Pantoprazole
Newborn use only

2021

Alert	Short- and long-term safety data in infants are limited. The bioavailability of the in-house pharmacy suspension made from the contents of the capsule may be up to 25% less than that of the capsule itself. Dose may need to be adjusted if no clinical response.
Indication	Treatment of gastroesophageal reflux disease (GORD) Post-operative prophylaxis in congenital tracheoesophageal fistula and oesophageal atresia (role unclear)
Action	Bind to the hydrogen/potassium ATPase enzyme system (proton pump), inhibiting both stimulated and basal acid secretion.
Drug type	Proton pump inhibitor
Trade name	IV: Pantoprazole Sandoz 40 mg Powder for Injection, Pantoprazole Sun Powder for injection, Somac Injection (Powder for injection). ORAL: Multiple brands available. Refer to presentation section.
Presentation	IV: 40 mg/vial of pantoprazole in dry powder form. Oral: 2 mg/mL dispersion (compounded by Pharmacy) Australian Pharmaceutical Formulary Handbook formula.
Dose	IV 0.5 mg/kg/dose 12 hourly Oral: 0.6–1.2 mg/kg/dose daily
Dose adjustment	Therapeutic hypothermia – No information. ECMO – No information. Renal impairment – No adjustment is required. Hepatic impairment – No dose adjustment is required.
Maximum dose	
Total cumulative dose	
Route	IV, oral
Preparation	**IV infusion**: Add 10 mL of sodium chloride 0.9% to 40 mg powder to make a volume of 10 mL with a concentration of 4 mg/mL. Draw up 1 mL (4 mg) of pantoprazole and add 9 mL of sodium chloride 0.9% to make a final volume of 10 mL with a concentration of 0.4 mg/mL. **IV bolus**: Add 10 mL of sodium chloride 0.9% to 40 mg powder for reconstitution to make a volume of 10 mL with a concentration of 4 mg/mL
Administration	IV: IV infusion — over 15 min IV bolus — over at least 2 minutes. Oral: Give ½ hour before feed. Shake well before use.
Monitoring	Serum magnesium periodically during prolonged therapy. Consider transaminase levels
Contraindications	Liver disease.
Precautions	Short- and long-term safety data in infants are limited but there have been several safety concerns with long term usage in adults. Current FDA's maximum recommended duration of therapy of PPIs is up to 8 weeks.
Drug interactions	Concurrent use of ketoconazole may result in decreased ketoconazole exposure. Concurrent use of ampicillin may result in loss of ampicillin efficacy.
Adverse reactions	Limited data available, though appears well tolerated and to have few side effects. Uncommon reports of nausea, vomiting and skin rash. Reported adverse events in adults: Abdominal pain (3%), diarrhea (4%), flatulence (4%) Neurologic: Headache (5%) Atrophic gastritis, *Clostridium difficile* diarrhea Haematological: thrombocytopenia (less than 1%) Immunological: Stevens-Johnson syndrome, toxic epidermal necrolysis Musculoskeletal: fracture of bone, osteoporosis-related hip fracture, rhabdomyolysis Renal: Interstitial nephritis, acute
Compatibility	**Fluids** (14-15): Glucose 5%, glucose 10% (Somac only), sodium chloride 0.9%.

	Y site (14-15): Acetazolamide, alprostadil, aminophylline, amoxicillin-clavulanate, amphotericin B lipid complex, amphotericin B liposome, ampicillin, azithromycin, ceftriaxone, doxycycline, fluorouracil, fosphenytoin, ganciclovir, imipenem-cilastatin, penicillin G, pentobarbital, piperacillin, potassium chloride, procainamide, succinylcholine, theophylline, ticarcillin, ticarcillin-clavulanate, vasopressin, zidovudine. **Variable compatibility:** Aciclovir, amikacin, amiodarone, calcium gluconate, cefazolin, cefoxitin, ceftazidime, cefuroxime, clindamycin, cloxacillin, digoxin, dopamine, enalaprilat, epinephrine, furosemide, gentamicin, heparin, hydrocortisone sodium succinate, insulin, magnesium sulfate, midazolam, morphine, nitroglycerin, nitroprusside, norepinephrine, octreotide, phenobarbital, piperacillin-tazobactam, sodium bicarbonate, sulfamethoxazole-trimethoprim, thiopental, tobramycin, vancomycin
Incompatibility	Fluids: Amino acid solutions and lipid emulsions.(extrapolated from TPN 3:1 solutions compatibility data)(14) Y site (14): Amphotericin B conventional colloidal, atenolol, atracurium, atropine, caffeine citrate, calcium acetate, calcium chloride, cefepime, cefotaxime, ciprofloxacin, dexamethasone, dexmedetomidine, diazepam, dobutamine, ephedrine, fentanyl, fluconazole, glycopyrrolate, hydralazine, indometacin, labetalol, lidocaine, linezolid, meropenem, methylprednisolone, metronidazole, milrinone, naloxone, pancuronium, phenytoin, potassium acetate, potassium phosphates, propranolol, ranitidine, remifentanil, rocuronium, salbutamol, sodium acetate, sodium phosphates, vecuronium, verapamil.
Stability	IV: Somac Injection: Use as soon as practicable after reconstitution/preparation. If storage is necessary, hold at 2°C-8°C for not more than 12 hours. Pantoprazole Sun Powder: The reconstituted solution should be stored at 2°C to 8°C for not more than 12 hours. No information on Pantoprazole Sandoz 40 mg Powder for injection. Oral: As per the Australian Pharmaceutical Formulary handbook recommendation.
Storage	IV: Store below 25°C. Protect from light. Oral: As per the Australian Pharmaceutical Formulary handbook recommendation.
Excipients	Somac Injection: 1 mg disodium edetate and 0.24 mg sodium hydroxide. Pantoprazole Sandoz and Sun Powder for Injection do not contain any excipients. Multiple tablet brands available, Somac granules: check individual Product Information for list of excipients.
Special comments	Bioavailability of oral dispersion is approximately 75% of intact capsule.
Evidence	**Treatment of gastroesophageal reflux disease (GORD)** NICE Guidelines(1) 1. Do not offer acid-suppressing drugs, such as proton pump inhibitors (PPIs) or H_2 receptor antagonists (H_2RAs), to treat overt regurgitation in infants and children occurring as an isolated symptom. 2. Consider a 4-week trial of a PPI or H_2RA for those who are unable to tell you about their symptoms (for example, infants and young children and those with a neurodisability associated with expressive communication difficulties) who have overt regurgitation with 1 or more of the following: unexplained feeding difficulties (for example, refusing feeds, gagging or choking), distressed behaviour, faltering growth. 3. Consider a 4-week trial of a PPI or H_2RA for children and young people with persistent heartburn, retrosternal or epigastric pain. 4. Assess the response to the 4-week trial of the PPI or H_2RA, and consider referral to a specialist for possible endoscopy if the symptoms: do not resolve or recur after stopping the treatment. 5. When choosing between PPIs and H_2RAs, take into account: The availability of age-appropriate preparations, the preference of the parent (or carer), child or young person (as appropriate) and local procurement costs. 6. Offer PPI or H_2RA treatment to infants, children and young people with endoscopy-proven reflux oesophagitis, and consider repeat endoscopic examinations as necessary to guide subsequent treatment. 7. Do not offer metoclopramide, domperidone or erythromycin to treat GOR or GORD without seeking specialist advice and taking into account their potential to cause adverse events. ESPGHAN and NASPGHAN Guidelines(2) For healing of erosive esophagitis and relief of GERD symptoms, PPIs are superior to H_2RAs. Both medications are superior to placebo. Administration of long-term acid suppression without a diagnosis is

	inadvisable. When acid suppression is required, the smallest effective dose should be used. Most patients require only once-daily PPI; routine use of twice-daily dose is not indicated. No PPI has been approved for use in infants < 1 year of age and there are special concerns pertaining to prescription of PPIs in infants, as described in the Guideline. H_2RAs exhibit tachyphylaxis or tolerance but PPIs do not. Tachyphylaxis is a drawback to chronic use. H_2RAs have a rapid onset of action and, like buffering agents, are useful for on-demand treatment. **Post-operative prophylaxis in congenital oesophageal atresia and tracheoesophageal fistula** In a systematic review by Shawyer et al(3) of 25 studies (1,663 patients for analysis), most were single centre studies (92 %) and retrospective (76 %); there were no randomised control trials. The quality of literature regarding anti-reflux medication for GER post EA-TEF repair is poor. **Pharmacokinetics** Kierkus et al, studied the pharmacodynamics and safety of oral pantoprazole in neonates, preterm infants and infants in two open-label studies. Neonates and preterm infants (study 1, 1.2 mg/kg [high dose]) and infants 1 through 11 months (study 2,0.6 [low dose] or 1.2 mg/kg [high dose]) received once-daily pantoprazole. Treatment was administered for ≤6 weeks. In studies 1 and 2, 21 and 24 patients, respectively. The high dose improved pH-metry parameters significantly: mean gastric pH and percent time gastric pH>4 increased, and refluxate pH increased. Ward et al, in a multicentre, randomised, open label trial, assessed the PK of pantoprazole granules after single and multiple doses in 40 neonates and preterm infants. Pantoprazole plasma concentration values were highly variable after single and multiple doses. They found in preterm infants and neonates, pantoprazole granules for oral suspension were generally safe and well tolerated. Mean exposures with the pantoprazole 2.5 mg dose were slightly higher than those in older children and adults who received 40 mg and, while the half-life was longer, there was no evidence of accumulation following repeated dose administration.
Practice points	
References	1. NICE Guideline 2015. Gastro-oesophageal reflux disease in children and young people: diagnosis and management. Published: 14 January 2015. nice.org.uk/guidance/ng1. 2. Vandenplas Y, Rudolph CD, Di Lorenzo C, Hassall E,Liptak G, Mazur L, Sondheimer J, Staiano,A, et al. Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society of Pediatric Gastroenterology, Hepatology, and Nutrition. 3. Shawyer AC, D'Souza J, Pemberton J, Flageole H. The management of postoperative reflux in congenital esophageal atresia-tracheoesophageal fistula: a systematic review. Pediatr Surg Int [Internet]. 2014 [cited 2014 Oct];30(10):987-96. In: Ovid MEDLINE(R) [Internet]. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=25011995. 4. TigheM, AfzalNA, BevanA,HayenA,MunroA, Beattie RM. Pharmacological treatment of children with gastro-oesophageal reflux. Cochrane Database of Systematic Reviews 2014, Issue 11. Art. No.: CD008550. DOI: 10.1002/14651858.CD008550.pub2. 5. Freedberg DE, Lamouse-Smith ES, Lightdale JR, Jin Z, Yang YX, Abrams JA. Use of Acid Suppression Medication is Associated With Risk for C. difficile Infection in Infants and Children: A Population-based Study. Clin Infect Dis [Internet]. 2015 [cited 2015 Sep 15];61(6):912-7. In: Ovid MEDLINE(R) [Internet]. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=26060292 6. Jimenez J, Drees M, Loveridge-Lenza B, Eppes S, delRosario F. Exposure to Gastric Acid-Suppression Therapy Is Associated With Health Care- and Community-Associated Clostridium difficile Infection in Children. J Pediatr Gastroenterol Nutr [Internet]. 2015 [cited 2015 Aug];61(2):208-11. In: Ovid MEDLINE(R) [Internet]. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=25806678 7. Cohen S, Bueno de Mesquita M, Mimouni FB. Adverse effects reported in the use of gastroesophageal reflux disease treatments in children: a 10 years literature review. Br J Clin Pharmacol [Internet]. 2015 [cited 2015 Aug];80(2):200-8. In: Ovid MEDLINE(R) [Internet]. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=25752807 8. Wheatley E, Kennedy KA. Cross-over trial of treatment for bradycardia attributed to gastroesophageal reflux in preterm infants. J Pediatr [Internet]. 2009 [cited 2009 Oct];155(4):516-21. In: Ovid MEDLINE(R) [Internet]. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med5&NEWS=N&AN=19540518.

9. Canani RB, Cirillo P, Roggero P, Romano C, Malamisura B, Terrin G, Passariello A, Manguso F, Morelli L, Guarino A, Working Group on Intestinal Infections of the Italian Society of Pediatric Gastroenterology, Hepatology and Nutrition (SIGENP). Therapy with gastric acidity inhibitors increases the risk of acute gastroenteritis and community-acquired pneumonia in children. Pediatrics [Internet]. 2006 [cited 2006 May];117(5):e817-20. In: Ovid MEDLINE(R) [Internet]. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med5&NEWS=N&AN=16651285.
10. Saiman L, Ludington E, Dawson JD, et al. Risk factors for Candida species colonization of neonatal intensive care unit patients. Pediatr Infect Dis J 2001;20:1119–24.
11. More K, Athalye-Jape G, Rao S, Patole S.Association of inhibitors of gastric acid secretion and higher incidence of necrotizing enterocolitis in preterm very low-birth-weight infants. Am J Perinatol. 2013 Nov;30(10):849-56.
12. Kierkus J, Furmaga-Jablonska W, Sullivan JE, et al. Pharmacodynamics and safety of pantoprazole in neonates, preterm infants, and infants aged 1 through 11 months with a clinical diagnosis of gastroesophageal reflux disease. Dig Dis Sci. 2011 Feb;56(2):425-34. doi: 10.1007/s10620-010-1321-3. Epub 2010 Jul 7.
13. Ward RM, Kearns GL. Proton Pump Inhibitors in Pediatrics. Mechanism of Action, Pharmacokinetics, Pharmacogenetics, and Pharmacodynamics. Pediatr Drugs (2013) 15:119–131. DOI 10.1007/s40272-013-0012-x.
14. Micromedex solutions. Pantoprazole. Accessed on 24 March 2021.
15. Australian Injectable Drugs Handbook. Pantoprazole. Accessed on 24 March 2021.

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