Stilamin®

Somatostatin Serono

FOR INTRAVENOUS INFUSION ONLY

Presentation

Ampoules of Stilamin® (Somatostatin Serono) contain synthetic somatostatin (as the acetate) as a white, freeze-dried, sterile and pyrogen-free powder.

One strength is available: 3 mg.

Each ampoule of Stilamin® contains:

Somatostatin	3.0 mg*
D-Mannitol (excipient)	5.0 mg

* Corresponding to 3.6 mg of somatostatin acetate.

Indications and use

Stilamin® is indicated for:

- Severe acute haemorrhage from oesophageal varices.
- Severe acute haemorrhage from gastric or duodenal ulcers,or accompanying acute erosive or haemorrhagic gastritis.
- Adjuvant treatment in pancreatic, biliary and intestinal fistulae.
- Prophylaxis and treatment of postoperative complications following pancreatic surgery.
- Adjuvant treatment in diabetic ketoacidosis.

Pharmacodynamic properties

Stilamin® is a synthetic cyclic 14 amino-acid peptide, which is identical in structure and action

to natural somatostatin.

By i.v. infusion in humans, 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 gastro-intestinal 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 G.I., haemorrhage. Furthermore, somatostatin is capable of reducing remarkably splanchnic blood flow without causing significant variations in the systemic arterial pressure, which proves to be valuable for the management of oesophageal variceal haemorrhage.

Somatostatin reduces both pancreatic endocrine and exocrine secretion which makes it effective in the prophylaxis and treatment of postoperative complications of pancreatic surgery.

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

Pharmacokinetics

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

Following i.v. 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, between 2,6 and 4,9 minutes in subjects with chronic renal failure.

Following an i.v. infusion at a rate of 75 µg/h, the plateau level was obtained within 15 minutes and reached 1250 ng/L. The metabolic clearance rate was around 1L/min. and the half-life around 2,7 min.

After i.v. injection of 2 µg of 125-I-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.

Dosage and administration

Stilamin® is given intravenously, by slow bolus injection (3 to 5 minutes) of 250 µg or by continuous infusion at a rate of 250 µg/hour (equivalent of approximately 3,5 µg/kg body weight/hour).

The lyophilised powder should be reconstituted with the physiological sodium chloride solution immediately prior to use.

For continuous infusion Stilamin® contents should be used to prepare a 12 hours infusion. The solution may be either saline or 5% dextrose and should be adjusted to guarantee an outflow of 250 µg somatostatin/hour. The use of a perfusion syringe is recommended.

- Treatment of severe acute bleeding from the upper gastro-intestinal tract, including from oesophageal varices.
  It is recommended to start by a slow intravenous injection of 250 µg of Stilamin® as loading dose, then immediately followed by an intravenous infusion at a rate of 250 µg/h. In case of interruption of more than3 to5 minutes between two infusions, an additional slow i.v. injection of 250 µg is recommended to ensure a continuous treatment.
  Once the haemorrhage has stopped (usually in less than 12 to 24 hours), treatment should be continued for 48-72 hours in order to avoid rebleeding.
  Treatment up to 120 hours has been routinely performed in this indication.
- Adjuvant treatment in pancreatic, biliary and intestinal fistulae:
  A continuous infusion of Stilamin® at a rate of 250 µg/h is recommended until closure of the fistula (2-20 days). This infusion should be performed in addition to total parenteral nutrition. Once the fistula has been closed, treatment should be continued for 1 to 3 days and stopped progressively in order to avoid rebound effect.
- Prophylactic treatment of postoperative complications following pancreatic surgery:
  Stilamin® is administered at the beginning of the surgical intervention at a rate of 250 µg/h and treatment is continued for 5 days.
- Adjuvant treatment in diabetic ketoacidosis:
  In patients with ketoacidosis, infusion of 100-500 µg/h of somatostatin associated with insulin therapy (bolus of 10 I.U. + infusion of 1-4.8 I.U./h) was capable of restoring euglycemia within 4 hours and resolving acidosis within 3 hours.

Contraindications

- Known hypersensitivity to somatostatin or any of the excipients of Stilamin®

- During pregnancy and the immediate post- partum period (puerperium) as well as during lactation. There is no evidence of the drug's safety in human pregnancy nor is there evidence from animal work that is free from hazard.
  Avoid in pregnancy unless there is no safer alternative.

Warnings and Precaution

Due to its inhibitory effect on the secretion of insulin and glucagon, the administration of Stilamin® can, at the onset of treatment, lead to a transient fall in blood glucose level. Caution is, therefore, called for in insulin-dependent diabetic patients in whom blood glucose should be measured every 3-4 hours. Simultaneous administration of insulin requiring sugars should, if possible, be avoided. If necessary, insulin should be administered.

Interaction with other drugs

Since somatostatin lengthens the time of hexobarbital-induced sleep and potentiates the action of pentetrazol, Stilamin® should not be administered concomitantly with these drugs or with drugs exerting the same effects.

Adverse Reactions

Nausea, vertigo and flushing have been reported rarely. Nausea and vomiting have been reported

when the infusion rate is greater than 50 µg/min.

The following definitions apply to the frequency terminology used hereafter:

Very common (≥ 1/10)

Common (≥ 1/100 to < 1/10)

Uncommon (≥ 1/1,000 to < 1/100)

Rare (≥ 1/10,000 to < 1/1,000) Very rare (< 1/10,000)

Frequency not known (cannot be estimated from the available data)

Cardiovascular disorders:

Frequency not known:	Flushing, bradycardia

Immune system disorders:

Frequency not known:	Allergic reaction (e.g., rash, pruritus), anaphylactoid reaction, anaphylactic shock (e.g., dyspnoea, blood pressure decreased)

Metabolism and nutrition disorders:

Frequency not known:	Hypoglycaemic reaction, hypoglycaemia, blood sugar decreased, blood sugar increased, hyperglycaemia

Incompatibilities

Physical incompatibilities with other drugs have not been tested, therefore Stilamin® should be administered alone in the syringe and in infusion solutions.

Stability and storage

Storage conditions and expiry date are indicated on the box. Solutions of Stilamin® in physiological sodium chloride or 5% dextrose are stable for 24 hours, at 25°C.

Package quantities

Ampoules of Stilamin® 3 mg are packed singly. Drugs should be stored out of reach of children.

Manufactured by:

Alfasigma S.p.A.

Via Enrico Fermi 1

65020 Alanno (PE)

Italy

Or

Merck Serono SA

Succursale d'Aubonne

Zone Industrielle de l'Ouriettaz

1170 Aubonne

Switzerland

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