

## SUMMARY OF PRODUCT CHARACTERISTICS

## 1. TRADE NAME OF THE MEDICINAL PRODUCT

**SOMATULINE P.R. 30 mg**, powder and solvent for suspension for prolonged release injection (I. M.).

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition of the powder

Lanreotide acetate, expressed as lanreotide .....	0.03000 g *
Copolymers (lactide-glycolide and lactic-glycolic) .....	0.15000 g
Mannitol .....	0.06375 g
Carmellose - Na .....	0.02250 g
Polysorbate 80 .....	0.00150 g

For one vial

Composition of the solvent

Mannitol .....	0.01600 g
Water for injection .....	2.00000 g

For one ampoule

\* Taking into account the characteristics of the pharmaceutical form, each vial contains a quantity of lanreotide acetate corresponding to 0.040 g of lanreotide.

## 3. PHARMACEUTICAL FORM

Powder and solvent for suspension for prolonged release injection (I. M.).

## 4. CLINICAL PARTICULARS

## 4.1 Therapeutic indications

Treatment of acromegaly

When the secretion of growth hormone remain abnormal after surgery and/or radiotherapy.

Treatment of the clinical symptoms of carcinoid tumours

After a test injection (cf. 4.2. Posology and method of administration).

Treatment of primary thyrotropic adenomas responsible for hyperthyroidism

As a preparation for or as a complement to surgery and/or radiotherapy, or where these therapies are unsuitable.

## 4.2 Posology and method of administration

The treatment should be adjusted to each patient in a specialised unit.

Taking into account the variability of the sensitivity of the tumours to somatostatin analogues, it is recommended to start treatment with a test injection, in order to evaluate the quality of the response (GH secretion, symptoms related to the carcinoid tumour, tumoral secretions...).

If no response to the first test injection is seen, the treatment should be reviewed.

In acromegaly

The frequency of administration of the prolonged release form should initially be set to one intramuscular injection every 14 days. In case of an insufficient response, as judged by the levels of growth hormone and IGF-1 (measured prior to the next injection), the frequency of injection may be increased to 1 every 10 days.

In carcinoid tumours

The frequency of administration of the prolonged release form should initially be set to one intramuscular injection every 14 days. In case of an insufficient response, judged by clinical symptoms (flushes, soft stools), the frequency of injection may be increased to 1 every 10 days.

In primary thyrotropic adenomas responsible for hyperthyroidism :

The frequency of administration of the prolonged release form should initially be set to one intramuscular injection every 14 days. In case of an insufficient response, as judged by the levels of thyroid hormone and TSH, the frequency of injection may be increased to 1 every 10 days.

NB: It is important that injection of the prolonged release form is performed exactly according to the instructions in the package insert. Each defective injection, which leaves a quantity greater than that which normally remains in the device used for injection, should be reported.

#### **4.3 Contra-indications**

Pregnancy and breast-feeding.

Hypersensitivity to one of the components including the active substance.

#### **4.4 Special warnings and special precautions for use**

- In the non-insulin dependent diabetic patients, a strict monitoring of glycemic control must be established.
- In the 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.
- In the non diabetic subject, some cases of transient increase of blood glucose levels have been observed during routine controls ; however, treatment with insulin was not required.
- Lanreotide may reduce gall bladder motility and therefore, gall bladder echography is advised at the start of treatment and every six months thereafter. If gallstones do occur, they are generally asymptomatic. Symptomatic stones should be treated as medically indicated.
- In acromegalic patients and patients presenting with primitive thyrotropic adenomas, use of lanreotide is not exempt from the monitoring of the volume of the pituitary tumour.
- In the carcinoid syndromes, lanreotide must not be prescribed before having eliminated the presence of an obstructive intestinal tumour.
- It is advised, during prolonged treatment, to perform before treatment and every 6 months, an echography of the gallbladder (cf. Undesirable effects).
- Fat concentrations in stools may increase to levels high enough to result in steatorrhea, requiring the use of appropriate corrective therapy .The appearance of a significant and lasting increase of steatorrhea justifies the complementary prescription of pancreatic extracts.
- In case of hepatic or renal insufficiency, the liver and kidney functions should be regularly monitored in order to adapt, if necessary, the interval between doses.
- In a rat fertility study, testicular abnormalities in males have been noted, as well as moderate abnormalities of fertility, gestation and offspring growth. The effects are related to the exaggerated physiopharmacological activity of the product.

The treated patients should be warned about possible abnormalities of their fertility and about the appropriateness of using a contraceptive during the treatment and over a period of 3 months after stopping.

#### **4.5 Interaction with other medicaments and other forms of interaction**

*Associations requiring precautions for use*

The gastrointestinal effects of Somatuline LA may reduce the intestinal absorption of co-administered drugs. As with other somatostatin analogues, Somatuline LA may reduce the intestinal absorption of cyclosporin A. Interactions with highly plasma bound drugs are unlikely in view of the moderate binding of lanreotide to serum proteins (78 % mean serum binding).

Insulin: risk of hypoglycemia : decrease in the needs of insulin following the decrease in endogen glucagon secretion. The patient must be informed of the risk of hypoglycemia, the glycemic and urinary selfmonitoring must be reinforced and the posology of insulin during treatment by lanreotide must be adapted.

#### **4.6 Pregnancy and lactation**

Studies in animals showed transitory growth retardation of offspring prior to weaning. Although no teratogenic effects have been observed in animals, in the absence of clinical experience, lanreotide must not be administered to pregnant or lactating women.

Children:

As there is no experience of the use of the product in children, the use of Somatuline LA in children cannot be advised.

#### **4.7 Effects on ability to drive and use machines**

Not applicable.

#### **4.8 Undesirable effects**

- Local : moderate transitory pain at the site of injection, sometimes associated with local redness.
- General tolerance : gastrointestinal side effects are the most common and include: diarrhoea or soft stools, abdominal pain, flatulence, anorexia, nausea and vomiting. In general, all these side effects are mild to moderate in intensity; in most cases the frequency and the intensity of such effects appear to diminish or to resolve with continued therapy.
- At a biological level, some rare cases of disorders of glucose regulation have been noted.
- Gallstones : in some patients, during prolonged treatment, cases of asymptomatic gallstones have been reported (cf. 4.4 Precautions for use).
- In rare instances, acute pancreatitis has been reported within a short time after the first administration.

#### **4.9 Overdose**

Symptomatic treatment of observed disorders (gastrointestinal, ionic balance).

To date, no life threatening cases have been reported.

### **5. PHARMACOLOGICAL PROPERTIES**

#### **5.1 Pharmacodynamic properties**

Hypothalamic hormone. Somatostatin analogue.

H : HORMONES

Like natural somatostatin, lanreotide is a peptide inhibitor of a number of endocrine, neuroendocrine, exocrine and paracrine functions. It shows good affinity for peripheral somatostatin receptors (hypophyseal and pancreatic). In contrast, its affinity for central receptors is much weaker. This profile confers a good specificity of action at the level of growth hormone as well as digestive hormone secretion. Lanreotide is clearly more active than natural somatostatin and shows a much longer duration of action.

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 acromegaly.

By inhibiting the synthesis of thyroid stimulating hormone (TSH), lanreotide normalised also the thyroid function on patient with thyrotropin-secreting adenomas. There was no significant reduction in the size of the adenoma

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. Pharmacokinetic properties

The absorption kinetics of lanreotide from SOMATULINE PR, administered intramuscularly in healthy volunteers, is characterised by a first phase of rapid release, corresponding to the release of peptide superficially associated with the microspheres, then by a second release phase, followed by a very slow decrease.

The first plasma peak ( $C_{max} 1: 6.8 \pm 3.8 \mu\text{g/l}$ ) occurs at  $1.4 \pm 0.8$  hours and the second ( $C_{max} 2 : 2.5 \pm 0.9 \mu\text{g/l}$ ) at  $1.9 \pm 1.8$  days. The absolute bioavailability is  $46.1 \pm 16.7\%$ . The mean residence time of  $8.0 \pm 1.0$  days and the apparent half-life of  $5.2 \pm 2.5$  days, confirm the prolonged release of the product.

In acromegalic patients, the pharmacokinetic profile is comparable and the level of growth hormone and IGF-1 are significantly reduced for a period of at least 14 days after a single administration.

With repeated administration over several months, there is no evidence of accumulation of the product. Studies of the binding of lanreotide to blood components show that the medicinal interactions are not very likely at this level.

#### **5.2 Preclinical safety data**

Studies of animal toxicology have not shown specific toxicity of the molecule. The observed effects are related to the pharmacological properties of the product on the endocrine system.

The resorption of the microspheres is complete in 45-60 days.

**6. PHARMACEUTICAL PARTICULARS**

**6.1 Incompatibilities**

The microspheres must be reconstituted immediately prior to use, using only the solution supplied in the package.

**6.2 Shelf-life**

2 years.

**6.3 Special precautions for storage**

To be stored at a temperature between + 2° C and + 8° C (in a refrigerator).

**6.4 Nature and contents of container**

Powder in a vial (glass) and 2 ml of solvent in an ampoule (glass).

**6.5 Instructions for use/handling**

The reconstitution of the powder in the specific solvent must be performed immediately before injection, by shaking the vial, gently, 20 to 30 times, in order to obtain an homogenous suspension with a milky appearance.

This must not be mixed with other medications.

**7. MARKETING AUTHORISATION NUMBER**

337 352-3 : powder in a vial (glass) + 2 ml of solvent in an ampoule (glass) box of 1 with 1 syringe and 2 needle

**8. MARKETING AUTHORIZATION HOLDER**

**BEAUFOR IPSEN PHARMA**

24 rue Erlanger

75016 PARIS

France

**DRUGS-ABOUT.COM**

**9. IMPORTER:**

**Medison Pharma**

10 Hashiloach St. POB 7090 Petach Tikva 49170