Stilamin®

Somatostatin
FOR INTRAVENOUS INFUSION ONLY

Presentation

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

Two strengths are available: 250µg and 3mg.

Each ampoule of Stilamin contains:

Somatostatin	250µg or 3.0mg
D-Mannitol (excipient)	5.0mg

* Corresponding to 300µg and 3.6mg of somatostatin acetate respectively.

Each ampoule of the strength 250µg is accompanied by a solvent ampoule containing 1ml of isotonic, sterile and pyrogen-free Sodium Chloride injection solution.

Indication 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 of pancreatic, biliary and intestinal fistulae.
- Prophylaxis and treatment of postoperative complications following pancreatic surgery.

Pharmacodynamic properties

Stilamin is a synthetic cyclic 14 amino-acid peptide, which is identical in structure and action to natural somatostatin.

By intravenous 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 gastro-intestinal tract and in the hypothalamus.

Somatostatin inhibits the release of gastrin, gastric acid, and pepsin which supports its indication in the treatment of upper gastro-intestinal 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 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, between 2.6 and 4.9 minutes in subjects with chronic renal failure.

Following an intravenous 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 minutes.

After intravenous injection of 2 µg of 125-I tyrosine 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 one 3 mg of Stilamin ampoule 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 than 3 to 5 minutes between two infusions, an additional slow intravenous 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 fistulae (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.

Precautionary statements

Contra-indications

Stilamin is contra-indicated:

a) 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 it is free from hazard.
Avoid in pregnancy unless there is no safer alternative.

b) In states of proven hypersensitivity to somatostatin

Warning

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.

Side-effects

Nausea, vertigo, and flushing have been reported rarely. Nausea and vomiting have been reported when the infusion rate is greater than 50 µg/min.

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 condition and expiry date are indicated on the box. Solutions of Stilamin in physiological sodium chloride are stable for 24 hours.

Package quantities

Ampoules of stilamin 250µg are packed singly and in boxes of five. Each ampoule is accompanied by an ampoule of 1 ml of physiological Sodium Chloride injection as solvent.

Ampoules of stilamin 3mg are packed singly.

Drugs should be stored out of reach of children.

Manufacturer:

Merck Serono SA Aubonne Branch
Zone Industrielle de l'Ouriettaz,
1170 Aubonne Switzerland

MERCK

施他寧 STILAMIN®

3 mg、250 μg

本藥限由醫師使用

Stilamin 3mg
衛署藥輸字第021333號
Stilamin 250 μg
衛署藥輸字第021436號

Somatostatin
僅供靜脈輸注用

成份：

Stilamin® 針劑 (Somatostatin) 含有合成的Somatostatin (as the acetate)，為白色、凍結乾燥、無菌且無熱原的粉末；有二種藥效強度可供選擇：250 μg和3mg。

每安瓿的Stilamin®含有：

Somatostatin.....250 μg或3.0mg

D-Mannitol (賦形劑).....5.0mg

※相當於300 μg或3.6mg 之Somatostatin醋酸鹽。

每一劑250 μg強度的安瓿，附有一安瓿含1 ml等張、無菌且無熱原的生理食鹽注射溶液。

適應症：

食道靜脈曲張引起的嚴重急性出血。胃潰瘍、十二指腸潰瘍、出血性胃炎引起的嚴重急性出血。胰臟手術後胰臟併發症之預防。胰臟、膽及腸道瘻管之輔助治療。

藥理作用：

Stilamin® 為合成的環形胜肽，含14個氨基酸，其結構與作用均與天然的Somatostatin相同。以靜脈輸注於人體，Somatostatin會抑制生長激素，甲狀腺刺激激素、胰島素、升血糖素和胃酸的分泌。它也會影響胃腸道的吸收、蠕動、內臟血流與營養功能。

生理上，Somatostatin大部份存在於胃腸道和下視丘。

Somatostatin對於胃泌素、胃酸和蛋白酶之釋放具有抑制作用，因此它適用於上消化道出血的治療。此外，Somatostatin會顯著地減少內臟的血流而不會引起全身動脈血壓的重大變化，因此對處理食道靜脈曲張引起的出血極具價值。

Somatostatin會減少胰臟的內分泌及外分泌，因此它對於胰臟手術後的併發症具有預防與治療作用。Somatostatin對於糖尿病引起的酮酸毒症有效的原因可歸因於它對升血糖素之分泌有抑制作用。

藥物動力學：

於正常人內生性的Somatostatin之血漿內濃度並不高，一般均低於175ng/L。

於靜脈輸注後，Somatostatin呈現很短的血漿內半衰期。依放射線免疫測試法，於正常人為1.1～3分鐘，於肝病變的人為1.2～4.8分鐘、而於慢性腎功能不良的人為2.6～4.9 分鐘。

以每小時75 μg之速度靜脈輸注後，血中的高原期可在15分鐘內得到，並會達到1250ng/L。其代謝排除率為1L/min，而其半衰期約為2.7分鐘。以靜脈注射125-I標記的thyrosine somatostatin 2 μg後，四小時後的尿液排出物含有40%的放射線活性，而24小時後的排泄物含有70%的放射線活性。

Somatostatin會很快的在肝臟被內胜肽酶和氨基胜肽酶代謝，使分子的N端與環狀部份接連的部位分裂。

劑量及投與方法：

Somatostatin只能經由靜脈投與，其方式有二：其一為250 μg之一次投與法，一次投與250 μg時必須用3～5分鐘之慢速度注入。其二為點滴輸注法，點滴的速度為一小時250 μg(大約相當於每一小時每公斤體重投與3.5 μg)。

凍結乾燥的粉末應在使用前才用生理食鹽注射液溶解。

要連續點滴時，應用一安瓿3mg的Stilamin調配12小時用之點滴液。點滴液可用生理食鹽水或5%葡萄糖調配，而且必須調整點滴的速度確實為每小時250 μg之Somatostatin。因此，應用點滴用的注射器。

－治療上消化道，包括食道靜脈曲張引起的嚴重的急性出血時，應先以慢速度注射一劑250 μg之Stilamin，接著以250 μg/h之速度進行靜脈點滴。如果為更換靜脈點滴而中斷點滴的時間超過3～5分鐘，則最好在更換期間補以一劑250 μg之緩慢的靜脈注射以確保連續治療。

出血停止(一般約於12～24小時內)後，仍應繼續治療48～72小時，以避免再出血。

對此適應症的治療通常均會施行達120小時。

－於胰臟、膽及腸道瘻管之輔助治療：

應以250 μg/h連續點滴到瘻管閉合(2～20天)。在施行本項的點滴時，應同時另行全靜脈營養劑的點滴。在瘻管閉合後，治療應再繼續1～3天，並應漸進地減量停藥，以免發生反彈作用而病症復發。

－胰臟手術後胰臟併發症之預防治療：

Stilamin® 應從手術開始時，即以250 μg/h的速度進行點滴，並應繼續治療5天。

注意事項：

治療禁忌：

於下列情況應禁用Stilamin®：

－懷孕期、產後期和哺乳期。在人類的懷孕期投與此藥的安全性尚未獲得證實。在動物實驗上，也尚未證實其對懷孕無害。於懷孕期，除非沒有更好的取代辦法，應避免使用。

－經證實對Somatostatin過敏者。

警告：

由於Stilamin® 對胰島素和升血糖素的分泌具有抑制作用，在剛開始治療時，會導致暫時的血糖值的降低，因此對於依賴胰島素的糖尿病患者需要加以注意。其血糖值應每3～4小時測量一次。如果可能，應避免同時服用須要胰島素的糖。如果必要，應投與胰島素。

藥物交互作用：

因為Somatostatin會延長hexobarbital（安眠藥）所作用的睡眠時間，並且會加強Pentetrazol（抗癲癇等）的作用。因此，Stilamin® 不應與此二種藥同時投與，或與其他具有與該兩種藥同作用之藥物併用。

副作用：

偶爾有人會發生噁心、暈眩和面部潮紅。當點滴速率快於50 μg/分鐘時，曾有人發生噁心、嘔吐。

配伍禁忌：

與其他藥物在物理上之不相容性尚未經試驗，因此，Stilamin® 應使用獨自的點滴注射器和點滴液來投與。

安定性及貯存：

貯存條件和有效期限標示於包裝盒。以生理食鹽水溶解的Stilamin®注射液安定性可達24小時。

包裝：

Stilamin® 250 μg以一安瓿包裝，附等支數1公撮安瓿裝溶劑，100支以下盒裝。

3mg一安瓿的Stilamin® 為每盒單獨一支裝。

本藥須慎防孩童觸及。

製造廠：Merck Serono SA. Aubonne Branch
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藥　商：台灣默克股份有限公司
地　址：台北市內湖區堤頂大道二段89號6樓
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