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	**Oral:** 1. Fever 2. Mild to moderate pain **IV: (Change to oral dosing as soon as possible)** 1. Postoperative pain where the oral route is not possible 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) **IV**:10mg/mL in 100mL glass vials
Dilution	Oral: Nil IV: can be diluted in 0.9% saline and 5% dextrose if needed
Dosage	<table><tr><th colspan="2">Corrected GA</th><th>< 32 weeks</th><th>32-36+6 weeks</th><th>≥ 37 weeks</th></tr><tr><td colspan="2">Oral</td><td>7.5mg/kg</td><td>10mg/kg</td><td>15mg/kg</td></tr><tr><td rowspan="2">IV</td><td>Loading Dose</td><td>15mg/kg</td><td>15mg/kg</td><td>15mg/kg</td></tr><tr><td>Maintenance Dose</td><td>7.5mg/kg</td><td>10mg/kg</td><td>10 mg/kg</td></tr></table> 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 dosing as soon as possible
Interval	6 hourly
Administration	**Oral:** Liquid **IV**: Infusion over 15 minutes

Intravenous Dose Compatible With	**Solution:** Sodium chloride 0.9% and 5% & 10% dextrose **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.
Intravenous Dose Incompatible With	Aciclovir, atropine, chlorpromazine, diazepam, metronidazole, phenobarbital, phenytoin, propofol. 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.
Interactions	Increased rate of metabolism of paracetamol when given in combination with carbamazepine, phenobarbital, phenytoin, rifampicin. Flucloxacillin + paracetamol may predispose to metabolic acidosis especially if patient has renal impairment Isoniazid + paracetamol may increase risk of formation of toxic paracetamol metabolites Zidovudine + paracetamol may increase risk of bone marrow suppression
Monitoring	**IV:** Review IV dosing after 5 days and if continuing check LFTs 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)
Stability	**Oral:** Months **IV:** If diluted, administer within 30 minutes. Vials are preservative free and are for single use only.
Storage	**Oral:** Store at room temperature **IV:** Do not store in the fridge, store at room temperature Single use only. Complete IV infusion within 1 hr of opening the vial

Adverse Reactions	Pain at injection site Rash, fever, bone marrow depression Beware of accumulation if used regularly Hepatotoxicity in neonates rare. Use with caution in hepatic or renal failure **Overdose:** hepatotoxicity, renal tubular acidosis, metabolic acidosis, encephalopathy. Monitor LFT and coag profile and treat with n-acetylcysteine
Metabolism	**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. **IV:** 100% bioavailability. Onset of pain relief within 5-10 mins, peak effect at 1 hour Metabolised in the liver by conjugation and metabolism by cytochrome P450. Excreted in the urine 90%
Comments	**IV:** Licensed for use in term newborns. Safety and efficacy data have not been established on preterm infants See Neofax for treatment of serious overdose Rectal paracetamol suppositories (25mg and 50mg) not available in 2023 and so rectal route is no longer an option
References	1. Treatment with paracetamol in infants. Acta Anaesthesiologica Scandinavica 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. *European J Clin Pharm* 2004 60:191-7 5. Allegaert K et al. Pharmacokinetics of single dose iv propacetamol in neonates: effect of GA. *Arch Dis Fetal Neonatal Ed* 2004;89:F25-28. 6. Palmer GM et al.IV acetaminophen pharmacokinetics in neonates after multiple doses. *BJA* 2008;101:523-30. *7.* Anderson BJ et al. Acetaminophen analgesia in children: placebo effect and pain resolution after tonsillectomy. *European J Clin Pharm 2001;57:559-69.* 8. Bartocci M, Lundeberg S. IV paracetamol: the “Stockholm protocol” for postoperative analgesia of term and preterm neonates. *Pediatr Anaesthesia* 2007:17, 111-21 9. Allegaert K et al. Not al iv paracetamol formulations are created equal… *Pediatr Anaesthesia* 2007:17, 809-18. 10. Anderson BJ, Allegaert K. IV neonatal paracetamol dosing: the magic of 10 days. *Pediatr Anasethesia* 2009:289-95. 11. Jasani B et al. Evidence based use of acetaminophen for hemodynamically significant ductus arteriosus in preterm infants. *Seminars in perinatology*. 2018: Jun; 42(4): 243-252. 12. King Edward Memorial Hospital and Perth Chidlren’s Hospital Neonatalogy. Neonatal Paracetamol Guidline. Accessed 1.9.18 13. Royal hospital for Women, Sydney. Paracetamol Guidline. Accessed 1.9.18 14. Ohlsson A. Paracetamol (acetaminophen) for patent ductus arteriosus in preterm or low birth weight infants. *Cochrane Database Systemic Review.* 2018 April 6: 4.

Updated By	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) A Lynn, B Robertshawe June 2023 (remove rectal route as an option)