Omeprazole
Newborn use only

2021

Alert	Short and long-term safety data in infants are limited.
Indication	Treatment of gastroesophageal reflux disease (GORD). Prophylaxis in congenital tracheoesophageal fistula and oesophageal atresia (role unclear).
Action	Proton pump inhibitor (PPI). Bind to the hydrogen/potassium ATPase enzyme system (proton pump), inhibiting both stimulated and basal acid secretion.
Drug Type	Proton Pump Inhibitor.
Trade Name	Oral tablet: Multiple brands available. Oral capsule: Multiple brands available. IV: Omeprazole Sandoz Powder for Injection.
Presentation	Oral: Available in 10mg and 20 mg. Available in capsules or enteric coated tablets. Oral suspension of 2 mg/mL, 5mg/mL or other strengths may be prepared in pharmacy. IV: 40mg/vial of Omeprazole in dry powder form.
Dose	PO: 1-2.5 mg/kg/day in 1 to 2 divided doses.(1,2) IV: 0.5 mg/kg/dose 12-24 hourly (3,4,5,6)
Dose adjustment	Therapeutic hypothermia – No information. ECMO – No information. Renal impairment – No dose adjustment is required. Hepatic impairment – Dose reduction is recommended. However, no specific information available.
Maximum daily dose	2.5 mg/kg/day (1)
Total cumulative dose	
Route	PO, IV
Preparation	**PO:** 2 mg/mL oral suspension (prepared by hospital pharmacy). **IV:** Add 10 mL of sodium chloride 0.9% to 40 mg powder for reconstitution to make 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.
Administration	PO: Administer prior to meals. Shake the bottle well before administration. IV: Infuse over 30 minutes.
Monitoring	Serum magnesium, in patients on prolonged therapy or who use digoxin or drugs that may cause hypomagnesaemia (e.g. diuretics) concomitantly. Serum vitamin B_{12} — every 1 to 2 years in patients on prolonged therapy.
Contraindications	Hypersensitivity to any component of the product.
Precautions	Short- and long-term safety data in infants are limited. There have been 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 fluconazole may result in increased plasma concentrations of omeprazole. Concurrent use of iron may result in reduced non-heme iron bioavailability. Omeprazole is mainly metabolised via hepatic cytochrome P450 system (CYP2C19) and may be expected to interact with the metabolism of other drugs metabolised by this enzyme. Omeprazole may reduce phenytoin clearance – monitor phenytoin levels. Omeprazole produces a profound and sustained inhibition of gastric acid secretion. The absorption of compounds whose absorption depends on gastric pH (e.g. ketoconazole, itraconazole, erlotinib etc.) may decrease and the absorption of drugs such as digoxin can increase during treatment with omeprazole. Monitor digoxin levels.
Adverse Reactions	Increased risk of neonatal intestinal and pulmonary infections. Hypomagnesaemia.
Compatibility	Fluids: Glucose 5%, sodium chloride 0.9% Y-site: Cisatracurium, Furosemide, Morphine sulfate, Temocillin
Incompatibility	Oral: No information. IV: Haloperidol, Lorazepam, midazolam, tacrolimus, tigecycline, vancomycin.
Stability	Oral: Suspension is stable for 30 to 60 days or as per product label. (16) Refrigerate. Protect from light. IV reconstituted solution and diluted solution: Stable for 6 hours below 25°C. Protect from light.
Storage	Oral suspension: Refrigerate (2–8°C) the prepared suspension. IV: Store below 25°C. Protect from light.

Excipients	ORAL: Check with hospital pharmacy. IV: disodium edetate and sodium hydroxide.
Special Comments	
Evidence	**Dose** **Oral route:** A double blind dose finding trial in neonates found that minimum effective dose depends on gestational age at birth and postnatal age. Optimal dose was higher in older neonates but born very prematurely than in younger neonates but born less prematurely. When studied at 35 weeks post-menstrual age or more, premature neonates of less than 32 weeks required a dose of 2.5 mg/kg/day whereas less premature and term neonates required 1 mg/kg/day.(1) A randomised, double blind, placebo-controlled, crossover design trial of omeprazole therapy was performed by Omari et al in 10 preterm infants (34–40 weeks postmenstrual age). Infants were given omeprazole 0.7 mg/kg daily for 7 days and then placebo for 7 days in randomised order. Compared to placebo, omeprazole therapy significantly reduced gastric acidity, oesophageal acid exposure and number of acid GER episodes.(7) **Intravenous route:** Andersson et al. studied eight patients, aged 8 days to 17 months, receiving intravenous omeprazole at doses of 0.4–1.2 mg/kg. They found that in neonates ≤ 10 days, half-life and clearance of omeprazole were substantially longer and lower than in children.(3) In a randomised trial in paediatric population, 0.5 mg/kg/dose or 1 mg/kg/dose 12 hourly were administered intravenously. Neither of the 2 omeprazole regimens achieved adequate alkalinization of the gastric pH during the first 24 hours. Between 24 and 48 hours, the 1 mg/kg dose maintained the gastric pH greater than 4 for a greater percentage of the time.(4) Kaufman et al studied 22 paediatric patients ranging in age from 0.9 to 108 months who underwent liver or intestinal transplantation. Intravenous Therapy was started after surgery at 0.5 mg/kg every 12 hours. A dosage of 0.5 mg/kg every 12 hours was sufficient for most patients, but dosing every 6 to 8 hours was required to assure maximal acid suppression in all.(5) Recommended doses of IV omeprazole in paediatric population ranged from 0.5 mg/kg/12 hourly to 1 mg/kg/dose daily.(6) **Treatment of gastroesophageal reflux disease (GORD)** NICE Guidelines (8) 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 infants and young children, and those with a neuro-disability 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. 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. **Prophylaxis in congenital oesophageal atresia and tracheoesophageal fistula** In a systematic review by Shawyer et al involving 1,663 patients for analysis, most were single centre studies and retrospective; there were no randomised controlled trials. The quality of literature regarding anti-reflux medication for GER post EA-TEF repair is poor.(9) **Pharmacokinetics** PPIs are metabolised by the hepatic cytochrome P450 (CYP) enzyme system. Despite rapid elimination of omeprazole from plasma (i.e. mean elimination half-life ≈ 1 hour), the effect can persist for 24 to 72 hours consequent to strong binding of the active form to its target receptor. Oral bioavailability of omeprazole ranges from 35% to 65% and it is 95% protein bound. (10) Dose may need adjustment if no clinical response. **Safety** Omeprazole is well tolerated clinically and with respect to laboratory tests. There are potential risks including increase of neonatal intestinal and pulmonary infections and occurrence of severe hypomagnesaemia.(1,11-15)
Practice points	

References	1. Kaguelidou F, Alberti C, Biran V, et al. Dose-Finding Study of Omeprazole on Gastric pH in Neonates with Gastro-Esophageal Acid Reflux Using a Bayesian Sequential Approach. PLoS One. 2016 Dec 21;11(12):e0166207. 2. Vandenplas Y, Rudolph CD, Di Lorenzo C, 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. JPGN 2009;49:498–547. 3. Andersson T, Gothberg G, Friberg L, et al. Pharmacokinetics of intravenous omeprazole in neonates and infants. J Pediatr Gastroenterol Nutr 2001; 33:424[abstract] 4. Solana MJ, López-Herce J, Sánchez A, et al. 0.5 mg/kg versus 1 mg/kg of intravenous omeprazole for the prophylaxis of gastrointestinal bleeding in critically ill children: a randomized study. The Journal of pediatrics. 2013 Apr 1;162(4):776-82. 5. Kaufman SS, Lyden ER, Brown CR et al. Omeprozole therapy in pediatric patients after liver and intestinal transplantation. J Pediatric Gastroenterology & Nutrition 2002;34(2):194-8. 6. Solana MJ, López-Herce J. Pharmacokinetics of intravenous omeprazole in critically ill paediatric patients. European Journal of Clinical Pharmacology 2010;66:323–330. 7. Omari TI; Haslam RR; Lundborg P; Davidson GP. Effect of omeprazole on acid gastroesophageal reflux and gastric acidity in preterm infants with pathological acid reflux. J Pediatric Gastroenterology & Nutrition 2007; 44(1):41-4. 8. NICE Guideline 2015. Gastro-oesophageal reflux disease in children and young people: diagnosis and management. Published: 14 January 2015. nice.org.uk/guidance/ng1. 9. 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 2014;30(10):987-96. 10. Kearns GL, Winter HS. Proton pump inhibitors in pediatrics: relevant pharmacokinetics and pharmacodynamics. J Pediatric Gastroenterology & Nutrition 2003; 37 Suppl 1:S52-9. 11. Canani RB, Cirillo P, Roggero P, et al. Therapy with gastric acidity inhibitors increases the risk of acute gastroenteritis and community-acquired pneumonia in children. Pediatrics. 2006; 117:e817-20. 12. Canani RB, Terrin G. Gastric acidity inhibitors and the risk of intestinal infections. Curr Opin Gastroenterol 2010; 26:31-5. 13. Guillet R, Stoll BJ, Cotten CM, et al. Association of H2-blocker therapy and higher incidence of necrotizing enterocolitis in very low birth weight infants. Pediatrics. 2006;117:e137-42. 14. Saiman L, Ludington E, Dawson JD, et al. Risk factors for Candida species colonization of neonatal intensive care unit patients. The Pediatr Infect Dis J. 2001; 20:1119-24. 15. Famularo G, Gasbarrone L, Minisola G. Hypomagnesemia and proton-pump inhibitors. Expert Opin Drug Saf. 2013; 12:709±16. 16. Whaley P.A. et al, B. Stability of omeprazole in SyrSepnd SF Alka. Int. J. Pharm Comp. 2012;16: 164-166

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