

Newborn Use Only

Pantoprazole

2016

Alert	Short- and long-term safety data in infants are limited but there have been several safety concerns with long term usage in adults. The bioavailability of the in-house pharmacy suspension made from the contents of the capsule may be less (up to 25% less) than that of the tablet 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	Proton pump inhibitor (PPI).
Drug Type	Proton pump inhibitor
Trade Name	Pantoprazole Sandoz 40 mg Powder for Injection (Sandoz), Somac Injection (Powder for injection) (Takeda Pharmaceuticals)
Presentation	IV: 40 mg/vial of pantoprazole in dry powder form. PO: 2 mg/mL dispersion (compounded by Pharmacy) Australia Pharmaceutical Formulary and Handbook formula
Dosage / Interval	IV 0.5 mg/kg/dose 12 hourly PO: 0.6–1.2 mg/kg/dose daily
Maximum daily dose	
Route	IV, PO
Preparation/Dilution	A) IV infusion option: 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. Draw up 1 mL (4 mg) 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. B) IV push option: 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 push — over at least 2 minutes. PO: 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, <i>Clostridium difficile</i> 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: Glucose 5%, glucose 10%, sodium chloride 0.9%. Y site: Acetazolamide, alprostadil, aminophylline, amoxicillin sodium-clavulanate,

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	amphotericin B phospholipid complex, amphotericin B liposomal, ampicillin, azithromycin, ceftriaxone, ganciclovir, imipenem-cilastatin, penicillin G, piperacillin, potassium chloride, theophylline, ticarcillin disodium, ticarcillin disodium-clavulanate, vasopressin, zidovudine.
Incompatibility	Fluids: Amino acid solutions and lipid emulsions. Y site: Atenolol, atracurium, atropine, caffeine citrate, calcium chloride, cefotaxime, dexamethasone, diazepam, dobutamine, ephedrine, fentanyl, fluconazole, hydralazine, indometacin, labetalol, lidocaine, meropenem, methylprednisolone, metronidazole, midazolam, milrinone, naloxone, pancuronium, phenytoin, propranolol, ranitidine, rocuronium, vecuronium
Stability	IV: Reconstituted solution is stable for 24 hours at 2 to 8°C. Diluted solutions must be used within 12 hours of preparation. Oral: 28 days shelf-life from date of manufacture.
Storage	IV: Store below 25°C. Protect from light. Oral: Store at 2–8°C. Protect from light.
Special Comments	Bioavailability of oral dispersion is approximately 75% of intact tablets.
Evidence summary	<p><u>Treatment of gastroesophageal reflux disease (GORD)</u></p> <p><u>NICE Guidelines¹</u></p> <ol style="list-style-type: none"> 1. Do not offer acid-suppressing drugs, such as proton pump inhibitors (PPIs) or H₂ receptor antagonists (H₂RAs), to treat overt regurgitation in infants and children occurring as an isolated symptom. 2. Consider a 4-week trial of a PPI or H₂RA 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 H₂RA 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 H₂RA, 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 H₂RAs, 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 H₂RA 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. <p><u>ESPGHAN and NASPGHAN Guidelines²</u></p> <p>For healing of erosive esophagitis and relief of GERD symptoms, PPIs are superior to H₂RAs. 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.</p> <p>H₂RAs exhibit tachyphylaxis or tolerance but PPIs do not. Tachyphylaxis is a drawback to chronic use. H₂RAs have a rapid onset of action and, like buffering agents, are useful for on-demand treatment.</p>

	<p>Post-operative prophylaxis in congenital oesophageal atresia and tracheoesophageal fistula</p> <p>In a systematic review by Shawyer et al,³ of 25 articles (1,663 patients for analysis), most were single center 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.</p> <p>Kierkus et al, studied the pharmacodynamics and safety of oral pantoprazole in neonates, preterm infants and infants aged 1 through 11 month. 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. Twentyfour- hour dual-electrode pH-metry parameters were compared between predose and steady state (C5 days) (two-sided, paired t test). Treatment was administered for ≤6 weeks. In studies 1 and 2, 21 and 24 patients, respectively, were enrolled for pharmacodynamic evaluation. The high dose provided similar responses in the two studies and improved these parameters significantly: mean gastric pH and percent time gastric pH>4 increased (p<0.05 both studies), normalized area under the curve (AUC) of gastric H+ activity decreased (p<0.05 study 2), and normalized AUC of esophageal H+ activity decreased (p<0.05 both studies). The AUC of esophageal pH<4 decreased. Normalized AUC of esophageal H+ activity decreased (p<0.05 both studies), indicating refluxate pH increased, although this was not reflected in any change in mean esophageal pH or reflux index. The normalized AUC of esophageal H+ activity was a more sensitive measure of changes in esophageal pH.</p> <p>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. Pantoprazole is primarily metabolized by the CYP2C19 enzyme and to a limited extent by CYP3A4. As such, pantoprazole PK would be expected to vary with the expression of these enzymes. These enzymes are not completely developed at birth and appear to be activated by a mechanism associated with birth that is independent of gestational age. In conclusion, they reported, 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.</p>
<p>References</p>	<ol style="list-style-type: none"> 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. <i>Pediatr Surg Int</i> [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. Tighe M, Afzal NA, Bevan A, Hayen A, Munro A, Beattie RM. Pharmacological treatment of children with gastro-oesophageal reflux. <i>Cochrane Database of Systematic Reviews</i> 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 <i>C. difficile</i> Infection in Infants and Children: A Population-based Study. <i>Clin Infect Dis</i> [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 <i>Clostridium difficile</i> Infection in Children. <i>J Pediatr Gastroenterol Nutr</i> [Internet]. 2015 [cited 2015 Aug];61(2):208-11. In: Ovid MEDLINE(R) [Internet].

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