Patient Information Leaflet

For the use of a Registered Medical Practitioner, or a Hospital, or a Laboratory only

PANTOPRAZOLE GASTRO-RESISTANT TABLETS IP 40 MG

PROPLEXCID™ 40

1. GENERIC NAME

Pantoprazole Gastro-Resistant Tablets IP 40 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each enteric coated tablet contains:

Pantoprazole Sodium IP	
eq. to Pantoprazole	40 mg
Excipients	q.s.

Colours: Ferric Oxide Yellow USP-NF & Titanium Dioxide IP

3. DOSAGE FORM AND STRENGTH

Oral Dosage Form (Tablets)

Pantoprazole 40 mg

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

It is indicated for the treatment of gastric ulcer, duodenal ulcer, moderate and severe reflux oesophagitis.

4.2 Posology and Method of Administration

Posology

Adults and adolescents 12 years of age and above:

Reflux oesophagitis

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 reflux oesophagitis. If this is not sufficient, healing will usually be achieved within a further 4 weeks.

Treatment of gastric ulcer

One tablet of Pantoprazole per day. In individual cases the dose may be doubled (increase to 2 tablets of 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.

Treatment of duodenal ulcer

One tablet of Pantoprazole per day. In individual cases the dose may be doubled (increase to 2 tablets of 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.

Special populations

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.

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.

Elderly

No dose adjustment is necessary in the elderly.

Paediatric population

Pantoprazole is not recommended for use in children below 12 years of age because of limited data on safety and efficacy in the age group.

4.3 Contraindications

Hypersensitivity to the active substance, substituted benzimidazoles.

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 hyper secretory 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* or *C.difficile*.

Hypomagnesaemia

Severe hypomagnesaemia has rarely 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 (and therewith associated hypocalcaemia and hypokalaemia) improved after magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPIs with digoxin or drugs 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 elderly 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.

Pantoprazole contains sodium

This medicine contains less than 1 mmol (23 mg) sodium per tablet, that is to say essentially 'sodium-free'.

4.5 Drug Interactions

Medicinal products with pH-Dependent Absorption Pharmacokinetics

Because of profound and long lasting inhibition of gastric acid secretion, pantoprazole may interfere with the absorption of other medicinal products where gastric pH is an important determinant of oral availability, e.g. some azole antifungals such as ketoconazole, itraconazole, posaconazole and other medicines such as erlotinib.

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.

If the combination of HIV protease inhibitors with a proton pump inhibitor is judged unavoidable, close clinical monitoring (e.g. virus load) is recommended. A pantoprazole dose of 20 mg per day should not be exceeded. Dosage of the HIV protease inhibitors may need to be adjusted.

Coumarin anticoagulants (phenprocoumon or warfarin)

Co-administration of pantoprazole with warfarin or phenprocoumon did not affect the pharmacokinetics of warfarin, phenprocoumon or INR. However, there have been reports of increased INR and prothrombin time in patients receiving PPIs and warfarin or phenprocoumon concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding, and even death. Patients treated with pantoprazole and warfarin or phenprocoumon may need to be monitored for increase in INR and prothrombin time.

Methotrexate

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

Other interactions studies

Pantoprazole is extensively metabolised in the liver via the cytochrome P450 enzyme system. The main metabolic pathway is demethylation by CYP2C19 and other metabolic pathways include oxidation by CYP3A4.

Interaction studies with medicinal products also metabolised with these pathways, like carbamazepine, diazepam, glibenclamide, nifedipine, and an oral contraceptive containing levonorgestrel and ethinyl oestradiol, did not reveal clinically significant interactions.

An interaction of pantoprazole with other medicinal products or compounds, which are metabolized using the same enzyme system, cannot be excluded.

Results from a range of interaction studies demonstrate that pantoprazole does not effect the metabolism of active substances metabolised by CYP1A2 (such as caffeine, theophylline), CYP2C9 (such as piroxicam, diclofenac, naproxen), CYP2D6 (such as metoprolol), CYP2E1 (such as ethanol) or does not interfere with p-glycoprotein related absorption of digoxin.

There were no interactions with concomitantly administered antacids.

Interaction studies have also been performed by concomitantly administering pantoprazole with the respective antibiotics (clarithromycin, metronidazole, amoxicillin). No clinically relevant interactions were found.

Medicinal products that inhibit or induce CYP2C19:

Inhibitors of CYP2C19 such as fluvoxamine could increase the systemic exposure of pantoprazole. A dose reduction may be considered for patients treated long-term with high doses of pantoprazole, or those with hepatic impairment.

Enzyme inducers affecting CYP2C19 and CYP3A4 such as rifampicin and St John´s wort *(Hypericum perforatum)* may reduce the plasma concentrations of PPIs that are metabolized through these enzyme systems.

4.6 Use in Specific Population

Pregnancy

A moderate amount of data on pregnant women (between 300-1000 pregnancy outcomes) indicate no malformative or feto/neonatal toxicity of Pantoprazole. Animal studies have shown reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of Pantoprazole during pregnancy.

Breast-feeding

Animal studies have shown excretion of pantoprazole in breast milk. There is insufficient information on the excretion of pantoprazole in human milk but excretion into human milk has been reported. A risk to the newborns/infants cannot be excluded. Therefore, a decision on whether to discontinue breastfeeding or to discontinue/abstain from Pantoprazole therapy taking into account the benefit of breast-feeding for the child, and the benefit of Pantoprazole therapy for the woman.

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. Adverse drug reactions, such as dizziness and visual disturbances may occur. If affected, patients should not drive or operate machines.

4.8 Undesirable Effects

Approximately 5 % of patients can be expected to experience adverse drug reactions (ADRs). The table below lists adverse reactions reported with pantoprazole, ranked under the following frequency classification: Very common (≥1/10); common (≥1/100 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.

Table 1: Adverse reactions with pantoprazole in clinical trials and post-marketing experience

Frequency / System Organ Class	Common	Uncommon	Rare	Very Rare	Not Known
Blood and lymphatic system disorders			Agranulocytosis	Thrombocytopenia; Leukopenia; Pancytopenia	
Immune system disorders			Hypersensitivity (including anaphylactic reactions and anaphylactic shock)		
Metabolism and nutrition disorders			Hyperlipidaemias and lipid increases (triglycerides, cholesterol); Weight changes		Hyponatraemia; Hypomagnesaemia ; Hypocalcaemia[1]; Hypokalaemia
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		Parathesia
Eye disorders			Disturbances in vision / blurred vision		
Gastrointestinal disorders	Fundic Gland Polyps (benign)	Diarrhoea; Nausea / vomiting; Abdominal distension and bloating; Constipation; Dry mouth; Abdominal pain and discomfort			Microscopic colitis
Hepatobiliary disorders		Liver enzymes increased (transaminases, γ-GT)	Bilirubin increased		Hepatocellular injury; Jaundice; Hepatocellular failure
Skin and subcutaneous tissue disorders		Rash / exanthema / eruption; Pruritus	Urticaria; Angioedema		Stevens-Johnson syndrome; Lyell syndrome; Erythema multiforme; Photosensitivity; Subacute cutaneous lupus erythematosus; drug rash with eosinophilia and systemic symptoms (DRESS)
Musculoskeletal and connective tissue disorders		Fracture of the hip, wrist or spine	Arthralgia; Myalgia		Muscle spasm [2]
Renal and urinary disorders					Interstitial nephritis (with possible progression to renal failure)
Reproductive system and breast disorders			Gynaecomastia		
General disorders and administration site conditions		Asthenia, fatigue and malaise	Body temperature increased; Oedema peripheral		

[1] Hypocalcaemia and hypokalaemia in association with hypomagnesaemia

[2] Muscle spasm as a consequence of electrolyte disturbance

➢ ***Acute Kidney Injury has been observed in patients taking PPIs including Pantoprazole.***

4.9 Overdose

- There are no known symptoms of overdose in man.
- Systemic exposure with 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 an overdose with clinical signs of intoxication, apart from symptomatic and supportive treatment, no specific therapeutic recommendations can be made.

5. PHARMACODYNAMIC & PHARMACOKINETIC 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 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. The inhibition is dose-dependent and affects both basal and stimulated acid secretion. In most patients, freedom from symptoms is achieved within 2 weeks. As with other proton pump inhibitors and H2 receptor inhibitors, treatment with 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 cell receptor level, it can inhibit hydrochloric acid secretion independently of stimulation by other substances (acetylcholine, histamine, gastrin). The effect is the same whether the product is given orally or intravenously.

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.

5.2 Pharmacodynamic Properties

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.

An influence of a long term treatment with pantoprazole exceeding one year cannot be completely ruled out on endocrine parameters of the thyroid according to results in animal studies.

5.3 Pharmacokinetic Properties

Absorption

Pantoprazole is rapidly absorbed and the maximal plasma concentration is achieved even after one single 40 mg oral dose. On average at about 2.5 h p.a. the maximum serum concentrations of about 2–3 µg/ml are achieved, and these values remain constant after multiple administration. Pharmacokinetics does 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. The absolute bioavailability from the tablet was found to be about 77%. Concomitant intake of food had no influence on AUC, maximum serum concentrations and thus bioavailability. Only the variability of the lag-time will be increased by concomitant food intake.

Distribution

Pantoprazole's serum protein binding is about 98%. Volume of distribution is about 0.15 l/kg.

Biotransformation

The substance is almost exclusively metabolised in the liver. The main metabolic pathway is demethylation by CYP2C19 with subsequent sulphate conjugation, other metabolic pathways include oxidation by CYP3A4.

Elimination

Terminal half-life is about 1 hour and clearance is about 0.1 l/h/kg. There were a few cases of subjects with delayed elimination. Because of the specific binding of pantoprazole to the proton pumps of 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 the serum and urine is desmethyl pantoprazole which is conjugated with sulphate. The half-life of the main metabolite (about 1.5 hours) is not much longer than that of pantoprazole.

Special populations

Poor metabolisers

Approximately 3 % of the European population lack a functional CYP2C19 enzyme and are called poor metabolisers. In these individuals the metabolism of pantoprazole is probably mainly catalysed by CYP3A4. After a single-dose administration of 40 mg pantoprazole, the mean area under the plasma concentration-time curve was approximately 6 times higher in poor metabolisers than in subjects having a functional CYP2C19 enzyme (extensive metabolisers). Mean peak plasma concentrations were increased by about 60 %. These findings have no implications for the posology of pantoprazole.

Renal impairment

No dose reduction is recommended when pantoprazole is administered to patients with impaired renal function (including dialysis patients). As with healthy subjects, pantoprazole's half-life is short. Only very small amounts of pantoprazole are dialysed. Although the main metabolite has a moderately delayed half-life (2 - 3 h), excretion is still rapid and thus accumulation does not occur.

Hepatic impairment

Although for patients with liver cirrhosis (classes A and B according to Child) the half-life values increased to between 7 and 9 h and the AUC values increased by a factor of 5 - 7, the maximum serum concentration only increased slightly by a factor of 1.5 compared with healthy subjects.

Elderly

A slight increase in AUC and C_{max} in elderly volunteers compared with younger counterparts is also not clinically relevant.

Paediatric population

Following administration of single oral dose of 20 or 40 mg pantoprazole to children aged 5 to 16 years AUC and C_{max} were in the range of corresponding values in adults.

Following administration of single i.v. doses of 0.8 or 1.6 mg/kg pantoprazole to children aged 2 - 16 years there was no significant association between pantoprazole clearance and age or weight. AUC and volume of distribution were in accordance with data from adults.

6. NONCLINICAL PROPERTIES

6.1. Animal Toxicology or Pharmacology

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

In a two-year carcinogenicity studies in rats neuroendocrine neoplasms were found. In addition, squamous cell papillomas were found in the forestomach of rats. 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 two-year rodent studies an increased number of liver tumors was observed in rats 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). 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 harmful effects on the thyroid glands are expected.

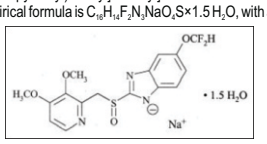
In a peri-postnatal rat reproduction study designed to assess bone development, signs of offspring toxicity (mortality, lower mean body weight, lower mean body weight gain and reduced bone growth) were observed at exposures (C_{max}) approximately 2x the human clinical exposure. By the end of the recovery phase, bone parameters were similar across groups and body weights were also trending toward reversibility after a drug-free recovery period. The increased mortality has only been reported in pre-weaning rat pups (up to 21 days age) which is estimated to correspond to infants up to the age of 2 years old. The relevance of this finding to the paediatric population is unclear. A previous peri-postnatal study in rats at slightly lower doses found no adverse effects at 3 mg/kg compared with a low dose of 5 mg/kg in this study.

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

The active ingredient Pantoprazole Gastro-resistant Tablets, a PPI, is a substituted benzimidazole, sodium 5-(difluoromethoxy)-2-[(3,4-dimethoxy-2-pyridinyl)methyl] sulfinyl]-1H-benzimidazole sesquihydrate, a compound that inhibits gastric acid secretion. Its empirical formula is $C_{16}H_{14}F_2N_3NaO_4S \times 1.5\,H_2O$, with a molecular weight of 432.4.



Pantoprazole sesquihydrate is a white to off-white crystalline powder and is racemic. Pantoprazole has weakly basic and acidic properties. Pantoprazole sesquihydrate is freely soluble in water, very slightly soluble in phosphate buffer at pH 7.4, and practically insoluble in n-hexane. The stability of the compound in aqueous solution is pH-dependent. The rate of degradation increases with decreasing pH. At ambient temperature, the degradation half-life is approximately 2.8 hours at pH 5 and approximately 220 hours at pH 7.8.

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

Not applicable.

8.2 Shelf Life

Please refer details on blister / carton.

8.3 Packaging Information

Alu-Alu Blister of 10 tablets.

8.4 Storage and Handling Instructions

Store protected from moisture, at a temperature not exceeding 25°C.

9. PATIENT COUNSELLING INFORMATION

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What Pantoprazole Tablets are and what they are used for?

Pantoprazole Tablets contain the active substance pantoprazole. Pantoprazole is a selective "proton pump inhibitor", a medicine which reduces the amount of acid produced in your stomach. It is used for treating acid-related diseases of the stomach and intestine.

Pantoprazole is used for treating:

Adults and adolescents 12 years of age and above:

- Reflux oesophagitis: An inflammation of your oesophagus (the tube that connects your throat to your stomach) accompanied by the regurgitation of stomach acid.

Adults:

- An infection with a bacterium called Helicobacter pylori in patients with duodenal ulcers and stomach ulcers in combination with two antibiotics (Eradication therapy). The aim is to get rid of the bacteria and so reduces the likelihood of these ulcers returning.
- Stomach and duodenal ulcers.
- Zollinger-Ellison-Syndrome and other conditions producing too much acid in the stomach.

What you need to know before you take Pantoprazole Tablets?

Do not take Pantoprazole Tablets:

- If you are allergic to pantoprazole, or any of the other ingredients of this medicine.
- If you are allergic to medicines containing other proton pump inhibitors.

Tell your doctor immediately, before or after taking this medicine, if you notice any of the following symptoms, which could be a sign of another more serious disease:

- An unintentional loss of weight.
- Repeated vomiting.
- Difficulty in swallowing or pain when swallowing.
- Vomiting blood: this may appear as dark coffee grounds in your vomit.
- You look pale and feel weak (anaemia).
- You notice blood in your stools: which may be black or tarry in appearance.
- Chest pain.
- Stomach pain.
- Severe and/or persistence diarrhoea, as pantoprazole has been associated with a small increase in infectious diarrhoea.

Your doctor may decide that you need some tests to rule out malignant disease because pantoprazole also alleviates the symptoms of cancer and could cause delay in diagnosing it. If your symptoms continue in spite of your treatment, further investigations will be considered.

Children and Adolescent

Pantoprazole is not recommended for use in children as it has not been proven to work in children below 12 years of age.

Other medicines and Pantoprazole

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

This is because Pantoprazole may influence the effectiveness of other medicines, so tell your doctor if you are taking:

- Medicines such as ketoconazole, itraconazole and posaconazole (used to treat fungal infections) or erlotinib (used for certain types of cancer) because pantoprazole may stop these and other medicines from working properly.
- Warfarin and phenprocoumon, which affect the thickening, or thinning of the blood. You may need further checks.
- Atazanavir (used to treat HIV-infection).
- Methotrexate (used to treat rheumatoid arthritis, psoriasis, and cancer) – if you are taking methotrexate your doctor may temporarily stop your Pantoprazole treatment because pantoprazole can increase levels of methotrexate in the blood.
- Fluvoxamine (used to treat depression and other psychiatric diseases) – if you are taking fluvoxamine your doctor may reduce the dose.
- Rifampicin (used to treat infections).
- St John's wort (Hypericum perforatum) (used to treat mild depression).

Pregnancy and breast-feeding

There are no adequate data from the use of pantoprazole in pregnant women. Excretion into human milk has been reported. If you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. You should use this medicine only if your doctor considers the benefit for you greater than the potential risk for your unborn child or baby.

Driving and using machines

Pantoprazole has no or negligible influence on the ability to drive and use machines. If you experience side effects like dizziness or disturbed vision, you should not drive or operate machines.

How to take Pantoprazole Tablets?

- Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.
- Take the tablets 1 hour before a meal without chewing of breaking them and swallow them whole with some water
- ***For treatment of an infection with a bacterium called Helicobacter pylori in patients with duodenal ulcers and stomach ulcers in combination with two antibiotics.*** One tablet, two times a day plus two antibiotic tablets of either amoxicillin, clarithromycin and metronidazole (or tinidazole), each to be taken two times a day with your Pantoprazole Tablet. Take the first Pantoprazole Tablet 1 hours before breakfast and the second Pantoprazole Tablet 1 hour before your evening meal. Follow your doctor's instructions and make sure you read the package leaflets for these antibiotics. The usual treatment period is one to two weeks.
- ***For the treatment of stomach and duodenal ulcers.*** The usual dose is one tablet a day. After consultation with your doctor, the dose may be doubled. Your doctor will tell you how long to take your medicine. The treatment period for stomach ulcers is usually between 4 and 8 weeks. The treatment period for duodenal ulcers is usually between 2 and 4 weeks.
- ***For the long-term treatment of Zollinger-Ellison Syndrome and of other conditions in which too much stomach acid is produced.*** The recommended starting dose is usually two tablets a day. Take the two tablets 1 hour before a meal. Your doctor may later adjust the dose, depending on the amount of stomach acid you produce. If prescribed more than two tablets a day, the tablets should be taken twice daily.

If your doctor prescribes a daily dose of more than four tablets a day, you will be told exactly when to stop taking the medicine.

Special patient groups:

- If you have kidney problems, moderate or severe liver problems, you should not take pantoprazole for eradication of Helicobacter pylori.
- If you suffer from severe liver problems, you should not take more than one tablet 20mg pantoprazole a day (for this purpose tablets containing 20 mg pantoprazole are available).
- Children below 12 years. These tablets are not recommended for use in children below 12 years.

If you take more Pantoprazole Tablets than you should

Tell your doctor or pharmacist. There are no known symptoms of overdose.

If you forget to take Pantoprazole Tablets

Do not take a double dose to make up for a forgotten dose. Take your next normal dose at the usual time.

If you stop taking Pantoprazole Tablets

Do not stop taking these tablets without first talking to your doctor or pharmacist.

If you have any further questions about the use of this medicine, ask your doctor, pharmacist or nurse.

Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

➢ ***Acute Kidney Injury has been observed in patients taking PPIs including Pantoprazole.***

Common

- Benign polyps in the stomach.

Uncommon

- Headache
- Dizziness
- Diarrhoea
- Feeling sick, vomiting
- Bloating and flatulence (wind)
- Constipation
- Dry mouth
- Abdominal pain and discomfort
- Skin rash, exanthema, eruption, itching
- Feeling weak, exhausted or generally unwell
- Sleep disorders
- Fractures in the hip, wrist or spine.
- An increase in liver enzymes.

Rare

- Distortion or complete lack of the sense of taste
- Disturbance in visions such as blurred vision
- Hives
- Pain in the joints, muscle pains
- Weight changes
- Raised body temperature, high fever.
- Swelling of the extremities (peripheral oedema).
- Allergic reactions.
- Depression.
- Disorientation, an increase in bilirubin.
- Increased fat levels in blood.
- Sharp drop in circulating granular white blood cells, associated with high fever, an increase in bilirubin.
- Increased fat levels in blood.
- Sharp drop in circulating granular white blood cells, associated with high fever.

10. DETAILS OF MANUFACTURER

Windlas Biotech Limited (Plant-3),
(WHO-GMP Certified Company)
Plot No. 39, Pharmacity, Selaqui,
Dehradun-248197, Uttarakhand.

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

License Number: 30/UA/2020 **Dated:** 07/09/2021

12. DATE OF REVISION

NA

Marketed by:

PLEXCURE

PLEXCURE HEALTHCARE PVT. LTD.

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