

PARACETAMOL – For Analgesia

Trade Name	Oral: Children’s Panadol, Paracetamol IV: Paracetamol Kabi (Fresenius Kabi NZ)			
Class	Antipyretic and analgesic			
Mechanism of Action	Inhibits prostaglandin synthesis within the CNS. Acts peripherally by blocking pain impulse generation. Relieves fever by central action in hypothalamic heat regulating centre.			
Indications	<p>Oral and Rectal:</p> <ol style="list-style-type: none"> 1. Fever 2. Mild to moderate pain <p>IV: (Change to oral or pr dosing as soon as possible)</p> <ol style="list-style-type: none"> 1. Postoperative pain where the oral and rectal routes are not possible or the onset of action from the rectal route is deemed to be too slow 2. As an adjunct to allow weaning of morphine 			
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	Oral: Liquid – 120mg/5mL, (250mg/5mL also available) Rectal: Suppository – 25mg, 50mg IV: 10mg/mL in 100mL glass vials			
Dilution	Oral and Rectal: Nil IV: can be diluted in 0.9% saline and 5% dextrose if needed			
Dosage Oral and Rectal ...	Corrected GA	< 32 weeks	32-36⁺⁶ weeks	≥ 37 weeks
	Oral	7.5mg/kg	10mg/kg	15mg/kg
	Rectal	7.5mg/kg	10mg/kg	15mg/kg
	Dosing rounded to the nearest half or full suppository size. Unable to dose accurately if <1kg so do not use pr	1-2kg 12.5mg	1-1.7kg 12.5 mg 1.8-2.9 25 mg ≥3kg 37.5 mg	<2kg 25 mg 2-2.9 37.5mg 3-3.9 50 mg 4-4.9 62.5mg ≥5kg 75 mg
If a baby does not fit this rectal dosing matrix due to extreme weight differences for GA, calculate a dose with appropriate rounding as above				

... Dosage Intravenous	IV Loading dose	15mg/kg	15mg/kg	15mg/kg
	IV Maintenance dose	7.5mg/kg	10mg/kg	10 mg/kg
Review IV dosing after <u>5 days</u> and if to continue check <u>LFTs</u> . Trough paracetamol levels are not routinely needed. Change to oral or rectal dosing as soon as possible				
Interval	6 hourly			
Administration	<p>Oral: Liquid</p> <p>Rectal: Suppository If half of the suppository is required, cut it lengthwise through the tip. In babies < 1 kg the rectal dose will be less than half a 25mg suppository so dosing is too inaccurate to use the rectal route</p> <p>IV: Infusion over 15 minutes</p>			
Intravenous Dose Compatible With	<p>Solution: Sodium chloride 0.9% and 5% & 10% dextrose</p> <p>Terminal Y-site: 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>			
Intravenous Dose Incompatible With	<p>Aciclovir, atropine, chlorpromazine, diazepam, metronidazole, phenobarbital, phenytoin, propofol.</p> <p>Information on compatibility of IV paracetamol with other medicines is relatively limited. 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>			
Interactions	Increased rate of metabolism of paracetamol when given in combination with carbamazepine, phenobarbital, phenytoin, rifampicin.			

	<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>
Monitoring	<p>IV:</p> <p>Review IV dosing after 5 days and if continuing check LFTs</p> <p>Trough paracetamol levels are not routinely needed but if there are any concerns about toxicity then the trough level for analgesia to target is < 60 micromol/L* (equates to 10mg/L)</p>
Stability	<p>Oral and Rectal: Months</p> <p>IV: If diluted, administer within 30 minutes.</p> <p>Vials are preservative free and are for single use only.</p>
Storage	<p>Oral and Rectal: Store at room temperature</p> <p>IV: Do not store in the fridge, store at room temperature</p> <p>Single use only. Complete IV infusion within 1 hr of opening the vial</p>
Adverse Reactions	<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>
Metabolism	<p>Oral: Peak serum concentration occurs approximately 60 min after an oral dose. First-pass hepatic metabolism 10-40% of oral dose. Most metabolised in the liver, primarily by sulphation and excreted in the urine. Half life 5hrs in infants over 32 wks, up to 11 hrs in more immature infants.</p> <p>IV: 100% bioavailability.</p> <p>Onset of pain relief within 5-10 mins, peak effect at 1 hour</p> <p>Metabolised in the liver by conjugation and metabolism by cytochrome P450. Excreted in the urine 90%</p> <p>Rectal: Absorption is slower and more variable.</p>
Comments	<p>IV: 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>References</p>	<ol style="list-style-type: none"> 1. Treatment with paracetamol in infants. <i>Acta Anaesthesiologica Scandinavica</i> 2001; 45: 20-29 2. Medsafe data sheet 3. *Princess Margaret Hospital Perth. Paracetamol protocol June 2008 4. Allegaert K et al. IV paracetamol pharmacokinetics in term + preterm infants. <i>European J Clin Pharm</i> 2004 60:191-7 5. Allegaert K et al. Pharmacokinetics of single dose iv propacetamol in neonates: effect of GA. <i>Arch Dis Fetal Neonatal Ed</i> 2004;89:F25-28. 6. Palmer GM et al. IV acetaminophen pharmacokinetics in neonates after multiple doses. <i>BJA</i> 2008;101:523-30. 7. 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. 8. 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 9. Allegaert K et al. Not all iv paracetamol formulations are created equal... <i>Pediatr Anaesthesia</i> 2007;17, 809-18. 10. Anderson BJ, Allegaert K. IV neonatal paracetamol dosing: the magic of 10 days. <i>Pediatr Anaesthesia</i> 2009:289-95. 11. 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. 12. King Edward Memorial Hospital and Perth Children's Hospital Neonatology. Neonatal Paracetamol Guideline. Accessed 1.9.18 13. Royal hospital for Women, Sydney. Paracetamol Guideline. Accessed 1.9.18 14. 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.
<p>Updated By</p>	<p>J McKie November 2001 P Schmidt & B Robertshawe January 2005 A Lynn, B Robertshawe June 2010 A Lynn, B Robertshawe Nov 2012 (re-order profile) A Lynn June 2014 (decrease GA to 28 weeks) A Lynn, B Dixon 2018 (combined PO,PR,IV, decreased GA, new PDA drug profile) A Lynn, M Wallenstein Jan 2021 – incompatibilities made clearer A Lynn, B Robertshawe March 2022 (brand update, compatibilities and interactions, simplify dosing and intervals, add in <32 week dosing)</p>