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PANTOPRAZOLE

PANTOCAR™-40

40 mg Tablet
PROTON PUMP INHIBITOR

PRODUCT NAME: Pantoprazole

DOSAGE FORM AND STRENGTH: Pantoprazole Tablets 40 mg

PHARMACOLOGIC CATEGORY: Drugs for acid related disorders, Proton pump inhibitors

PRODUCT DESCRIPTION: Light yellow coloured, circular, biconvex delayed release tablets with plain on both surfaces

FORMULATION/COMPOSITION:

Each enteric-coated tablet contains :

Pantoprazole Sodium Sesquihydrate equivalent to
Pantoprazole 40 mg

PHARMACODYNAMICS/PHARMACOKINETICS:

Pharmacodynamics:

Pantoprazole is substituted benzimidazoles 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 sulphonamide, 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 inhibitor and H₂ receptor inhibitors. 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, and gastrin). The effect is the same whether the active substance is given orally or intravenously.

Pharmacokinetics:

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.

INDICATIONS:

Used for short treatment (up to 8 weeks) in the healing and symptomatic relief of erosive esophagitis (damage to the esophagus from stomach acid cause by gastroesophageal reflux disease or GERD).

Pantoprazole is also used to treat Zollinger-Ellison Syndrome and other conditions involving excess stomach acid.

DOSAGE AND MODEL ROUTE OF ADMINISTRATION:

Posology

The recommended dose is 20 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.

Special populations

No dose adjustment is necessary in elderly patients or in those with impaired renal or liver function.

Paediatric population

Pantoprazole Control is not recommended for use in children and adolescents below 12 years of age due to insufficient data on safety and efficacy.

Method of administration

The tablets should not be chewed or crushed, and should be swallow whole 1 hour before meal with some water.

CONTRAINDICATIONS & PRECAUTION(S), WARNING(S)

Hypersensitivity to the active substance, or to any of the excipients

PRECAUTIONS & WARNINGS:

Patients should be instructed to consult a doctor if:

- They have unintentional weight loss, anaemia, gastrointestinal bleeding, dysphagia, persistent vomiting or vomiting with blood, since it may alleviate symptoms and delay diagnosis of a severe condition. In these cases, malignancy should be excluded.
- They have had previous gastric ulcer or gastrointestinal surgery.
- They are on continuous symptomatic treatment of indigestion or heartburn for 4 or more weeks.
- They have jaundice, hepatic impairment, or liver disease.
- They have any other serious disease affecting general well-being.
- They are aged over 55 years with new or recently changed symptoms.

Patients with long-term recurrent symptoms of indigestion or heartburn should see their doctor at regular intervals. Especially, patients over 55 years taking any non-prescription indigestion or heartburn remedy on a daily basis should inform their pharmacist or doctor.

Patients should not take another proton pump inhibitor or H₂ antagonist concomitantly.

Patients should consult their doctor before taking this medicinal product if they are due to have an endoscopy or urea breath test.

Patients should be advised that the tablets are not intended to provide immediate relief.

Patients may start to experience symptomatic relief after approximately one day of treatment with pantoprazole, but it might be necessary to take it for 7 days to achieve complete heartburn control. Patients should not take pantoprazole as a preventive medicinal product.

Gastrointestinal infections caused by bacteria

Decreased gastric acidity, due to any means - including proton pump inhibitors - increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with acid-reducing medicinal products leads to a slightly increased risk of gastrointestinal infections such as *Salmonella*, *Campylobacter*, or *Clostridium difficile*.

Sub acute 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 Control. 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 Control 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.

PREGNANCY AND LACTATION:

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.

Size: 210 x 280 mm

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 breast-feeding.

Fertility

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

INTERACTIONS:

Pantoprazole Control 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 co-administered with atazanavir.

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 PPI and warfarin or phenprocoumon concomitantly. Increase 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.

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 high-dose 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, and theophylline and an oral contraceptive containing levonorgestrel and ethynodiol 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.

ADVERSE 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.

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

Frequency	Uncommon	Rare	Very rare	Not known
System Organ Class				
Blood and lymphatic system disorders		Agranulocytosis	Thrombocytopenia; Leukopenia, Pancytopenia	
Immune system disorders		Hypersensitivity (incl. anaphylactic reactions and anaphylactic shock)		
Metabolism and nutrition disorders		Hyperlipidemias 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 pre-disposed patients, as well as the aggravation of these symptoms in case of pre-existence)
Nervous system disorders	Headache; Dizziness	Taste disorders		Paresthesia
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, y-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 Sub acute cutaneous lupus erythematosus
Musculoskeletal and connective tissue disorders	Fracture of the hip, wrist or spine	Arthralgia; Myalgia		Muscle spasm
Renal and urinary disorders				Interstitial nephritis
Reproductive system and breast disorders		Gynaecomastia		
General disorders and administration site conditions	Asthenia, fatigue and malaise	Body temperature increased; Oedema peripheral		

OVERDOSAGE AND TREATMENT:

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.

STORAGE CONDITION: Store at temperatures not exceeding 30°C.

DOSAGE FORMS AND PACKAGING AVAILABLE: Alu/Alu Blister Pack or 10's (Box of 30's and 100's)

INSTRUCTIONS AND SPECIAL PRECAUTIONS FOR HANDLING AND DISPOSAL (IF APPLICABLE): Not Applicable

NAME AND ADDRESS OF MARKETING AUTHORIZATION HOLDER:

Marketing Authorization Holder

Brown & Burk Philippines Inc.

U-501, 5/F., SEDCCO 1 Bldg., 120 Rada cor.,
Legaspi Sts., Legaspi Village, Makati City, Philippines

NAME AND ADDRESS OF MANUFACTURER:

MICRO LABS LIMITED

92, Sipcot Industrial Complex,
Hosur – 635 126, India.

CAUTION STATEMENT: FOODS, DRUGS, DEVICES, AND COSMETICS ACT PROHIBITS DISPENSING WITHOUT PRESCRIPTION.

ADR REPORTING STATEMENT:

"FOR SUSPECTED ADVERSE DRUG REACTION, REPORT TO THE FDA: www.fda.gov.ph

Seek medical attention immediately at the first sign of Adverse Drug Reaction.

REGISTRATION NUMBER: DRP-1018

DATE OF FIRST AUTHORIZATION: Aug. 2018

DATE OF REVISION OF PACKAGE INSERT: April 2019

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