Panosec
Tablet 40 mg
2058532

Panosec Tablet 40mg

Name of Product
Pantoprazole Gastro-Resistance Tablets 40mg

Name and Strength of Active Ingredient
Name : Pantoprazole Sodium Sesquihydrate
Strength : 40mg

Route of Administration: Oral

Product Description
Yellow to pale yellow, oval, biconvex delayed release tablets imprinted with 'H126' on one side with black ink and plain on the other side.

Pharmacodynamics
Mechanism of action
Pantoprazole is a substituted benzimidazole which inhibits the secretion of hydrochloric acid in the stomach by specific blockade of the p r oton 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. 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).
During treatment with antisecretory medicinal products, serum gastrin increases in response to the decreased acid secretion. Also CgA increases due to 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.

Pharmacokinetics
Absorption
Pantoprazole is rapidly absorbed and the maximal plasma concentration is achieved even after one single 40 mg oral dose. On average at about 2.0 h - 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 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. The absolute bioavailability from the tablet was found to be about 77%.
Concomitant intake of food had no influence on AUC, maximum serum concentration 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 metabolized on the liver. The main metabolic pathway is demethylation by CYP2C19 with subsequent sulphate conjugation, other metabolic pathway include oxidation by CYP3A4.

Elimination
Terminal half-life is about 1 hour and clearance is about 0.1 l/h/kg. 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 desmethylpantoprazole which is conjugated with sulphate. The half-life of the main metabolite (about 1.5 hours) is not much longer than that of pantoprazole.

Children
Following administration of single oral doses of 20 or 40 mg pantoprazole to children aged 5 - 16 years AUC and Cmax 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.

Indications
In combination with two appropriate antibiotics for the eradication of Helicobacter pylori in patients with peptic ulcers with the objective of reducing the recurrence of duodenal and gastric ulcers caused by this microorganism. Duodenal ulcer. Gastric ulcer. Moderate and severe cases of inflammation of the esophagus (reflux esophagitis). Zollinger-Ellison-Syndrome and other pathological hypersecretory conditions.

Recommended dose
Recommended Dose for Pantoprazole 40mg
The following information applies unless Panosec 40 mg has been otherwise prescribed by your doctor. Please follow these instructions, as otherwise Panosec 40 mg may not have the desired effect!

Adults and adolescents 12 years of age and above:
Treatment of moderate and severe reflux oesophagitis
One tablet of Panosec Tablet 40mg per day. In individual cases the dose may be doubled (increase to 2 tablets Panosec Tablet 40mg daily) especially when there has been no response to other treatment.

Adults:
Eradication of H. pylori in combination with two appropriate antibiotics
In cases of duodenal or gastric ulcer in which infection with Helicobacter pylori has been confirmed, the microorganism should be eradicated by combination treatment. Depending on the resistance pattern, the following combinations are recommended:
2 x 1 Panosec 40 mg gastro-resistant tablet / day
+ 2 x 1000 mg amoxicillin / day
+ 2 x 500 mg clarithromycin /day

2 x 1 Panosec 40 mg gastro-resistant tablet / day
+ 2 x 500 mg metronidazole / day
+ 2 x 500 mg clarithromycin / day

2 x 1 Panosec 40 mg gastro-resistant tablet / day
+ 2 x 1000 mg amoxicillin / day
+ 2 x 500 mg metronidazole / day

Treatment of gastric and duodenal ulcer
One tablet of Panosec Tablet 40mg per day. In individual cases the dose may be doubled (increase to 2 tablets Panosec Tablet 40mg daily) especially when there has been no response to other treatment.

Zollinger-Ellison-Syndrome and other pathological hypersecretory conditions
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 "Panosec Tablet 40mg"). Thereafter, the dosage 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. A temporary increase of the dosage above 160 mg pantoprazole is possible but should not be applied longer than required for adequate acid control. Treatment duration in Zollinger-Ellison-Syndrome and other pathological hypersecretory conditions is not limited and should be adapted according to clinical needs.

Children below 12 years of age:
Panosec Tablet 40mg is not recommended for use in children below 12 years of age due to limited data in this age group.

Type and duration of treatment
Combination therapy for eradication of Helicobacter pylori infection usually lasts 7 days and can be extended to a maximum of 2 weeks. If after this time further treatment with Panosec Tablet 40 mg is indicated to ensure that the ulcer heals completely, the dose recommendations for gastric and duodenal ulcers must be observed. In the majority of cases, a duodenal ulcer heals completely within 2 weeks. If a two-week treatment period is not sufficient, healing will be achieved in almost all cases within a further 2 weeks. Gastric ulcers and reflux esophagitis usually require a 4-week course of treatment. If this should be inadequate, healing will in most cases be achieved within a further 4 weeks. Treatment should not exceed 8 weeks as experience with long-term use is limited. Treatment duration in Zollinger-Ellison-Syndrome and other pathological hypersecretory conditions is not limited and should be adapted according to clinical needs.

Instructions for use / handling
Panosec Tablet 40 mg must not be chewed or crushed and must be swallowed whole with water 1 h before breakfast. In combination therapy for eradication of Helicobacter pylori infection the second Panosec Tablet 40 mg should be taken before the evening meal.

Contraindications
Hypersensitivity to the active substance, substituted benzimidazoles, or to any of the other excipients of Panosec tablet 40mg.

Warnings and precautions
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 alarm symptom (e.g. significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis, anaemia or maleana) 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.
Vitamin B12 deficiency
In patients with Zollinger-Ellison syndrome and other pathological hypersecretory conditions requiring long-term treatment, pantoprazole, as all acid-blocking medicines. Daily treatment with any acid suppressing medications over a long period of time (e.g. longer than 3 years) may lead to malabsorption of cyanocobalamin (vitamin B12) caused by hypo- or achlorhydria. Rare reports of cyanocobalamin deficiency occurring with acid-suppressing therapy have been reported in the literature. This diagnosis should be considered if clinical symptoms consistent with cyanocobalamin deficiency 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, 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 PPI 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.
Fractures
Proton pump inhibitors, especially if used in high doses and over long durations (>1year), 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 subacute cutaneous lupus erythematosus (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. If patient(s) are due to have a test on Chromogranin A level, Pantoprazole treatment should be stopped for at least 5 days before CgA measurements to avoid this interference (see section Pharmacodynamic). 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.
Regular Surveillance
Patients on proton pump inhibitor treatment (particularly those treated for long term) should be kept under regular surveillance.
Clostridium Difficile Diarrhea
Published observational studies suggest that PPI therapy may be associated with an increased risk of Clostridium difficile associated diarrhea, especially in hospitalized patients. The diagnosis should be considered for diarrhea that does not improve. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.

This medicinal product contains the colouring agent Ponceau 4R aluminium lake (E124), which may cause allergic reactions.

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

Size: 240 x 350mm
Pharmacodes: Front: 241 & Back: 242
No of colours: 01- Black
Die cut

Note: Pharma code position and Orientation are tentative, will be changed based on folding size.
If required pharma code shall be elongated along the length at the supplier end to suit pharmacode position at center after folding.

Interaction with other medicaments
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 bioavailability, e.g. some azole antifungals as ketoconazole, itraconazole, posaconazole and other medicine 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 20mg 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. 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.
Other interactions studies
Pantoprazole is extensively metabolized 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 metabolized with these pathways, like carbamazepine, diazepam, glibenclamide, nifedipine, and an oral contraceptive containing levonorgestrel and ethinyl oestradiol did not reveal clinically significant interactions.
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 administering pantoprazole concomitantly 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
Pregnancy and Lactation
Pregnancy
As a precautionary measure, it is preferable to avoid the use of Pantoprazole during pregnancy.
Breast-feeding
There is insufficient information on the excretion of pantoprazole into human breast milk. During breastfeeding, pantoprazole should only be used if the benefit to the woman outweighs the potential risk to the foetus or child.

Side Effects
The most commonly reported ADRs are diarrhoea and headache. The table below lists adverse reactions reported with pantoprazole. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

a) **Blood and lymphatic system disorders**
Rare : Agranulocytosis
Very rare : Thrombocytopenia; Leukopenia Pancytopenia
b) **Immune system disorders**
Rare : Hypersensitivity (including anaphylactic reactions and anaphylactic shock)
c) **Metabolism and nutrition disorders**
Vitamin B12 deficiency
Rare : Hyperlipidaemias and lipid increases (triglycerides, cholesterol); Weight changes
Not known : Hyponatraemia, Hypomagnesaemia, Hypocalcaemia in association with hypomagnesemia; Hypokalaemia
d) **Psychiatric disorders**
Uncommon : Sleep disorders
Rare : Depression (and all aggravations)
Very rare : Disorientation (and all aggravations)
Not known : Hallucination; Confusion (especially in pre-disposed patients, as well as the aggravation of these symptoms in case of pre-existence)
e) **Nervous system disorders**
Uncommon : Headache; Dizziness
Rare : Taste disorders
Not known : Paraesthesia
f) **Eye disorders**
Rare : Disturbances in vision/ blurred vision
g) **Gastrointestinal disorders**
Common : Fundic gland polyps (benign)
Uncommon : Diarrhoea; Nausea/vomiting;Abdominal distension and bloating; Constipation; Dry mouth; Abdominal pain and discomfort
Frequency 'not known': Microscopic Colitis
h) **Hepatobiliary disorders**
Uncommon : Liver enzymes increased (transaminases, γ-GT)
Rare : Bilirubin increased
Not known : Hepatocellular injury; Jaundice; Hepatocellular failure
i) **Skin and sub- cutaneous tissue disorders**
Uncommon : Rash/exanthema/eruption; Pruritus
Rare : Urticaria; Angioedema
Not known : Stevens- Johnson syndrome; Lyell syndrome; Subacute cutaneous lupus erythematosus
j) **Musculoskeletal and connective tissue disorders**
Uncommon : Fracture of the hip, wrist or spine
Rare : Arthralgia; Myalgia
Not known : Muscle spasm as a consequence of electrolyte disturbances
K) **Renal and urinary disorders**
Interstitial nephritis
l) **Reproductive system and breast disorders**
Rare : Gynaecomastia
m) **General disorders and administration site conditions**
Uncommon : Asthenia, fatigue and malaise
Rare : Body temperature increased; Oedema peripheral
n) **Infections and Infestation**
Clostridium difficile associated diarrhea

Symptoms and Treatment of Overdose
There are no known symptoms of over dosage 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 overdose with clinical signs of intoxication, apart from symptomatic and supportive treatment, no specific therapeutic recommendations can be made.

Storage Conditions
Store below 30°C and protect from moisture.

Shelf Life
24 months

Pack Size
1 x 10's, 3 x 10's, 6 x 10's, 9 x 10's, 10 x 10's and 50 x 10's blister pack

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