PANTOSPEY

Instructions for the medicinal product

Composition: Each vial contains:
Pantoprazole Sodium USP eq. to Pantoprazole 40 mg

Product Description
Physical properties: White to pale yellow coloured lyophilized cake or discontinued agreegates or free flowing powder freezed dried powder 10 ml clear glass vial.
Chemical name: Pantoprazole Sodium.
Molecular weight: 864.749111 g/mol.
Empirical / Structural formula: C32H34F4N6Na2O11S2.

ATC Classification: A02BC02.

Pharmacologic property:
Pharmacodynamics:
Pantoprazole is a substituted benzimidazole which inhibits the secretion of hydrochloric acid in the stomach by specific action on 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.
Pharmacokinetics:
Pharmacokinetics does not vary after single or repeated administration. In the dose range of 10 to 80 mg, the plasma kinetics of pantoprazole is linear after both oral and intravenous administration.
Pantoprazole's serum protein binding is about 98%. Volume of distribution is about 0.15 l/kg.
The substance is almost exclusively metabolized in the liver. The main metabolic pathway is demethylation by CYP2C19 with subsequent sulphate conjugation, other metabolic pathway include oxidation by CYP3A4. 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 are 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.

Indication:
- Reflux oesophagitis;
- Gastric and duodenal ulcer;
- Zollinger-Ellison-Syndrome and other pathological hypersecretory conditions.

Recommended Dose and Mode of Administration:
Intravenous administration of Pantospey is recommended only if oral administration is not appropriate. Data are available on intravenous use for up to 7 days. Therefore, as soon as oral therapy is possible, treatment with Pantospey IV should be discontinued and 40 mg pantoprazole p.o. should be administered instead.
Gastric and duodenal ulcer, reflux oesophagitis:
The recommended intravenous dose is 1 vial of Pantospey (40 mg pantoprazole) per day.
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 Pantospey. 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. A temporary increase of the dose above 160 mg pantoprazole is possible but should not be applied longer than required for adequate acid control.
In case a rapid acid control is required, a starting dose of 2 x 80 mg Pantospey is sufficient to manage a decrease of acid output into the target range (<10 mEq/h) within one hour in the majority of patients.
Paediatric population:
The experience in children is limited. Therefore, Pantospey is not recommended for use in patients below 18 years of age until further data become available.
Hepatic Impairment:
A daily dose of 20 mg Pantospey (half a vial of 40 mg Pantospey) should not be exceeded in patients with severe liver impairment.
Renal Impairment:
No dose adjustment is necessary in patients with impaired renal function.
Elderly:
No dose adjustment is necessary in elderly patients.
Method of administration:
A ready-to-use solution is prepared in 10 ml of sodium chloride 9 mg/ml (0.9 %) solution for injection. For instructions for preparation of the medicinal product before administration. The prepared solution may be administered directly or may be administered after mixing it with 100 ml sodium chloride 9 mg/ml (0.9 %) solution for injection or glucose 55 mg/ml (5 %) solution for injection.
After preparation the solution must be used within 12 hours.
The medicinal product should be administered intravenously over 2 - 15 minutes.

Contraindications:
- Hypersensitivity to the active substance, substituted benzimidazoles, or to any of the excipients;
- Children under 18 years old.
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Warnings and Precautions:
In patients with severe liver impairment, the liver enzymes should be monitored during therapy. In the case of a rise of the liver enzymes, the treatment should be discontinued.
Pantospey, like all proton pump inhibitors (PPIs), might be expected to increase the counts of bacteria normally present in the upper gastrointestinal tract. Treatment with Pantospey may lead to a slightly increased risk of gastrointestinal infections caused by bacteria such as Salmonella and Campylobacter.
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 drugs that may cause hypomagnesaemia (e.g., diuretics), health care professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.
Effects on 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.

Interactions with Other medicaments:
Effect of pantoprazole on the absorption of other medicinal products.
Because of profound and long lasting inhibition of gastric acid secretion, pantoprazole may reduce the absorption of drugs with a gastric pH dependent bioavailability, e.g. some azole antifungals as ketoconazole, itraconazole, posaconazole and other medicine as erlotinib.
HIV medications (atazanavir).
Co-administration of atazanavir and other HIV medications whose absorption is pH-dependent with proton-pump inhibitors might result in a substantial reduction in the bioavailability of these HIV medications and might impact the efficacy of these medicines. Therefore, the co-administration of proton pump inhibitors with atazanavir is not recommended.
Coumarin anticoagulants (phenprocoumon or warfarin).
Although no interaction during concomitant administration of phenprocoumon or warfarin has been observed. 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.
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 drugs 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.

Pregnancy and Lactation:
Pantospey should not be used during pregnancy unless clearly necessary.
Excretion into human milk has been reported. Therefore a decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with Pantospey should be made taking into account the benefit of breast-feeding to the child and the benefit of Pantospey therapy to woman.

Undesirable Effects:
Blood and lymphatic system disorders: thrombo-cytopenia; leukopenia.
Immune system disorders: hyper-sensitivity (including anaphylactic reactions and anaphylactic shock).
Metabolism and nutrition disorders: hyperlipi-daemias and lipid increases (triglycerides, cholesterol); weight changes; hyponatraemia, hypomagnesaemia.
Nervous system disorders: headache, dizziness.
Gastrointestinal disorders: diarrhoea; nausea / vomiting; abdominal distension and bloating; constipation; dry mouth; abdominal pain and discomfort.
Skin and sub-cutaneous tissue disorders: rash / exanthema / eruption; pruritus; urticaria; angioedema; tevens-John-son syndrome; lyell syndrome; erythema multiforme; photosensitivity.
Renal and urinary disorders: interstitial nephritis.

Overdose and 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.
Pantospey is extensively protein bound, it is not readily dialyzable.
In the case of overdose with clinical signs of intoxication, apart from symptomatic and supportive treatment, no specific therapeutic recommendations can be made.

Dosage Forms and Packaging Available:
1x1, 10 ml vial in a monocarton.

Storage:
Keep in dry place protected from light at a temperature below 30°C. Keep out of reach of children.

Shelf life:
2 years. Do not use after expiry date.

Distribution Condition:
Prescription only medicine (POM).