

6. Toren P, *et al.* Ondansetron treatment in Tourette's disorder: a 3-week, randomized, double-blind, placebo-controlled study. *J Clin Psychiatry* 2005; **66**: 499–503.
7. Hewlett WA, *et al.* Pilot trial of ondansetron in the treatment of 8 patients with obsessive-compulsive disorder. *J Clin Psychiatry* 2003; **64**: 1025–30.

Substance dependence. Ondansetron is being studied in the management of alcohol dependence (p.1626). However, in one study¹ a significant reduction in alcohol consumption was found only in lighter drinkers after subgroup analysis. Another study² found a reduction in alcohol consumption by patients with early-onset alcoholism (onset before age 25) who took ondansetron compared with placebo. No such effect was seen, however, in patients with late-onset alcoholism. Further study found that ondansetron also effectively ameliorated mood disturbances including symptoms of depression, anxiety, and hostility, in early-onset alcoholics.³ Self-reported alcohol consumption also reduced in adolescents (between ages 14 and 20) with alcohol dependence who were given ondansetron in an open study.⁴

- Sellers EM, *et al.* Clinical efficacy of the 5-HT₃ antagonist ondansetron in alcohol abuse and dependence. *Alcohol Clin Exp Res* 1994; **18**: 879–85.
- Johnson BA, *et al.* Ondansetron for reduction of drinking among biologically predisposed alcoholic patients. *JAMA* 2000; **284**: 963–71.
- Johnson BA, *et al.* Ondansetron reduces mood disturbance among biologically predisposed, alcohol-dependent individuals. *Alcohol Clin Exp Res* 2003; **27**: 1773–9.
- Dawes MA, *et al.* A prospective, open-label trial of ondansetron in adolescents with alcohol dependence. *Addict Behav* 2005; **30**: 1077–85.

Preparations

USP 31: Ondansetron Hydrochloride Oral Suspension; Ondansetron Injection; Ondansetron Oral Solution; Ondansetron Orally Disintegrating Tablets.

Proprietary Preparations (details are given in Part 3)

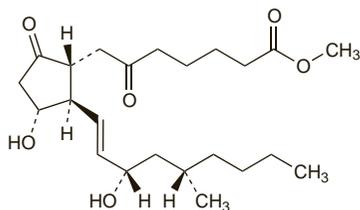
Arg.: Cetron; Dantenk; Dismolan; Emivox†; Espasevit; Finaber; Finoxi; Tiosalis; Zofran; **Austral.:** Ondaz; Onsetron; Zofran; **Austria:** Glaxosetron; Ondanglax; Ondansan; Zofran; **Belg.:** Zofran; **Braz.:** Ansetron; Injextra; Modifical; Nauseudron; Ontra; Vonau; Zofran; **Canada:** Zofran; **Chile:** Amilene; Gardoton; Zofran; Odanex; Oncoemet; Tronix; **Cz.:** Danemet; Emeset; Emetron†; Novetron; Ondemet; Setron†; Setronon; Zofran; **Denm.:** Hexatron; Zofran; **Fin.:** Zofran; **Fr.:** Zophren; **Ger.:** Zofran; **Gr.:** Biosetron; Cruzafen; Dentrion; Fedral; Odnatron; Onda; Ondametron; Ondaren; Ondaseprol; Setrodan; Vefron; Zetron; Zodatron; Zofron; Zophralen; **Hong Kong:** Zofran; **Hung.:** Antivom; Emetron; Ondagen; Zofran; **India:** Emeset; Periset; Vomiof; **Indon.:** Cedatron; Dantroxal; Entron; Frazon; In-vomit; Narfoz; Ondavell; Onetic 4; Vomceran; Zantron; Zofran; **Irl.:** Emital; Zofran; **Israel:** Zofran; **Ital.:** Zofran; **Malaysia:** Osetron; Zofran; **Mex.:** Danac; Modifical; Precirux; Zofran; **Neth.:** Zofran; **Norw.:** Zofran; **NZ:** Onsetron; Zofran; **Philipp.:** Emodan; Zofran; **Pol.:** Atossa; Emetron; Setronon; Zofran; **Port.:** Nausiend; Otobrol; Zofran; **Rus.:** Emetron (Эметрон); Setronon (Сетронон); Zofran (Зофран); **S.Afr.:** Dantron; Nauseudron; Zofran; **Singapore:** Zofran; **Spain:** Fixca†; Yatrox; Zofran; **Swed.:** Zofran; **Switz.:** Zofran; **Thai.:** Dantron; Emeset; Onsia; Vomitron†; Zetron; Zofran; **Turk.:** Zofan; Zofran; Zoltem; **UK:** Ondemet; Zofran; **USA:** Zofran; **Venez.:** Dismolan; Emeset; Tructum; Zofran.

Ornoprostil (rINN)

Ornoprostilo; Ornoprostilum; OU-1308. Methyl (-)-(1R,2R,3R)-3-hydroxy-2-[(E)-(3S,5S)-3-hydroxy-5-methyl-1-nonyl]-ε,5-dioxocyclopentaneheptanoate.

Орнопростил

C₂₂H₃₈O₆ = 410.5.
CAS — 70667-26-4.



Profile

Ornoprostil is a synthetic prostaglandin analogue that has been used in the treatment of peptic ulcer disease.

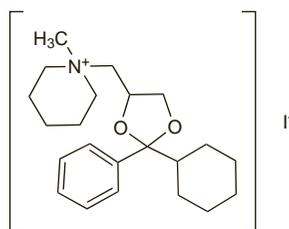
Oxapium iodide (rINN)

Ciclonium iodide; Cyclonium Iodide; Ioduro de oxapio; Oxapii Iodidum; Oxapium, Iodure d'; SH-100. 1-(2-Cyclohexyl-2-phenyl-1,3-dioxolan-4-ylmethyl)-1-methylpiperidinium iodide.

Оксапия Йодид

C₂₂H₃₄INO₂ = 471.4.
CAS — 6577-41-9.

The symbol † denotes a preparation no longer actively marketed



NOTE. Distinguish from ciclonium bromide, p.1716, an unrelated antispasmodic.

Pharmacopeias. In *Jpn.*

Profile

Oxapium iodide is an antimuscarinic that has been used as an antispasmodic in the treatment of gastrointestinal disorders and renal calculi.

Preparations

Proprietary Preparations (details are given in Part 3)

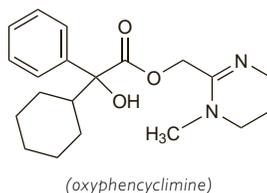
Jpn: Esperan.

Oxyphencyclimine Hydrochloride (BANM, rINN)

Hidrocloruro de oxifenclimina; Oksifensiklimin Hidroklorür; Oxyphencyclimine, Chlorhydrate d'; Oxyphencyclimini Hydrochloridum. 1,4,5,6-Tetrahydro-1-methylpyrimidin-2-ylmethyl α-cyclohexylmandelate hydrochloride.

Оксифенциклимина Гидрохлорид

C₂₀H₂₈N₂O₃.HCl = 380.9.
CAS — 125-53-1 (oxyphencyclimine); 125-52-0 (oxyphencyclimine hydrochloride).
ATC — A03AA01.
ATC Vet — QA03AA01.



Profile

Oxyphencyclimine hydrochloride is a tertiary amine antimuscarinic with effects similar to those of atropine (p.1219). It has been used as an adjunct in the treatment of peptic ulcer disease and for the relief of smooth muscle spasms in gastrointestinal disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Hong Kong: Daricon; **Thai.:** Daricon†; Med-Spastic†; Oxyno; Proclimine.

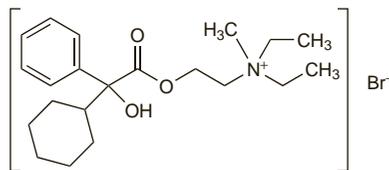
Multi-ingredient: **Hong Kong:** Rudd-U†; **Turk.:** Spazmo-Valibrin.

Oxyphenonium Bromide (BAN, rINN)

Bromuro de oxifenonio; Oksyfenoniowy bromek; Oxphenonii Bromidum; Oxyphenonii Bromidum; Oxyphenonium Bromatum; Oxyphénonium, Bromure d'. 2-(α-Cyclohexylmandeloyloxy)ethyl-diethylmethylammonium bromide.

Оксифенония Бромид

C₂₁H₃₄BrNO₃ = 428.4.
CAS — 14214-84-7 (oxyphenonium); 50-10-2 (oxyphenonium bromide).
ATC — A03AB03.
ATC Vet — QA03AB03.



Pharmacopeias. In *Pol.*

Profile

Oxyphenonium bromide is a quaternary ammonium antimuscarinic with peripheral effects similar to those of atropine (p.1219). It has been given orally to relieve visceral spasms.

Preparations

Proprietary Preparations (details are given in Part 3)

India: Antreny†; **Pol.:** Spasmophen; **S.Afr.:** Spastrex†.

Multi-ingredient: **Cz.:** Endiform†.

Palonosetron Hydrochloride

(USAN, rINN)

Hidrocloruro de palonosetron; Palonosetron, Chlorhydrate de; Palonosetroni Hydrochloridum; RS-25259-197. (3aS)-2,3,3a,4,5,6-Hexahydro-2-[(3S)-3-quinuclidinyl]-1H-benz[de]isoquinolin-1-one hydrochloride.

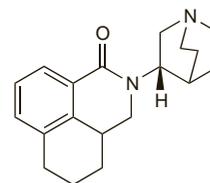
Палоносетрона Гидрохлорид

C₁₉H₂₄N₂O.HCl = 332.9.

CAS — 135729-56-5 (palonosetron); 135729-55-4 (palonosetron hydrochloride); 135729-62-3 (palonosetron hydrochloride).

ATC — A04AA05.

ATC Vet — QA04AA05.



(palonosetron)

Stability. The stability of palonosetron hydrochloride at concentrations of 5 and 30 micrograms/mL was assessed in polyvinyl chloride bags of the following 4 infusion solutions: glucose 5%, sodium chloride 0.9%, glucose 5% in sodium chloride 0.45%, and glucose 5% in lactated Ringer's solution. All solutions were considered to be physically and chemically stable for at least 48 hours at room temperature exposed to light, and for 14 days under refrigeration.¹

Palonosetron 50 micrograms/mL was found to be physically and chemically stable during simulated Y-site administration with the following drugs: fentanyl citrate 50 micrograms/mL, hydromorphone hydrochloride 500 micrograms/mL, morphine sulfate 15 mg/mL, pethidine hydrochloride 10 mg/mL, and sufentanil citrate (12.5 micrograms/mL of sufentanil).²

- Trissel LA, Xu QA. Physical and chemical stability of palonosetron HCl in 4 infusion solutions. *Ann Pharmacother* 2004; **38**: 1608–11.
- Trissel LA, *et al.* Physical and chemical stability of palonosetron hydrochloride with five opiate agonists during simulated Y-site administration. *Am J Health-Syst Pharm* 2007; **64**: 1209–13.

Adverse Effects and Precautions

As for Ondansetron, p.1757, although no dosage reduction is considered necessary in hepatic impairment. Diarrhoea, fatigue, and abdominal pain may also occur. Patients with a history of constipation or signs of subacute intestinal obstruction should be monitored if given palonosetron.

Effects on the cardiovascular system. For a discussion of the effects of 5-HT₃ antagonists on the cardiovascular system, see under Ondansetron, p.1757.

Interactions

As for Ondansetron, p.1757.

Pharmacokinetics

Palonosetron has a volume of distribution of around 7 to 8 litres/kg; plasma protein binding is about 62%. About 50% of a dose is metabolised in the liver by cytochrome P450 isoenzymes (notably CYP2D6, but also CYP3A4 and CYP1A2). About 80% of a dose is recovered in the urine within 144 hours, as palonosetron and its metabolites. The mean elimination half-life is reported to be about 40 hours.

◇ References.

- Hunt TL, *et al.* Evaluation of safety and pharmacokinetics of consecutive multiple-day dosing of palonosetron in healthy subjects. *J Clin Pharmacol* 2005; **45**: 589–96.
- Shah A, *et al.* Pharmacokinetic evaluation and safety profile of a 15-minute versus 30-second infusion of palonosetron in healthy subjects. *J Clin Pharmacol* 2006; **46**: 1139–45.

Uses and Administration

Palonosetron is a 5-HT₃ antagonist used in the prevention of nausea and vomiting induced by cytotoxic chemotherapy and for the prevention of postoperative nausea and vomiting. Palonosetron is given as the hydrochloride but doses are expressed in terms of the base; 280.8 micrograms of palonosetron hydrochloride is equivalent to about 250 micrograms of palonosetron.

For the prevention of acute and delayed **nausea and vomiting** associated with initial and repeat courses of moderately or highly emetogenic cancer **chemotherapy**, a dose of 250 micrograms is given intravenously over 30 seconds about 30 minutes before chemotherapy. Repeated dosing within 7 days is not recommended.

For the prevention of **postoperative** nausea and vomiting, for up to 24 hours after surgery, a single dose of 75 micrograms is given intravenously over 10 seconds immediately before the induction of anaesthesia. Efficacy beyond 24 hours has not been demonstrated.

References.

- Eisenberg P, et al. Improved prevention of moderately emetogenic chemotherapy-induced nausea and vomiting with palonosetron, a pharmacologically novel 5-HT₃ receptor antagonist: results of a phase III, single-dose trial versus dolasetron. *Cancer* 2003; **98**: 2473–82.
- Gralla R, et al. Palonosetron improves prevention of chemotherapy-induced nausea and vomiting following moderately emetogenic chemotherapy: results of a double-blind randomized phase III trial comparing single doses of palonosetron with ondansetron. *Ann Oncol* 2003; **14**: 1570–7.
- Anonymous. Palonosetron (Aloxi) for prevention of nausea and vomiting due to cancer chemotherapy. *Med Lett Drugs Ther* 2004; **46**: 27–8.
- Siddiqui MAA, Scott LJ. Palonosetron. *Drugs* 2004; **64**: 1125–32.

Preparations

Proprietary Preparations (details are given in Part 3)

Braz.: Onicit; **Chile**: Onicit; **Cz.**: Aloxi; **Gr.**: Aloxi; **Hung.**: Aloxi; **Indon.**: Paloxi; **Ir.**: Aloxi; **Ital.**: Aloxi; **Mex.**: Onicit; **Neth.**: Aloxi; **Pol.**: Aloxi; **UK**: Aloxi; **USA**: Aloxi; **Venez.**: Onicit.

Pantoprazole (BAN, USAN, rINN)

BY-1023; Pantopratsoli; Pantoprazol; Pantoprazolum; SKF-96022. 5-Difluoromethoxybenzimidazol-2-yl 3,4-dimethoxy-2-pyridylmethyl sulphoxide.

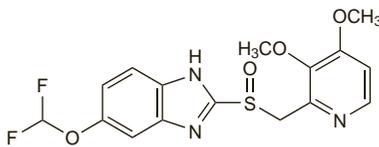
Пантопразол

C₁₆H₁₃F₂N₃O₄S = 383.4.

CAS — 102625-70-7.

ATC — A02BC02.

ATC Vet — QA02BC02.



Pantoprazole Sodium (BANM, USAN, rINN)

Natrii Pantoprazolum; Pantoprazol sódico; Pantoprazole sodique; Pantoprazolum natrium. Pantoprazole sodium sesquihydrate.

Натрий Пантопразол

C₁₆H₁₄F₂N₃NaO₄S · 1/2 H₂O = 432.4.

CAS — 138786-67-1 (anhydrous pantoprazole sodium); 164579-32-2 (pantoprazole sodium sesquihydrate).

ATC — A02BC02.

ATC Vet — QA02BC02.

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

Ph. Eur. 6.2 (Pantoprazole Sodium Sesquihydrate). A white or almost white powder. Freely soluble in water and in alcohol; practically insoluble in hexane. Protect from light.

Stability. A suspension of pantoprazole 2 mg/mL in sterile water and sodium bicarbonate was deemed to be physically and chemically stable¹ in amber polyethylene terephthalate bottles for 62 days at 2° to 8°.

- Dentinger PJ, et al. Stability of pantoprazole in an extemporaneously compounded oral liquid. *Am J Health-Syst Pharm* 2002; **59**: 953–6.

Adverse Effects and Precautions

As for Omeprazole, p.1753. Dosage may need to be reduced in severe hepatic impairment; liver function should be monitored regularly, and therapy stopped if liver enzymes are elevated.

Incidence of adverse effects. In a postmarketing surveillance study of the 6-month period after the launch of pantoprazole in England (UK), the adverse effects reported most frequently were diarrhoea, nausea, and headache. Other effects included malaise or lassitude, rash, other gastrointestinal disturbances, myalgia, and oedema.¹

- Wilton LV, et al. The pharmacovigilance of pantoprazole: the results of postmarketing surveillance on 11 541 patients in England. *Drug Safety* 2003; **26**: 121–32.

Effects on the blood. For a report of thrombocytopenia with pantoprazole, see under Omeprazole, p.1753.

Effects on the kidneys. For reports of interstitial nephritis associated with pantoprazole see p.1753.

Effects on the skin. For mention of skin reactions to pantoprazole, see p.1754.

Interactions

As for Omeprazole, p.1755.

For reference to a lack of effect of pantoprazole on diazepam, see Gastrointestinal Drugs, p.991, and for a lack of effect on theophylline, see p.1145. Licensed product information states that there are reports of increased prothrombin time in patients taking pantoprazole and warfarin, but for reports suggesting a lack of effect on warfarin, see p.1430. For a report of severe generalised myalgia and bone pain attributed to the use of methotrexate with pantoprazole, see Gastrointestinal Drugs, p.748.

Pharmacokinetics

Pantoprazole is rapidly absorbed and peak plasma-pantoprazole concentrations are achieved about 2 to 2.5 hours after an oral dose. The oral bioavailability is about 77% with the enteric-coated tablet formulation, and does not vary after single or multiple doses. Pantoprazole is about 98% bound to plasma proteins. It is extensively metabolised in the liver, primarily by the cytochrome P450 isoenzyme CYP2C19, to desmethyl-pantoprazole; small amounts are also metabolised by CYP3A4, CYP2D6, and CYP2C9. Metabolites are excreted mainly (about 80%) in the urine, with the remainder being excreted in faeces via the bile. The terminal elimination half-life is about 1 hour, and is prolonged in hepatic impairment; the half-life in patients with cirrhosis was 3 to 6 hours. Although the elimination half-life has been reported to be 3.5 to 10 hours in slow metabolisers (see also Metabolism under Omeprazole, p.1755), minimal accumulation occurs with once-daily dosing.

References.

- Pue MA, et al. Pharmacokinetics of pantoprazole following single intravenous and oral administration to healthy male subjects. *Eur J Clin Pharmacol* 1993; **44**: 575–8.

Bioavailability. A suspension of pantoprazole in sodium bicarbonate solution was rapidly absorbed, and peak plasma concentrations were comparable to that of the tablet. However, bioavailability of the suspension was about 25% lower than that of the tablet; the amount of sodium bicarbonate used may affect the bioavailability.¹

- Ferron GM, et al. Oral bioavailability of pantoprazole suspended in sodium bicarbonate solution. *Am J Health-Syst Pharm* 2003; **60**: 1324–9.

Uses and Administration

Pantoprazole is a proton pump inhibitor with actions and uses similar to those of omeprazole (p.1755). It is given as the sodium salt but doses are expressed in terms of the base. Pantoprazole sodium 11.28 mg is equivalent to about 10 mg of pantoprazole. Once-daily doses should be taken in the morning.

In the treatment of **gastro-oesophageal reflux disease** (p.1696), the usual oral dose is 20 to 40 mg once daily for 4 weeks, increased to 8 weeks if necessary; in the USA, up to 16 weeks of therapy is permitted for healing of erosive oesophagitis. For maintenance therapy, treatment can be continued with 20 to 40 mg daily. Alternatively, for recurring symptoms, an on-demand regimen of 20 mg daily may be given.

The usual dose for the treatment of **peptic ulcer disease** (p.1702) is 40 mg once daily. Treatment is usually

given for 2 to 4 weeks for duodenal ulceration, or 4 to 8 weeks for benign gastric ulceration. For the eradication of *Helicobacter pylori* pantoprazole may be combined with two antibacterials in a 1-week **triple therapy** regimen. Effective regimens include pantoprazole 40 mg twice daily combined with clarithromycin 500 mg twice daily and amoxicillin 1 g twice daily, or combined with clarithromycin 250 mg twice daily and metronidazole 400 mg twice daily.

Patients who require prophylaxis for **NSAID-associated ulceration** may take 20 mg daily.

In the treatment of pathological hypersecretory states such as the **Zollinger-Ellison syndrome** (p.1704), the initial dose is 80 mg daily, adjusted as required. Doses of up to 240 mg daily have been used. Daily doses greater than 80 mg should be given in 2 divided doses.

PARENTERAL DOSAGE.

Pantoprazole may also be given intravenously, as the sodium salt, over 2 to 15 minutes, either as a slow injection or a short-term infusion. For peptic ulceration or gastro-oesophageal reflux disease, the recommended dose is 40 mg daily. A dose of 80 mg once or twice daily may be used for Zollinger-Ellison syndrome; up to 240 mg daily may be given in divided doses. Patients should be switched to oral therapy as soon as possible.

Doses of pantoprazole may need to be reduced in patients with hepatic impairment (see below).

References.

- Anonymous. Pantoprazole—a third proton pump inhibitor. *Drug Ther Bull* 1997; **35**: 93–4.
- Poole P. Pantoprazole. *Am J Health-Syst Pharm* 2001; **58**: 999–1008.
- Cheer SM, et al. Pantoprazole: an update of its pharmacological properties and therapeutic use in the management of acid-related disorders. *Drugs* 2003; **63**: 101–32.
- Gisbert JP, et al. Pantoprazole based therapies in *Helicobacter pylori* eradication: a systematic review and meta-analysis. *Eur J Gastroenterol Hepatol* 2004; **16**: 89–99.
- Lehmann FS, Beglinger C. Role of pantoprazole in the treatment of gastro-oesophageal reflux disease. *Expert Opin Pharmacother* 2005; **6**: 93–104.

Administration. The safety and tolerability profiles of intravenous pantoprazole given in 10 mL of sodium chloride 0.9% over 2 minutes were similar to those given over 15 minutes in 100 mL.¹

- Micalizzi M, et al. Comparative tolerability of 2- and 15-minute intravenous infusions of pantoprazole. *Am J Health-Syst Pharm* 2007; **64**: 1822–6.

Administration in hepatic impairment. Dosage of pantoprazole may need to be reduced in severe hepatic impairment, or doses given only on alternate days. A maximum dose of 20 mg daily orally or intravenously, or 40 mg orally on alternate days, has been suggested. Doses above 40 mg daily have not been studied in patients with hepatic impairment. Liver enzymes should be monitored during therapy, and pantoprazole should be stopped if elevations occur.

Administration in renal impairment. Most studies have not found the pharmacokinetics of pantoprazole to be altered in patients with renal impairment¹ and licensed drug information in the UK and US generally does not recommend dosage adjustment in this group; however some UK sources, including the *BNF*, suggest that a maximum dose of 40 mg daily should be observed.

- Cheer SM, et al. Pantoprazole: an update of its pharmacological properties and therapeutic use in the management of acid-related disorders. *Drugs* 2003; **63**: 101–132.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Gastromax; Pangest; Pantocax; Pantop; Pantus; Peptazol; Sipar; Supracam; Ulserch; Zuralc; **Austral.**: Somac; **Austria**: Pantoloc; Zuralc; **Belg.**: Pantozol; Zuralc; **Braz.**: Gastropan; Noprop; Pantocal; Pantopaz; Pantozol; Pantrat; Peptovit; Ziprol; Zuralc; **Canad.**: Pantop; Pantozol; Singastri; Ulcemex; Zuralc; **Cz.**: Apo-Panto; Controloc; Nolpaz; Panogastin; **Denm.**: Pantoloc; **Fin.**: Somac; **Fr.**: Eupantoli; Inipomp; **Ger.**: Pantozol; Pantozol-Rifun; Rifun; **Gr.**: Controloc; Zuralc; Zircapoli; **Hong Kong**: Pantoloc; **Hung.**: Controloc; Nolpaz; Pantacid; Zimpac; **India**: Eracid; Pantodac; Pantop; Pantosec; Pentaloc; Praize; **Indon.**: Pantozol; **Ir.**: Prolium; **Israel**: Controloc; **Ital.**: Pantecta; Pantopan; Pantoric; Peptazol; **Malaysia**: Controloc; **Mex.**: Pantozol; Prazolani; Tecta; Zolpra; Zuralc; **Neth.**: Pantoric; Pantozol; **Norw.**: Somac; **NZ**: Somac; **Philipp.**: Pantoloc; Ulcepraz; **Pol.**: Controloc; **Port.**: Apton; Pantoc; Praoz; Zuralc; **Rus.**: Sunpraz (Санпраз); **S.Afr.**: Controloc; Pantocid; Pantoloc; Topzole; **Singapore**: Controloc; **Spain**: Anagastra; Pantecta; Pantocarm; Ulcotenal; **Swed.**: Pantoloc; **Switz.**: Pantozol; Zuralc; **Thail.**: Controloc; **Turk.**: Pantec; Pantoc; Pantipaz; Pulcet; **UK**: Prolium; **USA**: Protonix; **Venez.**: Pantop.

Multi-ingredient: **Austral.**: Somac-MA; **Austria**: Helipac; **Ger.**: ZacPac; **India**: Pantosec D; Praize-D; **Malaysia**: Klacid HP 7; **Neth.**: PantoPAC.