by cytochrome P450. Excreted in the urine 90%</p>
<p>Comments</p>	<p>Licensed for use in term newborns.</p>

	<p>Safety and efficacy data have not been established on preterm infants</p> <p>See Neofax for treatment of serious overdose</p> <p>Probably works better when given as first line treatment for PDA but may be given after Indomethacin treatment has failed</p> <p>Comparable efficacy to indomethacin and ibuprofen and more favourable adverse effect profile</p>		
<p>References</p>	<ol style="list-style-type: none"> 1. Medsafe data sheet 2. *Princess Margaret Hospital Perth. Paracetamol protocol June 2008 3. Allegaert K et al. IV paracetamol pharmacokinetics in term + preterm infants. <i>European J Clin Pharm</i> 2004 60:191-7 4. Allegaert K et al. Pharmacokinetics of single dose iv propacetamol in neonates: effect of gestational age. <i>Arch Dis Fetal Neonatal Ed</i> 2004;89:F25-28. 5. Palmer GM et al. IV acetaminophen pharmacokinetics in neonates after multiple doses. <i>BJA</i> 2008;101:523-30. 6. Anderson BJ et al. Acetaminophen analgesia in children: placebo effect and pain resolution after tonsillectomy. <i>European J Clin Pharm</i> 2001;57:559-69. 7. Bartocci M, Lundeberg S. IV paracetamol: the "Stockholm protocol" for postoperative analgesia of term and preterm neonates. <i>Pediatr Anaesthesia</i> 2007;17, 111-21 8. Allegaert K et al. Not all iv paracetamol formulations are created equal... <i>Pediatr Anaesthesia</i> 2007;17, 809-18. 9. Anderson BJ, Allegaert K. IV neonatal paracetamol dosing: the magic of 10 days. <i>Pediatr Anaesthesia</i> 2009:289-95. 10. Jasani B et al. Evidence based use of acetaminophen for hemodynamically significant ductus arteriosus in preterm infants. <i>Seminars in perinatology</i>. 2018; Jun; 42(4): 243-252. 11. King Edward Memorial Hospital and Perth Children's Hospital Neonatology. Neonatal Paracetamol Guideline. Accessed 1.9.18 12. Royal hospital for Women, Sydney. Paracetamol Guideline. Accessed 1.9.18 13. Ohlsson A. Paracetamol (acetaminophen) for patent ductus arteriosus in preterm or low birth weight infants. <i>Cochrane Database Systemic Review</i>. 2018 April 6: 4. 14. Trissel IV compatibilities in www.micromedexsolution.com 15. Neofax in www.micromedexsolutions.com 		
<p>Updated By</p>	<table border="0" style="width: 100%;"> <tr> <td style="width: 50%; vertical-align: top;"> <p>A Lynn, R Sinclair, B Dixon A Lynn, M Wallenstein A Lynn, B Robertshawe and interactions)</p> </td> <td style="width: 50%; vertical-align: top;"> <p>Oct 2018 (new profile for PDA treatment) Jan 2021 – incompatibilities clearer March 2022 (- brand update, compatibilities)</p> </td> </tr> </table>	<p>A Lynn, R Sinclair, B Dixon A Lynn, M Wallenstein A Lynn, B Robertshawe and interactions)</p>	<p>Oct 2018 (new profile for PDA treatment) Jan 2021 – incompatibilities clearer March 2022 (- brand update, compatibilities)</p>
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