
PANSPED 40

1. Generic Name

Pantoprazole Tablets I.P.

2. Qualitative and quantitative Composition:

Each enteric coated tablet contains:

Pantoprazole Sodium I.P.

(as sesquihydrate)

Equivalent to Pantoprazole 40 mg

Colour: Titanium Dioxide I.P.

The excipients used are Mannitol, Crospovidone, Sodium Carbonate anhydrous, Hydroxypropylcellulose, Sodium Carbonate anhydrous, Crospovidone, Calcium Stearate, Hydroxypropylmethylcellulose, Titanium Dioxide, Propylene Glycol, Triethyl Citrate, Eudragit, Talc.

3. Dosage form and strength

Dosage form: Enteric coated tablet

Strength: 40 mg

4. Clinical particulars

4.1. Therapeutic indication

Gastric ulcer, Duodenal ulcer, Zollinger-Ellison-syndrome and Gastro-esophageal reflux diseases (GERD).

4.2. Posology and method of administration

Posology

Gastro-esophageal reflux diseases

The recommended dose is 40 mg pantoprazole (one tablet) per day. It might be necessary to take the tablets for 2-3 consecutive days to achieve improvement of symptoms. Once complete relief of symptoms has occurred, treatment should be discontinued. The treatment should not exceed 4 weeks without consulting a doctor. If no symptom relief is obtained within 2 weeks of continuous treatment, the patient should be instructed to consult a doctor.

Gastric ulcer

One tablet of Pantoprazole per day. In individual cases the dose may be doubled (increase to 2 tablets Pantoprazole daily) especially when there has been no response to other treatment. A 4-week period is usually required for the treatment of gastric ulcers. If this is not sufficient, healing will usually be achieved within a further 4 weeks.

Duodenal ulcer

One tablet of Pantoprazole per day. In individual cases the dose may be doubled (increase to 2 tablets Pantoprazole daily) especially when there has been no response to other treatment. A duodenal ulcer generally heals within 2 weeks. If a 2-week period of treatment is not sufficient, healing will be achieved in almost all cases within a further 2 weeks.

Zollinger-Ellison-Syndrome

For the long-term management of Zollinger-Ellison-Syndrome and other pathological hypersecretory conditions patients should start their treatment with a daily dose of 80 mg (2 tablets of Pantoprazole 40 mg). Thereafter, the dose can be titrated up or down as needed using measurements of gastric acid secretion to guide. With doses above 80 mg daily, the dose should be divided and given twice daily. Treatment duration in Zollinger-Ellison syndrome and other pathological hypersecretory conditions is not limited and should be adapted according to clinical needs.

Special populations

Patients with hepatic Impairment

A daily dose of 20 mg pantoprazole (1 tablet of 20 mg pantoprazole) should not be exceeded in patients with severe liver impairment. Pantoprazole must not be used in combination treatment for eradication of *H. pylori* in patients with moderate to severe hepatic dysfunction since currently no data are available on the efficacy and safety of Pantoprazole in combination treatment of these patients.

Patients with renal Impairment

No dose adjustment is necessary in patients with impaired renal function. Pantoprazole must not be used in combination treatment for eradication of *H. pylori* in patients with impaired renal function since currently no data are available on the efficacy and safety of Pantoprazole in combination treatment for these patients.

Older people

No dose adjustment is necessary in elderly patients.

Paediatric population

Pantoprazole is not recommended for use in children and adolescents below 18 years of age due to insufficient data on safety and efficacy.

Method of administration

Pantoprazole 40 mg delayed release tablets should not be chewed or crushed and should be swallowed whole with liquid before a meal.

4.3. Contraindications

Hypersensitivity to the active substance, or to any of the excipients. Co-administration with atazanavir.

4.4. Special warnings and precautions for use

Hepatic Impairment

In patients with severe liver impairment, the liver enzymes should be monitored regularly during treatment with pantoprazole, particularly on long-term use. In the case of a rise of the liver enzymes, the treatment should be discontinued.

Combination therapy

In the case of combination therapy, the summaries of product characteristics of the respective medicinal products should be observed.

Gastric malignancy

Symptomatic response to pantoprazole may mask the symptoms of gastric malignancy and may delay diagnosis in the presence of any alarm symptom (e. g. significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis, anaemia or melaena) and when gastric ulcer is suspected or present, malignancy should be excluded. Further investigation is to be considered if symptoms persist despite adequate treatment.

Co-administration with HIV protease inhibitors

Co-administration of pantoprazole is not recommended with HIV protease inhibitors for which absorption is dependent on acidic intragastric pH such as atazanavir, due to significant reduction in their bioavailability.

Influence on vitamin B12 absorption.

In patients with Zollinger-Ellison syndrome and other pathological hypersecretory conditions requiring long-term treatment, pantoprazole, as all acid-blocking medicines, may reduce the absorption of vitamin B12 (cyanocobalamin) due to hypo- or achlorhydria. This should be considered in patients with reduced body stores or risk factors for reduced vitamin B12 absorption on long-term therapy or if respective clinical symptoms are observed.

Long term treatment

In long-term treatment, especially when exceeding a treatment period of 1 year, patients should be kept under regular surveillance.

Gastrointestinal infections caused by bacteria.

Treatment with Pantoprazole may lead to a slightly increased risk of gastrointestinal infections caused by bacteria such as Salmonella and Campylobacter and C. difficile.

Hypomagnesaemia

Severe hypomagnesaemia has been reported in patients treated with PPIs like pantoprazole for at least three months, and in most cases for a year. Serious manifestations of hypomagnesaemia such as fatigue, tetany, delirium, convulsions, dizziness and ventricular arrhythmia can occur but they may begin insidiously and be overlooked. In most affected patients, hypomagnesaemia improved after magnesium replacement and discontinuation of the PPI. For patients expected to be on prolonged treatment or who take PPIs with digoxin or medicinal products that may cause hypomagnesaemia (e.g., diuretics), health care professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.

Bone fractures

Proton pump inhibitors, especially if used in high doses and over long durations (>1 year), may modestly increase the risk of hip, wrist and spine fracture, predominantly in the older people or in presence of other recognised risk factors. Observational studies suggest that proton pump inhibitors may increase the overall risk of fracture by 10–40%. Some of this increase may be due to other risk factors. Patients at risk of osteoporosis should receive care according to current clinical guidelines and they should have an adequate intake of vitamin D and calcium.

Subacute cutaneous lupus erythematosus (SCLE)

Proton pump inhibitors are associated with very infrequent cases of SCLE. If lesions occur, especially in sun-exposed areas of the skin, and if accompanied by arthralgia, the patient should seek medical help promptly and the health care professional should consider stopping Pantoprazole. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

Interference with laboratory tests

Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, Pantoprazole treatment should be stopped for at least 5 days before CgA measurements. If CgA and gastrin levels have not returned to reference range after initial measurement, measurements should be repeated 14 days after cessation of proton pump inhibitor treatment.

4.5. Drugs interactions

Pantoprazole may reduce the absorption of active substances whose bioavailability is dependent on the gastric pH (e.g. ketoconazole).

It has been shown that co-administration of atazanavir 300 mg/ritonavir 100 mg with omeprazole (40 mg once daily) or atazanavir 400 mg with lansoprazole (60 mg single dose) to healthy volunteers resulted in a substantial reduction in the bioavailability of atazanavir. The absorption of atazanavir is pH dependent. Therefore, pantoprazole must not be coadministered with atazanavir.

Although no interaction during concomitant administration of phenprocoumon or warfarin has been observed in clinical pharmacokinetic studies, a few isolated cases of changes in International Normalised Ratio (INR) have been reported during concomitant treatment in the post-marketing period. Therefore, in patients treated with coumarin anticoagulants (e.g. phenprocoumon or warfarin), monitoring of prothrombin time/INR is recommended after initiation, termination or during irregular use of pantoprazole.

Concomitant use of high dose methotrexate (e.g. 300 mg) and proton-pump inhibitors has been reported to increase methotrexate levels in some patients. Therefore, in settings where highdose methotrexate is used, for example cancer and psoriasis, a temporary withdrawal of pantoprazole may need to be considered.

Pantoprazole is metabolized in the liver via the cytochrome P450 enzyme system. Interaction studies with carbamazepine, caffeine, diazepam, diclofenac, digoxin, ethanol, glibenclamide, metoprolol, naproxen, nifedipine, phenytoin, piroxicam, theophylline and an oral contraceptive containing levonorgestrel and ethinyl oestradiol did not reveal clinically

significant interactions. However, an interaction of pantoprazole with other substances which are metabolised by the same enzyme system cannot be excluded.

There were no interactions with concomitantly administered antacids.

4.6. Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

There are no adequate data from the use of pantoprazole in pregnant women. Studies in animals have shown reproductive toxicity. Preclinical studies revealed no evidence of impaired fertility or teratogenic effects. The potential risk for humans is unknown. Pantoprazole should not be used during pregnancy.

Breast-feeding

It is unknown whether pantoprazole is excreted in human breast milk. Animal studies have shown excretion of pantoprazole in breast milk. Pantoprazole should not be used during breastfeeding.

Fertility

There was no evidence of impaired fertility following the administration of pantoprazole in animal studies.

4.7. Effects on ability to drive and use machines.

Pantoprazole has no or negligible influence on the ability to drive and use machines. However, adverse reactions such as dizziness and visual disturbances may occur. If affected, patients should not drive or use machines.

4.8. Undesirable effects

Summary of the safety profile

Approximately 5% of patients can be expected to experience adverse reactions. The most commonly reported adverse reactions are diarrhoea and headache, both occurring in approximately 1% of patients.

Tabulated list of adverse reactions

The following adverse reactions have been reported with pantoprazole.

Within the following table, adverse reactions are ranked under the MedDRA frequency classification: Very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$), not known (cannot be estimated from the available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Adverse reactions with pantoprazole in clinical trials and post-marketing experience

Frequency	Uncommon	Rare	Very rare	Not known
System Organ Class				

Frequency	Uncommon	Rare	Very rare	Not known
Blood and lymphatic system disorders		Agranulocytosis	Thrombocytopenia; Leukopenia, Pancytopenia	
Immune system disorders		Hypersensitivity (incl. anaphylactic reactions and anaphylactic shock)		
Metabolism and nutrition disorders		Hyperlipidaemias and lipid increases (triglycerides, cholesterol); Weight changes		Hyponatraemia, Hypomagnesaemia
Psychiatric disorders	Sleep disorders	Depression (and all aggravations)	Disorientation (and all aggravations)	Hallucination; Confusion (especially in predisposed patients, as well as the aggravation of these symptoms in case of pre-existence)
Nervous system disorders	Headache; Dizziness	Taste disorders		
Eye disorders		Disturbances in vision / blurred vision		
Gastrointestinal disorders	Diarrhoea; Nausea / vomiting; Abdominal distension and bloating; Constipation; Dry mouth; Abdominal pain and discomfort			
Hepatobiliary disorders	Liver enzymes increased (transaminases, γ -GT)	Bilirubin increased		Hepatocellular injury; Jaundice; Hepatocellular failure

Frequency	Uncommon	Rare	Very rare	Not known
Skin and subcutaneous tissue disorders	Rash / exanthema / eruption; Pruritus	Urticaria; Angioedema		Stevens-Johnson syndrome; Lyell syndrome; Erythema multiforme; Photosensitivity Subacute cutaneous lupus erythematosus
Musculoskeletal and connective tissue disorders		Arthralgia; Myalgia		
Renal and urinary disorders				Interstitial nephritis; Acute Kidney Injury
Reproductive system and breast disorders		Gynaecomastia		
General disorders and administration site conditions	Asthenia, fatigue and malaise	Body temperature increased; Oedema peripheral		

Reporting of adverse reactions

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting By reporting side effects, you can help provide more information on the safety of this medicine.

4.9. Overdose

There are no known symptoms of overdose in man.

Doses up to 240 mg administered intravenously over 2 minutes were well tolerated. As pantoprazole is extensively protein bound, it is not readily dialysable.

In the case of overdose with clinical signs of intoxication, apart from symptomatic and supportive treatment, no specific therapeutic recommendations can be made.

5. Pharmacological properties

5.1. Mechanism of Action

Pantoprazole is a substituted benzimidazole which inhibits the secretion of hydrochloric acid in the stomach by specific blockade of the proton pumps of the parietal cells.

Pantoprazole is converted to its active form, a cyclic sulphenamide, in the acidic environment in the parietal cells where it inhibits the H⁺, K⁺-ATPase enzyme, i. e. the final stage in the production of hydrochloric acid in the stomach.

5.2. Pharmacodynamic properties

The inhibition of hydrochloric acid in the stomach is dose-dependent and affects both basal and stimulated acid secretion. In most patients, freedom from heartburn and acid reflux symptoms is achieved in 1 week. Pantoprazole reduces acidity in the stomach and thereby increases gastrin in proportion to the reduction in acidity. The increase in gastrin is reversible. Since pantoprazole binds to the enzyme distal to the receptor level, it can inhibit hydrochloric acid secretion independently of stimulation by other substances (acetylcholine, histamine, gastrin). The effect is the same whether the active substance is given orally or intravenously.

The fasting gastrin values increase under pantoprazole. On short-term use, in most cases they do not exceed the upper limit of normal. During long-term treatment, gastrin levels double in most cases. An excessive increase, however, occurs only in isolated cases. As a result, a mild to moderate increase in the number of specific endocrine (ECL) cells in the stomach is observed in a minority of cases during long-term treatment (simple to adenomatoid hyperplasia). However, according to the studies conducted so far, the formation of carcinoid precursors (atypical hyperplasia) or gastric carcinoids as were found in animal experiments have not been observed in humans.

During treatment with antisecretory medicinal products, serum gastrin increases in response to the decreased acid secretion. Also, CgA increases due to decreased gastric acidity. The increased CgA level may interfere with investigations for neuroendocrine tumours.

Available published evidence suggests that proton pump inhibitors should be discontinued between 5 days and 2 weeks prior to CgA measurements. This is to allow CgA levels that might be spuriously elevated following PPI treatment to return to reference range.

5.3. Pharmacokinetic properties

Pharmacokinetics do not vary after single or repeated administration. In the dose range of 10 to 80 mg, the plasma kinetics of pantoprazole are linear after both oral and intravenous administration.

Absorption

Pantoprazole is completely and rapidly absorbed after oral administration. The absolute bioavailability from the tablet was found to be about 77 %. On average, at about 2.0 h - 2.5 h post administration (t_{max}) of a single 20 mg oral dose, the maximum serum concentrations (C_{max}) of about 1-1.5 µg/ml are achieved, and these values remain constant after multiple administration. Concomitant intake of food had no influence on bioavailability (AUC or C_{max}), but increased the variability of the lag-time (t_{lag}).

Distribution

Volume of distribution is about 0.15 l/kg and serum protein binding is about 98%.

Biotransformation

Pantoprazole is almost exclusively metabolized in the liver.

Elimination

Clearance is about 0.1 l/h/kg, and terminal half-life ($t_{1/2}$) about 1 h. There were a few cases of subjects with delayed elimination. Due to the specific binding of pantoprazole to the proton pumps within the parietal cell, the elimination half-life does not correlate with the much longer duration of action (inhibition of acid secretion).

Renal elimination represents the major route of excretion (about 80%) for the metabolites of pantoprazole; the rest is excreted with the faeces. The main metabolite in both serum and urine is desmethylpantoprazole, which is conjugated with sulphate. The half-life of the main metabolite (about 1.5 h) is not much longer than that of pantoprazole.

Special populations

Renal impairment

No dose reduction is recommended when pantoprazole is administered to patients with impaired renal function (including patients on dialysis, which removes only negligible amounts of pantoprazole). As with healthy subjects, the half-life of pantoprazole is short. Although the main metabolite has a longer half-life (2-3h), excretion is still rapid and thus accumulation does not occur.

Hepatic impairment

After administration of pantoprazole to patients with liver impairment (Child-Pugh classes A, B and C) the half-life values increased to between 3 and 7 h and the AUC values increased by a factor of 3-6, whereas the C_{max} only increased slightly by a factor of 1.3 compared with healthy subjects.

Elderly

The slight increase in AUC and C_{max} in elderly volunteers compared with younger subjects was not clinically relevant.

6. Nonclinical properties

6.1. Animal Toxicology or Pharmacology

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity.

In the 2-year carcinogenicity studies in rats, neuroendocrine neoplasms were found. In addition, squamous cell papillomas were found in the forestomach of rats in one study. The mechanism leading to the formation of gastric carcinoids by substituted benzimidazoles has been carefully investigated and allows the conclusion that it is a secondary reaction to the massively elevated serum gastrin levels occurring in the rat during chronic high-dose treatment.

In the 2-year rodent studies an increased number of liver tumors was observed in rats (in one rat study only) and in female mice and was interpreted as being due to pantoprazole's high metabolic rate in the liver.

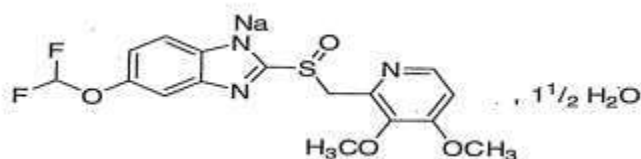
A slight increase of neoplastic changes of the thyroid was observed in the group of rats receiving the highest dose (200 mg/kg) in one 2-year study. The occurrence of these neoplasms is associated with the pantoprazole-induced changes in the breakdown of thyroxine in the rat liver. As the therapeutic dose in man is low, no side effects on the thyroid glands are expected.

In animal studies (rats) 5 mg/kg was the observed NOAEL (No Observed Adverse Effect Level) for embryotoxicity. Investigations revealed no evidence of impaired fertility or teratogenic effects.

Penetration of the placenta was investigated in the rat and was found to increase with advanced gestation. As a result, concentration of pantoprazole in the foetus is increased shortly before birth.

7. Description

Pantoprazole Sodium is sodium 5-(difluoromethoxy)-2-[(3,4-dimethoxy-pyridin-2-yl)methyl]sulphonyl-benzimidazol-1-ide, sesquihydrate. . having molecular formula of $C_{16}H_{14}F_2N_3NaO_4S \cdot 1.5 H_2O$ molecular weight is 432.4 the chemical structure is:



Pantoprazole is a white to off white powder.

Product Description: PANSPED 40 white to pale yellow colored, oval shape, biconvex, enteric coated tablets, plain on both sides.

8. Pharmaceutical particulars

8.1. Incompatibilities

None stated

8.2. Shelf-life

Do not use later than the date of expiry.

8.3. Packaging information

PANSPED 40 is packed in blister strips of 15 tablets

8.4. Storage and handing instructions.

Store at a temperature not exceeding 30° C, protected from light and moisture. Keep out of reach of children.

9. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

10. Details of manufacturer

Torrent Pharmaceuticals Ltd.

32 No. Middle Camp, NH-10,
East Districk, Gangtok, Sikkim-737 135

11. Details of permission or licence number with date

M/563/2010 issued on 23.12.2016

12. Date of revision

MAR 2025

MARKETED BY



TORRENT PHARMACEUTICALS LTD.

Torrent House, Off Ashram Road,

Ahmedabad-380 009, INDIA

IN/PANSPED 40/MAR 2025/05/PI