LUGANOR®
Pantoprazole

Sterile lyophilized powder for solution

Composition
Each vial contains:
Active ingredient: Pantoprazole sodium sesquihydrate equivalent to 40 mg pantoprazole.
Excipients: Disodium edetate and sodium hydroxide.

Indications
- Duodenal ulcer.
- Gastric ulcer.
- Gastro-œsophageal reflux disease.
- Long-term management of Zollinger Ellison syndrome and other pathological hypersecretory conditions.

Dosage
Intravenous administration of **Luganor** is generally recommended when oral application of proton pump inhibitors is not appropriate.
Luganor is for intravenous administration only and must not be given by any other route.

Duodenal ulcer, gastric ulcer, gastro-œsophageal reflux disease:
The recommended intravenous dosage is one vial (40 mg pantoprazole) **Luganor** per day.

Long-term management of Zollinger-Ellison syndrome and other pathological hypersecretory conditions:
The starting daily dose is 80 mg. 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.
In case a rapid acid control is required, a starting dose of 2 x 80 mg of **Luganor** is sufficient to manage a decrease of acid output into the target range (< 10 mEq/h) within one hour in the majority of patients.

Reconstitution and administration
The intravenous solution is prepared by injecting 10 ml of physiological sodium chloride solution (0.9 %) into the vial containing the dry substance. This solution should be administered intravenously by slow injection over 2 – 15 minutes or by infusion after mixing with 100 ml physiological sodium chloride solution (0.9 %) or 5 % Glucose.
After reconstitution, the solution should be administered immediately.

Contraindications
- Known hypersensitivity to pantoprazole and/or to any of the excipients.
- Pantoprazole, like other proton pump inhibitors, should not be co-administered with atazanavir (see Interactions).

Warnings
- As with other acid secretion inhibitors, pantoprazole may promote intragastric bacterial growth by reducing the volume and acidity of gastric acid.
- Cross-reactivity with the other proton pump inhibitors.

Precautions for use
- Children: the efficacy and safety of pantoprazole have not been established in children.
- Elderly patients: no dosage adjustment is necessary.
- Patients with renal insufficiency or on dialysis: no dosage adjustment is necessary.
- Patients with hepatic insufficiency: In patients with liver cirrhosis, the elimination half-life values increased to between 7 and 9 hours and the AUC values increased by a factor of 6 to 8, however the maximum plasma concentration only increased slightly by a factor of 1.5 compared with healthy subjects. It is recommended not to exceed a dose of 40 mg every 2 days.
- In case of gastric ulcer, it is recommended to confirm the benignity of the lesion prior to treatment.

Pregnancy and lactation
Pregnancy: There are currently insufficient data to evaluate a potential teratogenic or fetotoxic effect of this medicine when taken during pregnancy. Therefore, as a precautionary measure, it is best not to use **Luganor** during pregnancy except for very limited and valid indications.
Lactation: There is no information on the excretion of pantoprazole into human breast milk. The potential risk to the infant cannot be completely excluded. Interruption of breastfeeding is recommended when treatment with pantoprazole is needed.

Side effects
Pantoprazole is generally well tolerated. Only transient and reversible side effects have been reported.
The following side effects, listed by body system/organ and frequency (common: ≥ 1/100 and < 1/10; uncommon: ≥ 1/1000 and < 1/100; rare: ≥ 1/10 000 and < 1/1000; very rare: < 1/10 000, including isolated reports), have been reported with the use of pantoprazole and are more or less similar to those associated with other proton pump inhibitors:
Blood and lymphatic system disorders: Very rare: leucopenia, thrombocytopenia.
Gastrointestinal disorders: Common: upper abdominal pain, diarrhea, constipation, flatulence; Uncommon: nausea, vomiting; Rare: dry mouth.
General disorders and administration site conditions: Very rare: peripheral edema, injection site inflammation and/or superficial thrombophlebitis.
Hepatobiliary disorders: Very rare: severe hepatocellular damage and jaundice with or without hepatic failure.
Immune system disorders: Very rare: anaphylactic reactions including anaphylactic shock.
Investigations: Very rare: increased liver enzymes (transaminases, gamma-glutamyltranspeptidase), elevated triglycerides, increased body temperature, hyponatremia in the elderly.
Musculoskeletal and systemic disorders: Rare: arthralgia, fracture of the hip, wrist or spine; Very rare: myalgia.
Nervous system disorders: Common: headache; Uncommon: dizziness, disturbances in vision (blurred vision).
Psychiatric disorders: Rare: mental depression, hallucination, disorientation and confusion, particularly in susceptible patients and aggravation of symptoms existing prior to treatment.
Renal and urinary disorders: Very rare: Interstitial nephritis.
Skin and subcutaneous tissue disorders: Uncommon: allergic reactions such as pruritus and skin rash; Very rare: urticaria, angioedema, severe skin reactions such as Steven-Johnson syndrome, erythema multiforme, Lyell syndrome, photosensitivity.
Metabolism and nutrition disorders: Not known: Hyponatraemia; Hypomagnesaemia.
Other: Very rare: gynecomastia.

Overdosage
There are no known symptoms of overdosage in man.
Doses up to 240 mg were well tolerated. Apart from symptomatic treatment, no specific therapeutic recommendations can be made in case of overdose.

Interactions
Studies have shown a marked reduction in atazanavir exposure during concomitant proton pump inhibitor treatment. Pantoprazole is contraindicated during atazanavir treatment.
Pantoprazole may change the absorption of concomitant drugs whose bioavailability is pH dependent (ex. ketoconazole).
Pantoprazole is metabolized in the liver via the cytochrome P450 enzyme system. An interaction with compounds which are metabolized using the same enzyme system cannot be excluded. However, no clinically significant interactions were observed with diazepam, warfarin, theophylline, phenytoin, digoxin and oral contraceptive.
There were also no interactions with concomitantly administered antacids.

Pharmacodynamics
Pharmacotherapeutic group: proton pump inhibitors.
Pantoprazole is a specific proton pump (H+/K+ ATPase) inhibitor of the gastric parietal cell.
Due to its mechanism of action (action on the terminal phase of secretion), **Luganor** reduces gastric acid secretion whatever the nature of the stimulation.

Pharmacokinetics
Absorption and distribution: The peak serum concentration (Cmax) after a 15-min infusion is 5.52 µg/ml. These values

remain constant after multiple administration. In the dose range of 10 mg to 80 mg, the plasma kinetics of pantoprazole are linear.

Metabolism and elimination: Terminal half-life is 1 hour, volume of distribution is 11.0-23.6 L and clearance is 7.6-14.0 L/h. The serum protein binding of pantoprazole is about 98%. Because of the specific activation within the parietal cell, the serum elimination half-life does not correlate with the duration of action of the product.

Pantoprazole is almost exclusively eliminated by hepatic biotransformation. Renal elimination represents the major route of excretion (about 80%) for the metabolites of pantoprazole, the rest is excreted through the feces.

The main metabolite in both the serum and urine is desmethylpantoprazole as a sulphate conjugate.

The pharmacokinetic profile is not modified in the elderly and in patients with renal insufficiency.

Pantoprazole is poorly dialysable.

Presentation

Luganor sterile lyophilized powder for solution for I.V. injection or infusion is available in packs of 1 or 10 vials containing 40 mg pantoprazole.

Storage conditions

Store below 25°C. Protect from light.

After reconstitution: immediate use is recommended.

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