

lin 1 g and clarithromycin 500 mg, both twice daily. These regimens are given for 1 week. **Dual therapy** regimens such as omeprazole 20 mg twice daily or 40 mg daily with either amoxicillin 750 mg to 1 g twice daily or clarithromycin 500 mg three times daily, are less effective and must be given for 2 weeks. Omeprazole alone may be continued for a further 4 to 8 weeks.

Doses of 20 mg daily orally are used in the treatment of **NSAID-associated ulceration**; a dose of 20 mg daily may also be used for prophylaxis in patients with a history of gastroduodenal lesions who require continued NSAID treatment.

The initial recommended dosage for patients with the **Zollinger-Ellison syndrome** is 60 mg orally once daily, adjusted as required. The majority of patients are effectively controlled by doses in the range 20 to 120 mg daily, but doses up to 120 mg three times daily have been used. Daily doses above 80 mg should be given as divided doses (usually 2).

Omeprazole is also used for the prophylaxis of **acid aspiration** during general anaesthesia, in a dose of 40 mg the evening before surgery and a further 40 mg two to six hours before the procedure.

The dose of omeprazole may need to be reduced in patients with hepatic impairment (see below).

PARENTERAL DOSAGE.

In patients who are unsuited to receive oral therapy omeprazole sodium may be given on a short-term basis by intravenous infusion, in a usual dose equivalent to 40 mg of the base over a period of 20 to 30 minutes in 100 mL of sodium chloride 0.9% or glucose 5%. It may also be given by slow intravenous injection. Higher intravenous doses have been given to patients with Zollinger-Ellison syndrome.

General reviews.

- Richardson P, et al. Proton pump inhibitors: pharmacology and rationale for use in gastrointestinal disorders. *Drugs* 1998; **56**: 307–35.
- Langtry HD, Wilde MI. Omeprazole: a review of its use in Helicobacter pylori infection, gastro-oesophageal reflux disease and peptic ulcers induced by nonsteroidal anti-inflammatory drugs. *Drugs* 1998; **56**: 447–86.
- Berardi RR, Welage LS. Proton-pump inhibitors in acid-related diseases. *Am J Health-Syst Pharm* 1998; **55**: 2289–98.
- Brown GJE, Yeomans ND. Prevention of the gastrointestinal adverse effects of nonsteroidal anti-inflammatory drugs: the role of proton pump inhibitors. *Drug Safety* 1999; **21**: 503–12.
- Erdast BL. Proton-pump inhibitors for acute peptic ulcer bleeding. *Ann Pharmacother* 2001; **35**: 730–40.
- Robinson M, Horn J. Clinical pharmacology of proton pump inhibitors: what the practising physician needs to know. *Drugs* 2003; **63**: 2739–54.
- Dekel R, et al. The role of proton pump inhibitors in gastro-oesophageal reflux disease. *Drugs* 2004; **64**: 277–95.
- Anonymous. Proton pump inhibitors for GERD in children. *Med Lett Drugs Ther* 2007; **49**: 17–18.

Administration. Omeprazole is given orally as tablets or capsules containing enteric-coated pellets or granules, which should be swallowed whole and not crushed or chewed. In children or patients with swallowing difficulties, UK licensed product information (*Losec*; AstraZeneca) states that the tablet be dispersed in water and then mixed with fruit juice (with a pH less than 5) or yogurt before swallowing without chewing. Similarly the contents of the capsules can be mixed with water, fruit juice (with a pH less than 5) or yogurt and swallowed without chewing. A mixture of omeprazole and sodium bicarbonate as a powder for oral suspension is available in some countries.

Administration in children. Licensed UK oral doses of omeprazole for the treatment of gastro-oesophageal reflux disease in children 1 year of age and over are determined by body-weight as follows:

- 10 to 20 kg: 10 mg once daily
- over 20 kg: 20 mg once daily

These doses may be doubled if necessary. Treatment may be given for 4 to 12 weeks.

For gastro-oesophageal reflux disease, acid-related dyspepsia, treatment of duodenal and benign gastric ulcers including NSAID-associated ulceration, prophylaxis of acid aspiration, and Zollinger-Ellison syndrome, the *BNFC* recommends an oral dose of 700 micrograms/kg once daily in neonates and children 1 month to 2 years of age. If needed, doses may be increased in neonates after 7 to 14 days, to 1.4 mg/kg once daily; some neonates may require up to 2.8 mg/kg once daily. Children's doses may be increased up to 3 mg/kg (to a maximum of 20 mg) once daily.

For parenteral dosage in children the *BNFC* recommends an intravenous dose of 500 micrograms/kg (to a maximum of 20 mg)

once daily in children aged 1 month to 12 years; this may be increased to 2 mg/kg (to a maximum of 40 mg) once daily if needed.

For the eradication of *Helicobacter pylori* in children, the *BNFC* recommends an oral dose of omeprazole 1 to 2 mg/kg (to a maximum dose of 40 mg) once daily. This is given with antibacterial therapy under specialist supervision.

For administration of the tablets or capsules to children, see Administration, above.

Administration in hepatic impairment. Bioavailability and half-life of omeprazole can increase in patients with hepatic impairment. UK licensed product information recommends that a maximum daily oral dose of 20 mg be used in these patients; a daily intravenous dose of 10 to 20 mg is considered sufficient.

Asthma. Gastro-oesophageal reflux has been suggested as a potential exacerbating factor for asthma (p.1108), and acid suppressive therapy with omeprazole has been reported to reduce asthma symptoms in some¹ but not other² studies. A meta-analysis of acid suppressive therapy concluded it was not effective in improving asthma symptoms in most patients with gastro-oesophageal reflux,³ and the link between reflux and asthma symptoms has been disputed.⁴

- Harding SM, et al. Asthma and gastroesophageal reflux: acid suppressive therapy improves asthma outcome. *Am J Med* 1996; **100**: 395–405.
- Ford GA, et al. Omeprazole in the treatment of asthmatics with nocturnal symptoms and gastro-oesophageal reflux: a placebo-controlled cross-over study. *Postgrad Med J* 1994; **70**: 350–4.
- Gibson PG, et al. Gastro-oesophageal reflux treatment for asthma in adults and children. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2003 (accessed 11/12/07).
- Field SK. A critical review of the studies of the effects of simulated or real gastroesophageal reflux on pulmonary function in asthmatic adults. *Chest* 1999; **115**: 848–56.

Dyspepsia. Although earlier UK guidelines on the use of proton pump inhibitors in dyspepsia (p.1695) suggested that they should not be used routinely in non-ulcer dyspepsia,¹ subsequent guidelines on its general management in both the UK² and the US³ consider that a 1-month empirical trial in patients aged under 55 without symptoms suggestive of more serious disease is a valid first-line treatment.

- NICE. Guidance on the use of proton pump inhibitors in the treatment of dyspepsia (issued July 2000). Available at: <http://www.nice.org.uk/nicemedia/pdf/proton.pdf> (accessed 11/02/08)
- NICE. Dyspepsia: management of dyspepsia in adults in primary care (Clinical Guideline 17: issued August 2004, updated June 2005). Available at: <http://www.nice.org.uk/nicemedia/pdf/CG017NICEguideline.pdf> (accessed 11/02/08)
- American Gastroenterological Association. American Gastroenterological Association medical position statement: evaluation of dyspepsia. *Gastroenterology* 2005; **129**: 1753–5. Also available at: <http://download.journals.elsevierhealth.com/pdfs/journals/0016-5085/PIIS0016508505018172.pdf> (accessed 11/02/08)

Inflammatory bowel disease. There are a few reports^{1–3} of responses to omeprazole in patients with inflammatory bowel disease (p.1697). Combination of omeprazole with mesalazine has also been tried.²

- Heinzow U, Schlegelberger T. Omeprazole in ulcerative colitis. *Lancet* 1994; **343**: 477.
- Dickinson JB. Is omeprazole helpful in inflammatory bowel disease? *J Clin Gastroenterol* 1994; **18**: 317–19.
- Guslandi M, Tittoello A. Symptomatic response to omeprazole in inflammatory bowel disease. *J Clin Gastroenterol* 1996; **22**: 159–60.

Scleroderma. Gastro-oesophageal reflux is one of the gastrointestinal manifestations of systemic sclerosis, and proton pump inhibitors such as omeprazole play a major role in the management of such gastrointestinal disease.¹ For a discussion of the broader management of the condition see p.1817.

- Williamson DJ. Update on scleroderma. *Med J Aust* 1995; **162**: 599–601.

Preparations

BP 2008: Gastro-resistant Omeprazole Capsules; Gastro-resistant Omeprazole Tablets;
USP 31: Omeprazole Delayed-Release Capsules.

Proprietary Preparations (details are given in Part 3)

Arg.: Acimed; Aziatop; Brux; Danlox; Fabrazol; Fendiprazol; Gastec; Gastroprazol; Gastrotem; Klomeprax; Losec; Mucocox; Omeprasec; Pepticus; Pravil; Procelac; Phryma; Regulacid; Timezol; Ulcozol; Zoltenk. **Austria:** Acimax; Losec; Maxorl; Meprazol; Omepral; Probitor; **Austria:** Helicostad; Losec; Lostad; Medoprazol; Ome; Omeprax; Omepral; Probitor; Semiglen; **Belg.:** Docomepra; Logastric; Losec; Omepraprot; Sedacid; **Braz.:** Belprazol; Bioprazol; Elprazol; Estomepe; Eupete; Fegran; Gas-ec; Gaspiren; Gastrinb; Gastrum; Gastrozol; Klispe; Lomepral; Loprazol; Losaprol; Losart; Lozap; Lozaprel; Lozix; Meprax; Mesopran; Neoprazol; Novoprazol; Omeprax; Omenax; Omepr; Omepramed; Omeprazin; Omepraprot; Oprezon; Peprazol; Pepsicaps; Prazole; Prazonil; Prazotom; Ulcecaps; Ulcef; Ulcozol; Uniprazol; Victrix; Zolpramex; **Canada:** Losec; **Chile:** Lomex; Losec; Micromex; Omeprax; Pepticum; Prazolol; Ulic-Out; Ulicelac; Ulicurx; Zatro; Zomepral. **Cz.:** Apo-Ome; Gasec; Helicid; Lomac; Losec; Loseprazol; Omeprax; Omepral; Omolin; Onprelen; Oprezole; Orntanol; Pepticum; Probiok; Tulzol; Ultop; **Denm.:** Losec; **Fin.:** Losec; **Fr.:** Mopral; Zoltum; **Ger.:** Antra; Gastracid; Ome TAD; Ome-nertron; Ome-Puren; Ome-Q; Omebeta; Omedoc; Omegamma; OmeLich; OmeLind; OmeP; **Gr.:** Assoprol; Belifax; Elibactin; Elkostop; Elkoheran; Eselan; Esopraz; Ezipol; Gertalgin; Glaverin; Inhipelex; Kerlofin; Lanex; Lenar; Lomezec; Loproc; Lordin; Lozap; Lozaprin; Malortil; Meproren; Novex; Odamesol; Odazol; Ofnimarex; Omepral; Penrazol; Pipacid; Prazonil; Probitor; Rythmogastriy; Sedacid; Sieral; Silato; Ufonitren; Veralex; Zolledin; **Hong Kong:** Losec; **Hung.:** Losec; Omege; OmeP;

Omeprazin; Ulzol. **India:** Biocid; Lomac; Nogacid; Ocic; Olit; Omezol; Promisc; Ulzol; **Indon.:** Conral; Duadec; Loklor; Losec; Meisec; Norsec; Omevelt; OMe; Onic; Opm; Oprezol; Ozid; Prohibit; Promezol; Protop; Pumpitor; Redsec; Regasec; Rocer; Socid; Stomacer; Ulzol; Zepal; Zollicid; **Ir.:** BySec; Lopraz; Losamet; Losec; Losepine; **Israel:** Losec; Omepradex; **Ital.:** Antra; Losec; Mepral; Omeprazin; **Jpn:** Omepral; **Malaysia:** Gasec; Losec; Medoprazole; Omeleon; Omelec; Omeze; Omezele; Probitor; Romesc; Zenprol; Zomer; **Mex.:** Alboz; Aleprozil; Apopraz; Argaryn; Azoran; Danovag; Dimer; Gedex; Grizol; Hopram; Iba; Inhibitor; Logazil; Lopram; Losec; Medral; Mopral; Mornin; Olexin; Omecaps; Ometec; Opremid; Osiren; Ozoken; Panzer; Prastazol; Pentren; Prazidec; Prazolil; Sarox; Solcer; Sulfac; Tarzol; Uctal; Ulsem; Ultizol; Ultronep; Zulaltron; Vulcasid; Zoral; Zulmed; **Neth.:** Losec; Omeprazostad; Omeprad; Omepral; Omolin; Romisan; **Norw.:** Losec; **NZ:** Losec; Omezele; **Philipp.:** Gastrilic; Hovizol; Losec; Mepracid; Omenole; Omepron; Omizac; OMZ; Opehex; Peptisol; Premio; Promesc; Puroxel; Ritek; Tansi- nel; Ulsek; Zym; **Pol.:** Bioprazol; Gasec; Helicid; Losec; Ulzol; Omar; Orntanol; Polprazol; Prazol; Ulzol; **Port.:** Belmazol; Bloprazol; Eugastrin; Gasec; Losec; Mepraz; Novex; Nuodosina; Omepra; Omeratio; Omerol; Ometon; Omezeleon; Prazolot; Praxex; Prazolene; Proclor; Proton; **Rus.:** Gastrozol (Гастрозол); Helicid (Хелицид); Helol (Хелол); Losec (Лосек); Ocic (Оцид); Ome (Оме); Otipir (Отипир); Omilox (Омиток); Omizac (Омизак); Romesc (Ромесек); Sopral (Сопрал); Utop (Ультоп); Ulzol (Ульзол); Zerocid (Зероцид); **S.Afr.:** Altosec; Losec; Omeze; Omilox; Ulsec; **Singapore:** Losec; Ocic; Olit; Omelec; Omezele; Penrazole; Proceptin; Romesc; Zenpro; Zimer; **Spain:** Audazol; Aulcer; Belmazol; Ceprandal; Dolintol; Elgam; Emepron; Gastrimut; Indurgan; Ipirasa; Losec; Mliol; Mopral; Norpramin; Novex; Nuodosina; Omaren; Omprany; Parizac; Pepticum; Phryma; Samamidol; Ulsem; Ulcepep; Ulcometron; Zimor; **Swed.:** Losec; **Switz.:** Amano; Antra; Antrampus; Gastroprazol; Omed; omepra-basan; Omeze; Omepral; **Thai:** Airomet; Desec; Dosate; Duogas; Eselan; Eucid; Gaster; Gomec; Lomac; Losec; Madiprazole; Meiceral; Metsec; Miracid; Nocid; O-Sid; Olit; Ome; Omeic; Oprezol; Probitor; Severon; Stomec; Ulprazole; Zelfon; Zimor; **Turk.:** Demepazol; Erbolin; Losec; Omegeat; Omeprazol; Omepron; Prosek; **UAE:** Ritek; **UK:** Heartburn Relief; Losec; Zanprol; **USA:** Prilosec; **Venez.:** Fordex; Gastronil; Losec; Meproxt; Omeblox; Omevax; Omeze; Omeze; Parsolen; Prazol; Probitor; Promezol; Tocol; **Multi-ingredient:** Austral; Klacid HP 7; Losec Hp 7; **Braz.:** Erradic; Helicocid Triplec; Omeprazin; **Canada:** Losec 1-2-3 A; Losec 1-2-3 M; **Fin.:** Losec Helira; **India:** Helipac; Nogacid D; Okacid D; OTC HP Kit; **Malaysia:** Pylobact Comb; **NZ:** Klacid HP 7; Losec Hp 7; **Philipp.:** OAC Hp 7; **Rus.:** Pylobact (Пилобакт); **S.Afr.:** Losec 20 Triplec; **USA:** Zegerid.

Ondansetron (BAN, rINN)

GR-38032; Ondansetron; Ondansetron; Ondansetroni; Ondansetronum. (±)-1,2,3,9-Tetrahydro-9-methyl-3-(2-methylimidazol-1-ylmethyl)-carbazol-4(9H)-one.

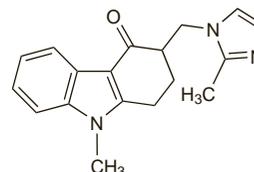
ОНДАНСЕТРОН

C₁₈H₁₉N₃O = 293.4.

CAS — 99614-02-5; 116002-70-1.

ATC — A04AA01.

ATC Vet — QA04AA01.



Pharmacopoeias. In *US*.

USP 31 (Ondansetron). A white to off-white powder. Sparingly soluble in water; very soluble in acid solutions. Store in airtight containers. Protect from light.

Ondansetron Hydrochloride (BANM, USAN, rINN)

GR-38032F; Hydrocloruro de ondansetron; Ondansetron, chlorhydrate d'; Ondansetron hydrochlorid; Ondansetronhydrochlorid; Ondansetroni hydrochloridum; Ondansetronhydrochloridi; Ondansetrono hydrochloridas; Ondansetroni Hydrochloridum; Ondansetronhydrochlorid; SN-307.

ОНДАНСЕТРОНА ГИДРОХЛОРИД

C₁₈H₁₉N₃O.HCl.2H₂O = 365.9.

CAS — 99614-01-4; 103639-04-9.

ATC — A04AA01.

ATC Vet — QA04AA01.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US*.

Ph. Eur. 6.2 (Ondansetron Hydrochloride Dihydrate). A white or almost white powder. Sparingly soluble in water and in alcohol; slightly soluble in dichloromethane; soluble in methyl alcohol. Protect from light.

USP 31 (Ondansetron Hydrochloride). A white to off-white powder. Sparingly soluble in water and in alcohol; very slightly soluble in acetone, in chloroform, and in ethyl acetate; slightly soluble in dichloromethane and in isopropyl alcohol; soluble in methyl alcohol. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

Incompatibility. Ondansetron hydrochloride and dexamethasone sodium phosphate were not compatible when high concentrations were combined in polypropylene syringes.¹ Lower concentrations (up to 640 micrograms/mL of ondansetron and 400 micrograms/mL of dexamethasone phosphate) were stable