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Somatostatin for Injection

ZOMATOR™ 0.25/3 ज़ोमेटोर ०.२५/३

COMPOSITION
ZOMATOR™ 0.25
Each vial contains:

Somatostatin BP	250mcg
Mannitol IP	q.s

ZOMATOR™ 3
Each vial contains:

Somatostatin BP	3mg
Mannitol IP	q.s

PHARMACEUTICAL FORM
Lyophilized cake or powder for injection

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic Properties
Pharmacotherapeutic group: Anti growth hormones
ATC code: H01CB01

Mechanism of Action
Somatostatin is a synthetic cyclic 14-amino acid peptide, which is identical in structure and action to natural somatostatin originally isolated from the hypothalamus of animals and later found in both epithelial cells and nerve fibres throughout the whole of the digestive system.

On intravenous infusion, somatostatin causes inhibition of growth hormone, thyroid stimulating hormone, insulin and glucagon secretion as well as inhibition of gastric acid secretion. It also affects the absorption, motility, splanchnic blood flow and trophic functions of the gastrointestinal tract.

Physiologically, somatostatin is found mainly in the gastrointestinal tract and in the hypothalamus.

Somatostatin inhibits the release of gastrin, gastric acid and pepsin, which supports its indication in the treatment of upper gastrointestinal haemorrhage. Furthermore, somatostatin is capable of reducing splanchnic blood flow remarkably without causing significant variations in the systemic arterial pressure, which proves to be valuable for the management of oesophageal variceal haemorrhage.

Somastostatin reduces both pancreatic endocrine and exocrine secretions, which makes it effective in the prophylaxis and treatment of postoperative complications of pancreatic surgery and pancreatic fistulae.

The positive effect of somatostatin in the management of diabetic ketoacidosis can be ascribed to its suppression activity of glucagon secretion.

Pharmacokinetic Properties
In healthy individuals the plasma level of endogenous somatostatin is low, generally well under 175 ng/L.

Following intravenous administration somatostatin shows a very short plasma half-life, which (as measured by radioimmunoassay) lies between 1.1 and 3 minutes in normal subjects, between 1.2 and 4.8 minutes in subjects with liver disease, and between 2.6 and 4.9 minutes in subjects with chronic renal failure.

Following an intravenous infusion at a rate 75 µg/h, the plateau was obtained within 15 minutes and reached 1250 ng/L. The metabolic clearance rate was around 1 L/min. and the half-life around 2.7 minutes.

After an intravenous injection of 2 µg of 125-L-thyrosine somatostatin, urinary excretion contained 40% of the radioactivity after 4 hours and 70% after 24 hours.

Somatostatin is rapidly metabolized in the liver through the action of endopeptidases and aminopeptidases, resulting in cleavage between the N-terminus and the cyclized portion of the molecule.

It has cytoprotective activity at the pancreatic parenchyma, liver and stomach.

Preclinical Safety Data
Nonclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, and toxicity to reproduction.

CLINICAL PARTICULARS
Therapeutic Indications
Treatment of severe acute gastrointestinal hemorrhage, resulting from gastric or duodenal ulcers, hemorrhagic gastritis and esophageal varices.

- Treatment of intestinal, biliary and pancreatic fistulae.
- Symptomatic treatment of excessive secretion from endocrine tumors of the gastrointestinal tract.
- Treatment of postoperative complications and prophylaxis following pancreatic surgery.
- Coadjuvant treatment in diabetic ketoacidosis.

Posology and Method of Administration
The recommended dose is 3.5 mcg/kg body weight, ie, one 250 mcg vial for a 75-kg patient, diluted immediately prior to use with a solvent of 2 mL sodium chloride 0.9 w/v provided and given as a slow intravenous bolus over not less than 1 minute. This should be immediately followed by a continual intravenous infusion of 3.5 mcg/kg per hour, ie, one 3 mg vial given over 12 hours. The solution may be either saline or 5% dextrose and should be adjusted to guarantee an outflow of 250 mcg somatostatin per hour.

The continual administration should last a minimum of 48 hours and a maximum of 120 hours (5 days).

Treatment of Acute, Severe Gastrointestinal Haemorrhage, Resulting From Gastric or Duodenal Ulcers, Haemorrhagic Gastritis and Oesophageal Varices:
A loading dose of 250 mcg by slow intravenous injection is recommended, then immediately followed by an intravenous infusion at a rate of 250 mcg/h. In case of interruption of more than 5 minutes between 2 infusions, an additional 250 mcg is recommended to ensure a continuous treatment. Even after the haemorrhage stops (usually stops in less than 12 to 24 hours), treatment should be continued for at least 48 to 72 hours and maximum of 120 hours in order to avoid recurrence of bleeding.

Treatment of Intestinal, Biliary and Pancreatic Fistulae:
Infusion at a rate of 250 mcg/h is recommended until closure of the fistula (2-20 days). The infusion should be performed in addition to other parenteral nutrition. The treatment should be continued for 1 to 3 days even after the fistula is closed in order to avoid a rebound effect.

Symptomatic Treatment of Excessive Secretion From Endocrine Tumours of the Gastrointestinal Tract:
A loading dose of 250 mcg by slow intravenous injection is recommended, then immediately followed by an intravenous infusion at a rate of 250 mcg/h. The treatment should be continued for at least 48 hours.

Treatment of Postoperative Complications and Prophylaxis Following Pancreatic Surgery:
At the beginning of the surgical intervention 250 mcg/hour needs to be administered and continued for 5 days.

Coadjuvant Treatment in Diabetic Ketoacidosis:
In patients with ketoacidosis, infusion of 100 to 500 mcg/h of somatostatin given concurrently with a bolus insulin injection (bolus of 10 IU + infusion of 1 to 4.8 IU/h) proved capable of normalizing glycaemia within 4 hours and abating acidosis within 3 hours.

Contraindications

- Known individual hypersensitivity to somatostatin.
- The risk of giving somatostatin during pregnancy and lactation has not yet been established. Somatostatin should not, therefore, be prescribed for pregnant or lactating women, nor should it be administered during the pre-and postnatal periods.

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

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Special Warnings and Precautions for Use
Somatostatin is intended for hospital use.
Half of the recommended dose should be given to patients with severe renal failure (creatinine clearance ≤ 30 mL/min). Patients receiving somatostatin should be kept under strict medical observation. The bolus doses should be given slowly over at least 1 minute. The infusion must be given continuously. At the beginning of the infusion, hypoglycaemia may occur, possibly followed by a rise in blood sugar 2 to 3 hours later due to alterations in the balance between the counter regulatory hormones, insulin and glucagon. For this reason, blood sugar must be measured every 4 to 6 hours.

Precaution is recommended in case of simultaneous administration of any form of sugar.

Somatostatin may induce the following pharmacodynamic cardiovascular effects: transient systemic hypertension, transiently reduced cardiac output, increased pulmonary arterial pressure, increased central venous pressure, systemic hypotension, bradycardia, atrioventricular block.

Consequently, patient's vital signs should be monitored during the initial phase of somatostatin administration, especially after a bolus injection. Caution should be exercised in patients with compromised cardiovascular status or history of cardiac arrhythmia, who may not be able to compensate for these effects.

As glomerular filtration rate, urine flow and sodium blood level may be decreased during somatostatin treatment, regular checks of the renal function and plasma electrolytes are recommended.

Somatostatin causes inhibition of the intestinal absorption of certain nutrients. It also inhibits other gastrointestinal hormone secretions. Abrupt interruption of infusion may result in a rebound effect, especially in patients treated for fistulae. Therefore, after healing of fistulae, only half of the dose should be infused for the next 48 hours, in order to avoid a possible rebound effect.

The effects of somatostatin on vital signs, glycaemia, and renal function should be taken into consideration for the patient's follow-up after treatment discontinuation.

Use in children and adolescents: No adequate clinical studies establishing safety and efficacy of somatostatin in children and adolescents have been done. Therefore, use is not recommended in this population of patients.

Drug Interactions
Taking into account the wide range of somatostatin pharmacodynamic effects on various regulating systems, there is a potential for many pharmacodynamic interactions.

Pharmacodynamic interactions with possible clinical relevance have been observed with drugs that also influence blood glucose regulation, plasma renin level and arterial blood pressure, showing that somatostatin may modify the effects of these drugs on these parameters.

Simultaneous administration of any form of sugar (including glucose and fructose solutions or total parenteral nutrition) favours glycaemic disturbances and requires a closer monitoring of blood sugar. Administration of insulin may be required.

Pregnancy and Lactation
Either animal-reproduction studies have not demonstrated a foetal risk but there are no controlled studies in pregnant women or animal-reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the 1st trimester (and there is no evidence of a risk in later trimesters).

Somatostatin should not be used during lactation.

Effects on Ability to Drive and Use Machines
None reported.

Undesirable Effects
The following adverse reactions have been spontaneously reported:

Cardiac Disorders: atrioventricular block, bradycardia, arrhythmia, ventricular extrasystole.

Gastrointestinal Disorders: abdominal pain, diarrhea, nausea, vomiting.

Metabolism and Nutrition Disorders: hyperglycaemia, hypoglycaemia.

Vascular Disorders: hypertension, hypotension, hot flushes. Abrupt interruption of continuous infusion may result in a rebound effect of the treated disease, especially in patients treated for fistula.

Overdose
Symptoms: Reported cases of somatostatin overdose did not reveal other safety hazard than the undesirable effects observed at recommended doses.

Treatment: Close monitoring of blood glucose level, cardiovascular parameters, renal function, and plasma electrolytes is recommended in case of somatostatin overdose. Interruption of the somatostatin administration will rapidly improve the symptoms, since the t½ of somatostatin in blood is short (about 2 minutes). Treatment of overdose is symptomatic and no specific antidote is known.

PHARMACEUTICAL PARTICULARS:
Incompatibilities
None reported.

Shelf Life

24 months.

Storage and Precautions
Store at a temperature between 2°C and 8°C
Protect from light.

Reconstitute with 0.9% Sodium Chloride Injection IP and use immediately. If not used immediately, store between 2°C and 8°C for 24 hrs. If any colour change or sedimentation is observed, do not use.

Keep out of reach of children.

Special Precautions for Disposal and Other Handling
Any unused product or waste material should be disposed in accordance with local requirements.

Nature and Contents of Container
- One vial of Somatostatin for Injection (lyophilized)
- One ampoule of 0.9% Sodium Chloride Injection IP.

MANUFACTURED BY:
Vins Bioproducts Limited
Survey No. 117, Thimmapur (V) - 509 325.
Kothur Mandal, Mahaboobnagar Dist., (AP)

MARKETED BY
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Electronics City
Bangalore 560100.

TM - Trademark of Biocon Limited

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