Uses and Administration

Palonosetron is a 5-HT_3 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.

1. 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.
2. 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.
3. Anonymous. Palonosetron (Aloxi) for prevention of nausea and vomiting due to cancer chemotherapy. *Med Lett Drugs Ther* 2004; **46:** 27–8.
4. 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; ***Irl.:*** 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.

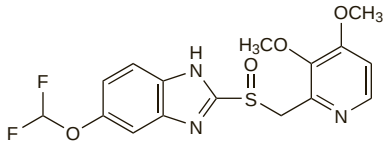
Пантопразол

$C_{16}H_{15}F_2N_3O_4S$ = 383.4.

CAS — 102625-70-7.

ATC — A02BC02.

ATC Vet — QA02BC02.



Pantoprazole Sodium *(BANM, USAN, rINNM)*

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

Натрий Пантопразол

$C_{16}H_{14}F_2N_3NaO_4S, 1/H_2O$ = 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 stable[1] in amber polyethylene terephthalate bottles for 62 days at 2° to 8°.

1. 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]

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 desmethylpantoprazole; 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.

1. 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]

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).

◊ Reviews.

1. Anonymous. Pantoprazole—a third proton pump inhibitor. *Drug Ther Bull* 1997; **35:** 93–4.
2. Poole P. Pantoprazole. *Am J Health-Syst Pharm* 2001; **58:** 999–1008.
3. 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.
4. 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.
5. 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]

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 impairment[1] 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.

1. 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; Pantocas; Pantop; Pantus; Peptazol; Sipar; Supracam; Ulserch†; Zurcal†; ***Austral.:*** Somac; ***Austria:*** Pantoloc; Zurcal; ***Belg.:*** Pantozol; Zurcale; ***Braz.:*** Gastropan; Noprop†; Pantocal; Pantopaz†; Pantozol; Pantrat; Peptovit†; Ziprol; Zurcal; ***Canad.:*** Panto; Pantoloc; ***Chile:*** Singastril†; Ulcemex; Zurcal; ***Cz.:*** Apo-Panto; Controloc; Nolpaza; Panogastin; ***Denm.:*** Pantoloc; ***Fin.:*** Somac; ***Fr.:*** Eupantol; Inipomp; ***Ger.:*** Pantozol; Pantozol-Rifun†; Rifun; ***Gr.:*** Controloc; Pantosec; Zurcazol; ***Hong Kong:*** Pantoloc; ***Hung.:*** Controloc; Nolpaza; Pantacid; Zimpax; ***India:*** Eracid†; Pantodac; Pantop; Pantosec; Pentaloc; Praize; ***Indon.:*** Pantozol; ***Irl.:*** Protium; ***Israel:*** Controloc; ***Ital.:*** Pantecta; Pantopan; Pantorc; Peptazol; ***Malaysia:*** Controloc; ***Mex.:*** Pantozol; Prazolan; Tecta; Zolpra; Zurcal; ***Neth.:*** Pantorc; Pantozol; ***Norw.:*** Somac; ***NZ:*** Somac; ***Philipp.:*** Pantoloc; Ulcepraz; ***Pol.:*** Controloc; ***Port.:*** Apton; Pantoc; Praoz; Zurcal; ***Rus.:*** Sunpraz (Санпраз); ***S.Afr.:*** Controloc; Pantocid; Pantoloc; Topzole; ***Singapore:*** Controloc; ***Spain:*** Anagastra; Pantecta; Pantocarm; Ulcotenal; ***Swed.:*** Pantoloc; ***Switz.:*** Pantozol; Zurcal; ***Thai.:*** Controloc; ***Turk.:*** Panthec; Panto; Pantpas; Pulcet; ***UK:*** Protium; ***USA:*** Protonix; ***Venez.:*** Pantop.

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