Rx PANTOPRAZOLE

SITIPRAZ

40 mg Lyophilized Powder for Injection (I.V.)

Proton Pump Inhibitor

FORMULATION:
Each vial contains:
Pantoprazole.....40 mg
(as Sodium Sesquihydrate)

PRODUCT DESCRIPTION:
White to almost white Lyophilized cake. After reconstitution with 0.9% sodium chloride solution it yields an almost colorless to light yellow color clear solution, free from any visible particles.

INDICATIONS:
For the treatment of gastro-esophageal reflux disease, peptic ulcer disease, and Zollinger-Ellison syndrome.

PHARMACODYNAMICS
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 H_2 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.

PHARMACODYNAMIC EFFECTS
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 (similar 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.

PHARMACOKINETICS
In the dose range of 10 to 80 mg the plasma kinetics of pantoprazole are linear after both oral and intravenous administration.
DISTRIBUTION
Pantoprazole's plasma 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 few cases of subjects with delayed elimination. Because of 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 are excreted in 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.

CONTRAINDICATIONS:
Pantoprazole (SITIPRAZ) should not be used in cases of known hypersensitivity to its constituents.

PRECAUTIONS:
The intravenous administration of Pantoprazole (SITIPRAZ) is recommended only if oral administration is not applicable.

Pantoprazole (SITIPRAZ) is not indicated for mild gastrointestinal complaints such as nervous dyspepsia.

Prior to treatment with Pantoprazole, the possibility of malignancy or a malignant disease of the esophagus should be excluded as the treatment with Pantoprazole (SITIPRAZ) may alleviate the symptoms of malignant ulcers and delay diagnosis. Diagnosis of reflux esophagitis should be confirmed by endoscopy.

The daily dose of 40 mg pantoprazole should not be exceeded in elderly patients or those with impaired renal function. In patients with severe liver impairment, the daily dose has to be reduced to 20 mg pantoprazole. Furthermore, in these patients, the liver enzymes should be monitored during Pantoprazole therapy. In case of a rise of liver enzyme, Pantoprazole should be discontinued.
To date there has been no experience with treatment in children.

Pregnancy and Lactation:
Clinical experience in pregnant women is limited. There is no information on the excretion of pantoprazole into human breast milk. Pantoprazole should only be used when the benefit to the mother is considered greater than the potential risk to the fetus/baby.

Effects on the ability to drive and to use machines or work without a firm support.
There are no known effects on the ability to drive and to use machines or work without a firm support.

DRUG INTERACTIONS:
Changes in absorption should be taken into account when

drugs whose absorption is pH-dependent (e.g. ketoconazole) are taken concomitantly.

Please note that this also applies for drugs taken a short time before Pantoprazole I.V.

Pantoprazole (SITIPRAZ) is metabolized in the liver via the cytochrome P450 enzyme system. An interaction of pantoprazole with other drugs or compounds, which are metabolized using the same enzyme cannot be excluded. However, no clinical significant interactions were observed in specific tests with a number of such drugs or compounds, namely carbamazepine, caffeine, diazepam, diclofenac digoxin, ethanol, glibenclamide, metoprolol, nifedipine, phenprocoumon, phenytoin, theophylline, warfarin, and an oral contraceptive. There were also no interactions with concomitantly administered antacids.

DOSAGE AND ADMINISTRATION:
The intravenous administration of Pantoprazole (SITIPRAZ) is recommended only if oral application is not appropriate.
The recommended intravenous dosage is one vial (40 mg Pantoprazole) per day. As soon as oral therapy is possible treatment with intravenous Pantoprazole (SITIPRAZ) should be discontinued and 40 mg Pantoprazole given orally should be administered instead. Duration of treatment with the active ingredient pantoprazole should not exceed 8 weeks.

INSTRUCTIONS FOR USE/HANDLING:
A ready-to-use solution is prepared by injecting 10mL of physiological sodium chloride solution into the vial containing the dry substance. This solution may be directly or may be administered after mixing with 100mL physiological sodium chloride solution with 5% or 10% glucose.

Pantoprazole (SITIPRAZ) must not be prepared or mixed with solvents other than those stated. The solution should have pH of 9. This drug should be administered intravenously over 2-15 minutes. The reconstituted solution must be used within 3 hours after preparation.

ADVERSE EFFECTS:
Gastrointestinal Disorders
Gastrointestinal complaints such as upper abdominal pain, diarrhea, constipation or flatulence were reported occasionally. There has been rare report of nausea.
Nervous System Disorder
Treatment with Pantoprazole (SITIPRAZ) can occasionally lead to headache. There have been rare reports of dizziness and disturbance in vision (blurred vision).
Skin and Subcutaneous Tissue Disorders
Allergic reactions such as pruritus and skin rash were reported occasionally. Wheals and swelling of the mucosa were reported in isolated cases.
Hepatobiliary Disorders
Increased liver (transaminases,Y-GT) were reported in individual cases. Severe hepatocellular damage leading to jaundice with or without hepatic failure has occurred very rarely. Musculoskeletal, Connective Tissue and
Bone Disorders
Myalgia subsiding after termination of therapy was reported in individual cases.
Psychiatric Disorders
Mental depression subsiding after termination of therapy was reported in individual cases.
General Disorders
There have been reports of injection site thrombophlebitis. Increased in body temperature was observed in individual cases, swelling of the lower arms and legs in isolated cases, both subsiding after termination of therapy.
Metabolic Disorders
Elevated triglycerides were reported in individual cases.
Immune System Disorders
Treatment with Pantoprazole can in isolated cases lead to anaphylactic reaction including anaphylactic shock with its typical symptoms such as dizziness, rapid pulse or profuse sweating.

If you experience any side effects not mentioned in this leaflet, please inform the doctor or pharmacist.

REPORTING OF SUSPECTED ADVERSE REACTIONS:
To allow continued monitoring of the benefit/risk balance of the medicinal product, reporting of suspected adverse reaction is necessary. Healthcare professional are encouraged to report any suspected adverse reactions directly to the importer/ distributor and/or report to FDA: www.fda.gov.ph.
Patients are advised to seek immediate medical attention at first sign/s of adverse reactions.

CAUTION:
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

OVER DOSE TREATMENT:
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 case of overdose with clinical signs of intoxication, apart from symptomatic and supportive treatment, no specific therapeutic recommendations can be made.

STORAGE:
Store at temperature not exceeding 30°C.

AVAILABILITY:
USP Type-I Clear, Colourless Glass Vial + 0.9% Sodium Chloride Injection x 10 mL (Box of 1's) .

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Manufactured by:
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