הודעה על החמרה (מידע בטיחות) בעלון לרופא

תאריך: 27.12.2016

שם תכשיר באנגלית ומספר הרישום : Somatuline PR 30 MG 117 93 22911 00

שם בעל הרישום : מדיסון פארמה בע"מ

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות		
טקסט חדש	**טקסט נוכחי**	**פרק בעלון**
4.4 **Special warnings and precautions for use** ▪ Lanreotide may reduce gallbladder motility and lead to gallstone formation. Therefore patients may need to be monitored periodically. It is advised, during prolonged treatment, to perform before treatment and every 6 months, an echography of the gallbladder (see section 4.8). ▪ Pharmacological studies in animals and humans show that lanreotide, like somatostatin and other somatostatin analogues, inhibits secretion of insulin and glucagon. Hence, patients treated with lanreotide may experience hypoglycaemia or hyperglycaemia. Blood glucose levels should be monitored when lanreotide treatment is initiated, or when the dose is altered. Any antidiabetic treatment should be adjusted accordingly. In insulin-treated diabetic patients, the insulin doses will initially be reduced by 25%, then adapted to the blood glucose level, which must be carefully controlled in these patients as soon as treatment begins. ▪ Slight decreases in thyroid function have been seen during treatment with lanreotide in acromegalic patients, though clinical hypothyroidism is rare. Thyroid function tests are recommended where clinically indicated. ▪ In acromegalic patients and patients presenting with primitive thyrotropic adenomas, use of lanreotide is not exempt from the monitoring of the	4.4 **Special warnings and precautions for use** ▪ Lanreotide may reduce gallbladder motility and lead to gallstone formation. Therefore patients may need to be monitored periodically. It is advised, during prolonged treatment, to perform before treatment and every 6 months, an echography of the gallbladder ▪ Pharmacological studies in animals and humans show that lanreotide, like somatostatin and other somatostatin analogues, inhibits secretion of insulin and glucagon. Hence, patients treated with lanreotide may experience hypoglycaemia or hyperglycaemia. Blood glucose levels should be monitored when lanreotide treatment is initiated, or when the dose is altered. Any antidiabetic treatment should be adjusted accordingly. In insulin-treated diabetic patients, the insulin doses will initially be reduced by 25%, then adapted to the blood glucose level, which must be carefully controlled in these patients as soon as treatment begins. ▪ Slight decreases in thyroid function have been seen during treatment with lanreotide in acromegalic patients, though clinical hypothyroidism is rare. Thyroid function tests are recommended where clinically indicated. ▪ In acromegalic patients and patients presenting with primitive thyrotropic	**4.4 Special warnings and precautions for use**

volume of the pituitary tumour.

▪ In patients without underlying cardiac problems, lanreotide may lead to a decrease of heart rate without necessarily reaching the threshold of bradycardia. In patients suffering from pre-existing cardiac disorders, sinus bradycardia may occur. Care should be taken when initiating treatment with lanreotide in patients with bradycardia (see section 4.5).

~~▪ In carcinoid tumours, lanreotide must not be prescribed before having eliminated the presence of an obstructive intestinal tumour.~~

▪ The appearance of a significant and lasting increase of steatorrhoea justifies the complementary prescription of pancreatic extracts.

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▪ The appearance of a significant and lasting increase of steatorrhoea justifies the complementary prescription of pancreatic extracts.

System organ class	Very common (≥1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)	Post-marketing safety experience (frequency known)
Metabolism and nutrition disorders		Hypoglycaemia, decreased appetite**, hyperglycaemia, diabetes mellitus	~~diabetes mellitus hyperglycaemia~~,	
Psychiatric disorders			Insomnia*	
Nervous system disorders		Dizziness, headache, lethargy**		
Cardiac disorders		Sinus bradycardia*		
Vascular disorders			Hot flushes*	
Gastrointestinal disorders	Diarrhoea, loose stools*, abdominal pain	Nausea, vomiting, constipation, flatulence, abdominal distension, abdominal discomfort, dyspepsia, steatorrhoea**	Faeces discoloured*	Pancreatitis
Hepatobiliary disorders	Cholelithiasis	Biliary dilatation*		
Musculoskeletal and connective tissue disorders		Musculoskeletal pain**, myalgia**		
Skin and subcutaneous tissue disorders		Alopecia, hypotrichosis*		

4.8 Undesirable effects

▪ **Investigations:**

Common: ALAT increased, ASAT abnormal, ALAT abnormal, blood bilirubin increased, blood glucose increased, glycosylated haemoglobin increased, weight decreased

Uncommon: ASAT increased, blood alkaline phosphatase increased, blood bilirubin abnormal , blood sodium decreased

▪ **Cardiac disorders**

Common: Sinus bradycardia

▪ **Nervous system disorders**

Common: Dizziness, headache

▪ **Gastrointestinal disorders**

Very common: Diarrhoea, loose stools, abdominal pain

Common: Nausea, vomiting, constipation, flatulence, abdominal distension, abdominal discomfort, dyspepsia

Uncommon: Faeces discoloured

▪ **Skin and subcutaneous tissue disorders**

Common: Alopecia, hypotrichosis

▪ **Metabolism and nutrition disorders**

Common: Hypoglycaemia

Uncommon: Diabetes mellitus, hyperglycaemia

▪ **Vascular disorders:**

Uncommon: Hot flush

▪ **General disorders and administration site conditions:**

Common: Fatigue, injection site reactions (pain, mass, induration, nodule, pruritus)

Uncommon: Asthenia

▪ **Hepatobiliary disorders**

Very common: Cholelithiasis

Common: Biliary dilatation

General disorders and administration site conditions		Asthenia, fatigue, injection site reactions (pain, mass, induration, nodule, pruritus)	~~Asthenia~~		▪ **Psychiatric disorders:** Uncommon: Insomnia	
Investigations		ALAT increased*, ASAT abnormal*, ALAT abnormal*, blood bilirubin increased*, blood glucose increased*, glycosylated haemoglobin increased*, weight decreased, pancreatic enzymes decreased**	ASAT increased*, blood alkaline phosphatase increased*, blood bilirubin abnormal*, blood sodium decreased*		**Post-marketing safety experience:** Post-marketing safety experience has not identified any other relevant information other than occasional reports of pancreatitis.	
Immune system disorders				Allergic reactions (including angioedema, anaphylaxis, hypersensitivity)		

* based on a pool of studies conducted in acromegalic patients

** based on a pool of studies conducted in patients with GEP-NETs

~~▪ Investigations:~~

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~~▪ Cardiac disorders~~

~~Common: Sinus bradycardia~~

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~~Common: Nausea, vomiting, constipation, flatulence, abdominal distension, abdominal discomfort, dyspepsia~~

~~Uncommon: Faeces discoloured~~

~~▪ Skin and subcutaneous tissue disorders~~

~~Common: Alopecia, hypotrichosis~~

~~▪ Metabolism and nutrition disorders~~

~~Common: Hypoglycaemia~~ ~~Uncommon: Diabetes mellitus, hyperglycaemia~~ ~~▪ Vascular disorders:~~ ~~Uncommon: Hot flush~~ ~~▪ General disorders and administration site conditions:~~ ~~Common: Fatigue, injection site reactions (pain, mass, induration, nodule, pruritus)~~ ~~Uncommon: Asthenia~~ ~~▪ Hepatobiliary disorders~~ ~~Very common: Cholelithiasis~~ ~~Common: Biliary dilatation~~ ~~▪ Psychiatric disorders:~~ ~~Uncommon: Insomnia~~ ~~**Post-marketing safety experience:**~~ ~~Post-marketing safety experience has not identified any other relevant information other than occasional reports of pancreatitis.~~ **Reporting of suspected adverse reactions** *R*eporting suspected adverse reaction after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il		
Pharmacotherapeutic group: Antigrowth hormones, ATC code: H01C B03. Lanreotide is an octapeptide analogue of natural somatostatin. Like somatostatin, lanreotide is an inhibitor of various endocrine, neuroendocrine, exocrine and paracrine functions. Lanreotide has a high affinity for human somatostatin receptors (SSTR) 2 and 5 and a reduced binding affinity for human SSTR1, 3, and 4. Activity at human SSTR 2 and 5 is the primary mechanism believed responsible for GH inhibition. In addition~~,~~ Its marked selectivity for the secretion of growth hormone compared to that of insulin, makes this a product suited to the treatment of	Pharmacotherapeutic group: Antigrowth hormones, ATC code: H01C B03. Lanreotide is an octapeptide analogue of natural somatostatin. Like somatostatin, lanreotide is an inhibitor of various endocrine, neuroendocrine, exocrine and paracrine functions. Lanreotide has a high affinity for human somatostatin receptors (SSTR) 2 and 5 and a reduced binding affinity for human SSTR1, 3, and 4. Activity at human SSTR 2 and 5 is the primary mechanism believed responsible for GH inhibition. Its marked selectivity for the secretion of growth hormone compared to that of insulin, makes this a product suited to the treatment of acromegaly.	**5.1 Pharmacodynamic properties**

acromegaly. By inhibiting the synthesis of thyroid stimulating hormone (TSH), lanreotide normalised also the thyroid function on patient with thyrotropin-secreting adenomas. Furthermore, the inhibitory action of lanreotide on intestinal exocrine secretion, digestive hormones and cellular proliferation mechanisms is particularly interesting for its application in the treatment of the symptoms of endocrine digestive tumours, especially carcinoids. Lanreotide, like somatostatin, exhibits a general exocrine anti-secretory action. It inhibits the basal secretion of motilin, gastric inhibitory peptide and pancreatic polypeptide, but has no significant effect on fasting secretin or gastrin secretion. Lanreotide markedly inhibits meal-induced increases in superior mesenteric artery blood flow and portal venous blood flow. Lanreotide significantly reduces prostaglandin E1-stimulated jejunal hydroelectrolytic secretion (water, sodium, potassium and chloride). Lanreotide reduces prolactin levels in acromegalic patients treated long term. Lanreotide is clearly more active than natural somatostatin and shows a much longer duration of action. A randomised, placebo controlled study has investigated the effects of lanreotide PR 30 mg administration every 10 days, on top of concomitant treatment regimen including intravenous corticoids, proton-pump inhibitors, antispasmodics, antiemetics and analgesics in 80 patients with upper intestinal obstruction of malignant origin due to confirmed peritoneal carcinomatosis in palliative care, having at least 2 vomiting episodes per day or a nasogastric tube and for whom, according to recent surgical advice, surgery was inappropriate. Patients having a bowel obstruction which could be explained by a non-malignant cause were excluded from the study. The primary objective was to assess the proportion of responders 7 days after a single injection of lanreotide PR 30mg versus placebo. Treatment response was defined as 1 or less vomiting episode per day for at least 3 consecutive days or no vomiting recurrence for at least 3 consecutive days for subjects in whom nasogastric tube had been removed. In the Intent-to-Treat [ITT] population, when based on subject diary record cards (DRC) assessed at day 7, the responders rate was more favourable for lanreotide than placebo although not statistically significant (41.9% [18/43] versus 29.7% [11/37], odds ratio=1.75 [95% CI 0.68, 4.49, p=0.24]).	By inhibiting the synthesis of thyroid stimulating hormone (TSH), lanreotide normalised also the thyroid function on patient with thyrotropin-secreting adenomas. Furthermore, the inhibitory action of lanreotide on intestinal exocrine secretion, digestive hormones and cellular proliferation mechanisms is particularly interesting for its application in the treatment of the symptoms of endocrine digestive tumours, especially carcinoids. Lanreotide, like somatostatin, exhibits a general exocrine anti-secretory action. It inhibits the basal secretion of motilin, gastric inhibitory peptide and pancreatic polypeptide, but has no significant effect on fasting secretin or gastrin secretion. Lanreotide markedly inhibits meal-induced increases in superior mesenteric artery blood flow and portal venous blood flow. Lanreotide significantly reduces prostaglandin E1-stimulated jejunal hydroelectrolytic secretion (water, sodium, potassium and chloride). Lanreotide reduces prolactin levels in acromegalic patients treated long term. Lanreotide is clearly more active than natural somatostatin and shows a much longer duration of action.	

In the Per Protocol (PP) population a significantly higher responders' rate, based on DRC data, was observed for lanreotide when compared to placebo (57.7% [15/26] and 30.4% [7/23], respectively [odds ratio=3.60, 95% CI 1.03, 12.62, p=0.045]).		