CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-074

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use Somatuline Depot safely and effectively. See full prescribing information for Somatuline Depot.

SOMATULINE® DEPOT (lanreotide) INJECTION
Initial U.S. Approval: 2007

----------INDICATIONS AND USAGE----------
Somatuline Depot (lanreotide) Injection is a somatostatin analog indicated for:

- the long-term treatment of acromegalic patients who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy (1)

----------DOSAGE AND ADMINISTRATION----------

- Dose range of 60 mg to 120 mg every 4 weeks (2)
- Recommended dose is 90 mg every 4 weeks for 3 months. Adjust thereafter based on GH and/or IGF-1 levels (2)
- Renal and Hepatic Impairment: Initial dose is 60 mg every 4 weeks for 3 months in moderate and severe renal or hepatic impairment. Adjust thereafter based on GH and/or IGF-1 levels. (2, 12.3)
- Injected in the superior external quadrant of the buttock Injection site should be alternated (2)
- Store at 2-8°C (36-46 °F) in the original package (16.2)

----------DOSAGE FORMS AND STRENGTHS----------
Single use syringe: 60, 90 and 120 mg (3)

----------CONTRAINDICATIONS----------
None

----------WARNINGS AND PRECAUTIONS----------

- Gallbladder: Gallstones may occur; consider periodic monitoring (5.1)
- Glucose Metabolism: Hypo- and/or hyperglycemia may occur. Glucose monitoring is recommended and anti-diabetic treatment adjusted accordingly (5.2)
- Cardiac Function: Decrease in heart rate may occur. Use with caution in at-risk patients (5.3)

----------ADVERSE REACTIONS----------
Most common adverse reactions are diarrhea, cholelithiasis, abdominal pain, nausea and injection site reactions (6)

To report SUSPECTED ADVERSE REACTIONS, contact Tercica at 1-866-837-2422 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

----------DRUG INTERACTIONS----------

- Hypoglycemia agents: Hypo- and/or hyperglycemia may occur. Glucose monitoring is recommended and anti-diabetic treatment adjusted accordingly (7.1)
- Cyclosporine: Somatuline may decrease the bioavailability of cyclosporine. Cyclosporine dose may need to be adjusted (7.2)
- Drugs affecting heart rate: Somatuline may decrease heart rate. Dose adjustment of coadministered drugs that decrease heart rate may be necessary (7.3)

----------USE IN SPECIFIC POPULATIONS----------

- Renal Impairment: Start dose is 60 mg in moderate and severe renal impairment (2, 8.6, 12.3)
- Hepatic Impairment: Start dose is 60 mg in moderate and severe hepatic impairment (2, 8.6, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 08/2007

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Somatuline Depot (lanreotide) Injection 60 mg, 90 mg and 120 mg is indicated for the long-term treatment of acromegalic patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option.

The goal of treatment in acromegaly is to reduce growth hormone (GH) and insulin growth factor-1 (IGF-1) levels to normal.

2 DOSAGE AND ADMINISTRATION

Patients should begin treatment with Somatuline Depot 90 mg given via the deep subcutaneous route, at 4 week intervals for 3 months.

After 3 months dosage may be adjusted as follows:

- GH >1 to ≤ 2.5 ng/mL, IGF-1 normal and clinical symptoms controlled: maintain Somatuline Depot dose at 90 mg every 4 weeks.
- GH > 2.5 ng/mL, IGF-1 elevated and/or clinical symptoms uncontrolled, increase Somatuline Depot dose to 120 mg every 4 weeks.
- GH ≤ 1 ng/mL, IGF-1 normal and clinical symptoms controlled: reduce Somatuline Depot dose to 60 mg every 4 weeks.

Thereafter, the dose should be adjusted according to the response of the patient as judged by a reduction in serum GH and /or IGF-1 levels; and/or changes in symptoms of acromegaly.

Somatuline Depot should be injected via the deep subcutaneous route in the superior external quadrant of the buttock. The skin should not be folded and the needle should be inserted perpendicular to the skin, rapidly and to its full length. The injection site should alternate between the right and left side.

The starting dose in patients with moderate and severe renal or moderate and severe hepatic impairment should be 60 mg via the deep subcutaneous route, at 4 week intervals for 3 months followed by dose adjustment as described above [*see Clinical Pharmacology (12.3)*].

3 DOSAGE FORMS AND STRENGTHS

60, 90 and 120 mg sterile, single-use, pre-filled syringes. The pre-filled syringes contain a white to pale yellow, semi-solid formulation.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Cholethiasis and Gallbladder Sludge

Lanreotide may reduce gallbladder motility and lead to gallstone formation therefore, patients may need to be monitored periodically [*see Adverse Reactions (6.1), Clinical Pharmacology (12.2)*].

5.2 Hyperglycemia and Hypoglycemia

Pharmacological studies in animals and humans show that lanreotide, like somatostatin and other somatostatin analogs, inhibits the secretion of insulin and glucagon. Hence, patients treated with Somatuline Depot may experience hypoglycemia or hyperglycemia. Blood glucose levels should be monitored when lanreotide treatment is initiated, or when the dose is altered; and antidiabetic treatment should be adjusted accordingly [*see Adverse Reactions (6.1)*].

5.3 Thyroid function Abnormalities

Slight decreases in thyroid function have been seen during treatment with lanreotide in acromegalic patients, though clinical hypothyroidism is rare (<1%). Thyroid function tests are recommended where clinically indicated.

5.4 Cardiovascular Abnormalities

The most common overall cardiac adverse reactions observed in three pooled Somatuline Depot Cardiac Studies in patients with acromegaly were sinus bradycardia (12/217, 5.5%), bradycardia (6/217, 2.8%) and hypertension (12/217, 5.6%) [*see Adverse Reactions (6.1)*].

In patients without underlying cardiac disease, lanreotide may lead to a decrease in heart rate without necessarily reaching the threshold of bradycardia. In patients suffering from cardiac disorders prior to lanreotide treatment, sinus bradycardia may occur. Care should be taken when initiating treatment with lanreotide in patients with bradycardia.

5.5 Drug Interactions

The pharmacological gastrointestinal effects of Somatuline Depot may reduce the intestinal absorption of concomitant drugs.

Lanreotide may decrease the relative bioavailability of cyclosporine. Concomitant administration of Somatuline Depot and cyclosporine may necessitate the adjustment of cyclosporine dose to maintain therapeutic levels [*see Drug Interactions (7.2)*].

5.6 Monitoring: Laboratory Tests

Serum GH and IGF-1 levels are useful markers of the disease and the effectiveness of treatment [*see Dosage and Administration (2.0)*].

6 ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

6.1 Clinical Studies Experience

The data described below reflect exposure to Somatuline Depot in 416 acromegalic patients in seven studies. One study was a fixed-dose pharmacokinetic study. The other six studies were open-label or extension studies, one had a placebo controlled run-in period and another had an active control. The population was mainly Caucasian (329/353, 93%) with a median age of 53.0 years of age (range 19-84 years). Fifty-four subjects (13%) were age 66-74 and eighteen subjects (4.3%) were ≥ 75 years of age. Patients were evenly matched for gender (205 males and 211 females). The median average monthly dose was 91.2 mg (e.g., 90 mg injected via the deep subcutaneous route every 4 weeks) over 385 days with a median cumulative dose of 1290 mg. Of the patients reporting acromegaly severity at baseline (N=265), serum GH levels were < 10 ng/mL for 69% (183/265) of the patients and ≥ 10 ng/mL for 31% (82/265) of the patients.

The most commonly reported adverse-reactions reported by > 5% of patients who received Somatuline Depot (N=416) in the overall pooled safety studies in acromegaly patients were gastrointestinal disorders (diarrhea, abdominal pain, nausea, constipation, flatulence, vomiting, loose stools), cholelithiasis and injection site reactions.

Tables 1 and 2 present adverse reaction data from clinical studies with Somatuline Depot in acromegalic patients. The tables include data from a single clinical study and pooled data from seven clinical studies.

<u>Adverse Reactions in Parallel Fixed-Dose Phase of Study 1:</u>
The incidence of treatment-emergent adverse reactions for Somatuline Depot 60 mg, 90 mg, and 120 mg by dose as reported during the first 4 months (fixed-dose phase) of Study 1 [*see Clinical Studies (14)*], are provided in Table 1.

Table 1 Adverse Reactions at an Incidence > 5% Lanreotide Overall and Occurring at Higher Rate in Drug than Placebo: Placebo-Controlled and Fixed-Dose Phase of Study 1 by Dose

	Placebo-Controlled Double-Blind Phase Weeks 0 to 4		Fixed-Dose Phase Double-Blind + Single-Blind Weeks 0 to 20			
Body System Preferred Term	**Placebo (N=25)** N (%)	**Lanreotide Overall (N=83)** N (%)	**Lanreotide 60 mg (N=34)** N (%)	**Lanreotide 90 mg (N=36)** N (%)	**Lanreotide 120 mg (N=37)** N (%)	**Lanreotide Overall (N=107)** N (%)
Gastrointestinal System Disorders	**1 (4%)**	**30 (36%)**	**12 (35%)**	**21 (58%)**	**27 (73%)**	**60 (56%)**
Diarrhea	0	26 (31%)	9 (26%)	15 (42%)	24 (65%)	48 (45%)
Abdominal pain	1 (4%)	6 (7%)	3 (9%)	6 (17%)	7 (19%)	16 (15%)
Flatulence	0	5 (6%)	0 (0%)	3 (8%)	5 (14%)	8 (7%)
Application Site Disorders (Injection site mass/ pain/ reaction/ inflammation)	**0 (0%)**	**5 (6%)**	**3 (9%)**	**4 (11%)**	**8 (22%)**	**15 (14%)**
Liver and Biliary System Disorders	**1 (4%)**	**3 (4%)**	**9 (26%)**	**7 (19%)**	**4 (11%)**	**20 (19%)**
Cholelithiasis	0	2 (2%)	5 (15%)	6 (17%)	3 (8%)	14 (13%)
Heart Rate & Rhythm Disorders	**0**	**8 (10%)**	**7 (21%)**	**2 (6%)**	**5 (14%)**	**14 (13%)**
Bradycardia	0	7 (8%)	6 (18%)	2 (6%)	2 (5%)	10 (9%)
Red Blood Cell Disorders	**0**	**6 (7%)**	**2 (6%)**	**5 (14%)**	**2 (5%)**	**9 (8%)**
Anemia	0	6 (7%)	2 (6%)	5 (14%)	2 (5%)	9 (8%)
Metabolic & Nutritional Disorders	**3 (12%)**	**13 (16%)**	**8 (24%)**	**9 (25%)**	**4 (11%)**	**21 (20%)**
Weight decrease	0	7 (8%)	3 (9%)	4 (11%)	2 (5%)	9 (8%)

A patient is counted only once for each body system and preferred term.
Dictionary = WHOART.

In Study 1, the adverse reactions of diarrhea, abdominal pain and flatulence increased in incidence with increasing dose of Somatuline Depot.

Adverse Reactions in Long-Term Clinical Trials:

Table 2 provides the most common adverse reactions that occurred in 416 acromegalic patients treated with Somatuline Depot in seven studies. The analysis of safety compares adverse reaction rates of patients at baseline from the two efficacy studies, to the overall pooled data from seven studies. Patients with elevated GH and IGF-1 levels were either naive to somatostatin analog therapy or had undergone a 3-month washout [*see Clinical Studies (14)*].

Table 2 Adverse Reactions at an Incidence > 5.0% in Overall Group Reported in Clinical Studies

System Organ Class	Number and Percentage of Patients			
	Studies 1 & 2 (N = 170)		Overall Pooled Data (N = 416)	
	N	%	N	%
Patients with any Adverse Reactions	**157**	**92**	**356**	**86**
Gastrointestinal disorders	**121**	**71**	**235**	**57**
Diarrhea	81	48	155	37
Abdominal pain	34	20	79	19
Nausea	15	9	46	11
Constipation	9	5	33	8
Flatulence	12	7	30	7
Vomiting	8	5	28	7
Loose stools	16	9	23	6
Hepatobiliary disorders	**53**	**31**	**99**	**24**
Cholelithiasis	45	27	85	20
General disorders and administration site conditions	**51**	**30**	**91**	**22**
(Injection site pain /mass /induration /nodule /pruritus)	28	17	37	9
Musculoskeletal and connective tissue disorders	**44**	**26**	**70**	**17**
Arthralgia	17	10	30	7
Nervous system disorders	**34**	**20**	**80**	**19**
Headache	9	5	30	7

Dictionary - MedDRA 7.1

In addition to the adverse reactions listed in Table 2, the following reactions were also seen:

- Sinus bradycardia occurred in 7% (12) of patients in the pooled Study 1 and 2 and in 3% (13) of patients in the overall pooled studies.
- Hypertension occurred in 7% (11) of patients in the pooled Study 1 and 2 and in 5% (20) of patients in the overall pooled studies.
- Anemia occurred in 7% (12) of patients in the pooled Study 1 and 2 and in 3% (14) of patients in the overall pooled studies.

Gastrointestinal Adverse Reactions

In the pooled clinical studies of Somatuline Depot therapy, a variety of gastrointestinal reactions occurred, the majority of which were mild to moderate in severity. One percent of acromegalic patients treated with Somatuline Depot in the pooled clinical studies discontinued treatment because of gastrointestinal reactions.

Gallbladder Adverse Reactions

In clinical studies involving 416 acromegalic patients treated with Somatuline Depot, cholelithiasis and gallbladder sludge were reported in 20% of the patients. Among 167 acromegalic patients treated with Somatuline Depot who underwent routine evaluation with gallbladder ultrasound, 17.4% had gallstones at baseline. New cholelithiasis was reported in 12.0% of patients. Cholelithiasis may be related to dose or duration of exposure [*see Cholelithiasis and Gallbladder Sludge (5.1)*].

Injection Site Reactions

In the pooled clinical studies, injection site pain (4.1%) and injection site mass (1.7%) were the most frequently reported local adverse drug reactions that occurred with the administration of Somatuline Depot. In a specific analysis 20 of 413 patients (4.8%) presented indurations at the injection site. Injection site adverse reactions were more commonly reported soon after the start of treatment and were less commonly reported as treatment continued. Such adverse reactions were usually mild or moderate but did lead to withdrawal from clinical studies in two subjects.

Glucose Metabolism Adverse Reactions

In the clinical studies in acromegalic patients treated with Somatuline Depot, adverse reactions of dysglycemia (hypoglycemia, hyperglycemia, diabetes) were reported by 14% (47/332) of patients and were considered related to study drug in 7% (24/332) of patients [*see Hyperglycemia and Hypoglycemia (5.2)*].

Cardiac Adverse Reactions

In the pooled clinical studies, sinus bradycardia (3.1%) was the most frequently observed heart rate and rhythm disorder. All other cardiac adverse drug reactions were observed in < 1% of patients. The relationship of these events to Somatuline Depot could not be established because many of these patients had underlying cardiac disease [*see Cardiovascular Abnormalities (5.4)*].

A comparative echocardiography study of lanreotide and another somatostatin analog demonstrated no difference in the development of new or worsening valvular regurgitation between the two treatments over one year. The occurrence of clinically significant mitral regurgitation (i.e., moderate or severe in intensity) or of clinically significant aortic regurgitation (i.e., at least mild in intensity) was low in both groups of patients throughout the study.

Other Adverse Reactions

For the most commonly occurring adverse reactions in the pooled analysis, diarrhea, abdominal pain and cholelithiasis, there was no apparent trend for increasing incidence with age. GI disorders and renal and urinary disorders were more common in patients with documented hepatic impairment; however, the incidence of cholelithiasis was similar between groups.

Laboratory investigations of acromegalic patients treated with Somatuline Depot in clinical studies show that the percentage of patients with putative antibodies at any time point after treatment is low (<1% to 4% of patients in specific studies whose antibodies were tested). The antibodies did not appear to affect the efficacy or safety of Somatuline Depot.

6.2 Postmarketing Experience

As adverse reactions experienced post approval use are reported voluntarily from a population of uncertain size it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The profile of reported adverse reactions for Somatuline Depot was consistent with that observed for treatment-related adverse reactions in the clinical studies. Those reported most

frequently being gastrointestinal disorders (abdominal pain and diarrhea) and general disorders and administration site conditions (injection site reactions).

7 DRUG INTERACTIONS

7.1 Insulin and Oral Hypoglycemic Drugs

Lanreotide, like somatostatin and other somatostatin analogs, inhibits the secretion of insulin and glucagon. Therefore, blood glucose levels should be monitored when lanreotide treatment is initiated or when the dose is altered and antidiabetic treatment should be adjusted accordingly.

7.2 Cyclosporine

Concomitant administration of cyclosporine with lanreotide may decrease the relative bioavailability of cyclosporine and, therefore, may necessitate adjustment of cyclosporine dose to maintain therapeutic levels.

7.3 Other Concomitant Drug Therapy

The pharmacological gastrointestinal effects of Somatuline Depot may reduce the intestinal absorption of concomitant drugs. Limited published data indicate that concomitant administration of a somatostatin analog and bromocriptine may increase the availability of bromocriptine.

Concomitant administration of bradycardia inducing drugs (e.g. beta-blockers) may have an additive effect on the reduction of heart rate associated with lanreotide. Dose adjustments of concomitant medication may be necessary.

Vitamin K absorption was not affected when concomitantly administered with lanreotide.

7.4 Drug Metabolism Interactions

The limited published data available indicate that somatostatin analogs may decrease the metabolic clearance of compounds known to be metabolized by cytochrome P450 enzymes, which may be due to the suppression of growth hormone. Since it cannot be excluded that lanreotide may have this effect, other drugs mainly metabolized by CYP3A4 and which have a low therapeutic index (e.g. quinidine, terfenadine) should therefore be used with caution. Drugs metabolized by the liver may be metabolized more slowly during lanreotide treatment and dose reductions of the concomitantly administered medications should be considered.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

Lanreotide has been shown to have an embryocidal effect in rats and rabbits. There are no adequate and well controlled studies in pregnant women. Somatuline Depot should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Reproductive studies in pregnant rats given 30 mg/kg by subcutaneous injection every 2 weeks (5-times the human dose based on body surface area comparisons) resulted in decreased embryo/fetal survival. Studies in pregnant rabbits given subcutaneous injections of 0.45 mg/kg/day, 2-times the human therapeutic exposures at the maximum recommended dose of 120 mg based on comparisons of relative body surface area shows decreased fetal survival and increased fetal skeletal/soft tissue abnormalities.

8.3 Nursing Mothers

It is not known whether lanreotide is excreted in human milk. Many drugs are excreted in human milk. As a result of serious adverse reactions in animals and potential in nursing infants from Somatuline, a decision should be made whether to discontinue nursing or discontinue the drug taking into account the importance of the drug to the mother.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

No overall differences in safety or effectiveness were observed between elderly patients compared with younger patients, and the other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. It is not necessary to alter the starting dose in elderly patients as expected lanreotide serum concentrations in the elderly are well within the range of serum concentrations safely tolerated in healthy young subjects. Similarly, it is not necessary to alter the titration or maintenance doses of Somatuline Depot as dose selection is based on therapeutic response [*see Dosage and Administration (2) and Clinical Pharmacology 12.3)*].

8.6 Renal Impairment

Lanreotide has not been studied in patients with mild, moderate and severe renal failure. It is recommended that patients with moderate and severe renal impairment receive a starting dose of lanreotide of 60 mg [*see Dosage and Administration (2) and Clinical Pharmacology (12.3)*].

8.7 Hepatic Impairment

It is recommended that patients with moderate and severe hepatic impairment receive a starting dose of lanreotide of 60 mg [*see Dosage and Administration (2) and Clinical Pharmacology (12.3)*].

10 OVERDOSAGE

If overdose occurs, symptomatic management is indicated.

There are no confirmed postmarketing cases of overdose with lanreotide that were serious or led to an adverse reaction.

Up-to-date information about the treatment of overdose can often be obtained from the National Poison Control Center at phone number 1-800-222-1222.

11 DESCRIPTION

Somatuline Depot (lanreotide) Injection 60, 90 and 120 mg is a prolonged-release formulation for deep subcutaneous injection containing the drug substance lanreotide acetate, a synthetic octapeptide with a biological activity similar to naturally occurring somatostatin, and water for injection.

Somatuline Depot is available as sterile, ready-to-use, pre-filled syringes containing lanreotide supersaturated bulk solution of 24.6% w/w lanreotide base.

Each syringe contains:	**Somatuline Depot 60 mg**	**Somatuline Depot 90 mg**	**Somatuline Depot 120 mg**
Lanreotide acetate	79.8 mg	116.4 mg	155.5 mg
Water for injection	186.2mg	271.6 mg	363 mg

Lanreotide acetate is a synthetic cyclical octapeptide analog of the natural hormone, somatostatin. Lanreotide acetate is chemically known as [cyclo S-S]-3-(2-naphthyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-L-threoninamide, acetate salt. Its molecular weight is 1096.34 (base) and its amino acid sequence is:

```
S----------------------------S
|                            |
D-βNal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH2, x(CH3COOH) where x = 1.6 to 3.4
```

For appearance of the formulation, see *Dosage Forms and Strengths (3).*

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Lanreotide, the active component of Somatuline Depot is an octapeptide analog of natural somatostatin. The mechanism of action of lanreotide is believed to be similar to that of natural somatostatin.

12.2 Pharmacodynamics

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. Like somatostatin, lanreotide is an inhibitor of various endocrine, neuroendocrine, exocrine and paracrine functions.

The primary pharmacodynamic effect of lanreotide is a reduction of GH and/or IGF-1 levels enabling normalization of levels in acromegalic patients [*see Clinical Studies (14)*]. In acromegalic patients, lanreotide reduces GH levels in a dose-dependent way. After a single injection of Somatuline Depot, plasma GH levels fall rapidly and are maintained for at least 28 days.

Lanreotide inhibits the basal secretion of motilin, gastric inhibitory peptide and pancreatic polypeptide, but has no significant effect on the secretion of secretin. Lanreotide inhibits post-prandial secretion of pancreatic polypeptide, gastrin and cholecystokinin (CCK). In healthy

subjects, lanreotide produces a reduction and a delay in post-prandial insulin secretion, resulting in transient, mild glucose intolerance.

Lanreotide inhibits meal-stimulated pancreatic secretions, and reduces duodenal bicarbonate and amylase concentrations, and produces a transient reduction in gastric acidity.

Lanreotide has been shown to inhibit gallbladder contractility and bile secretion in healthy subjects [*see Warnings and Precautions (5)*].

In healthy subjects, lanreotide inhibits meal-induced increases in superior mesenteric artery and portal venous blood flow, but has no effect on basal or meal-stimulated renal blood flow. Lanreotide has no effect on renal plasma flow or renal vascular resistance. However, a transient decrease in glomerular filtration rate (GFR) and filtration fraction has been observed after a single injection of lanreotide.

In healthy subjects, non-significant reductions in glucagon levels were seen after lanreotide administration. In diabetic non-acromegalic subjects receiving a continuous infusion (21 day) of lanreotide, serum glucose concentrations were temporarily decreased by 20-30% after the start and end of the infusion. Serum glucose concentrations returned to normal levels within 24 hours. A significant decrease in insulin concentrations was recorded between baseline and Day 1 only [*see Warnings and Precautions (5)*].

Lanreotide inhibits the nocturnal increase in thyroid-stimulating hormone (TSH) seen in healthy subjects. Lanreotide reduces prolactin levels in acromegalic patients treated on a long-term basis.

12.3 Pharmacokinetics

Somatuline Depot is thought to form a drug depot at the injection site due to the interaction of the formulation with physiological fluids. The most likely mechanism of drug release is a passive diffusion of the precipitated drug from the depot towards the surrounding tissues, followed by the absorption to the blood stream.

After a single deep, subcutaneous administration, the mean absolute bioavailability of Somatuline Depot in healthy subjects was 73.4, 69.0 and 78.4%, for the 60, 90 and 120 mg doses, respectively. Mean Cmax values ranged from 4.3 to 8.4 ng/mL during the first day. Single-dose linearity was demonstrated with respect to AUC and Cmax, and showed high inter-subject variability. Somatuline Depot showed sustained release of lanreotide with a half-life of 23 to 30 days. Mean serum concentrations were > 1 ng/mL throughout 28 days at 90 mg and 120 mg and > 0.9 ng/mL with 60 mg.

In a repeat-dose administration pharmacokinetics (PK) study in acromegalic patients, rapid initial release was seen giving peak levels during the first day after administration. At doses of Somatuline Depot between 60 and 120 mg linear pharmacokinetics were observed in acromegalic patients. At steady state mean Cmax values were 3.8 ± 0.5, 5.7 ± 1.7 and 7.7 ± 2.5 ng/mL increasing linearly with dose. The mean accumulation ratio index was 2.7 which is in line with the range of values for the half life of Somatuline Depot. The steady-state trough serum lanreotide concentrations in patients receiving Somatuline Depot every 28 days were 1.8 ± 0.3; 2.5 ± 0.9 and 3.8 ± 1.0 ng/mL at 60, 90 and 120 mg doses respectively. A limited initial burst effect and a low peak to trough fluctuation (81% to 108%) of the serum concentration at the plateau was observed.

For the same doses, similar values were obtained in clinical studies after at least four administrations (2.3 ± 0.9, 3.2 ± 1.1 and 4.0 ± 1.4 ng/mL, respectively).

Somatuline Depot has not been studied in special populations. For completeness, information on studies with an immediate-release formulation (IRF) of lanreotide administered intravenously is provided. A lthough some changes in elimination or distribution have been observed after IRF administration, no changes in the apparent half-life are expected with Somatuline Depot as the terminal phase is controlled by the release of lanreotide from the formulation.

Subjects with end-stage renal disease requiring dialysis showed an approximate 2-fold decrease in total serum clearance of lanreotide, with a consequent 2-fold increase in half-life and AUC.

Studies in healthy elderly subjects showed an 85% increase in half-life and a 65% increase in mean residence time (MRT) of lanreotide compared to those seen in healthy young subjects; however, there was no change in either AUC or Cmax of lanreotide in elderly as compared to healthy young subjects.

In moderately to severely hepatically-impaired subjects, a 30% reduction in clearance of lanreotide was observed.

Patients with moderate to severe renal impairment or moderate to severe hepatic impairment should begin treatment with Somatuline Depot 60 mg.

In studies evaluating excretion, <5% of lanreotide was excreted in urine and less than 0.5% was recovered unchanged in feces, indicative of some biliary excretion.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenicity, Mutagenicity, Impairment of Fertility

Standard lifetime carcinogenicity bioassays were conducted in mice and rats. Mice were given daily subcutaneous doses of lanreotide acetate at 0.5, 1.5, 5, 10 and 30 mg/kg for 104 weeks. Cutaneous and subcutaneous tumors of fibrous connective tissues at the injection sites were observed at the high dose of 30 mg/kg/day. Fibrosarcomas in both genders and malignant fibrous histiocytomas were observed in males at 30mg/kg/day resulting in exposures 3-times higher than the clinical therapeutic exposure at the maximum therapeutic dose of 120 mg given by monthly subcutaneous injection based on the AUC values. Rats were given daily subcutaneous doses of lanreotide acetate at 0.1, 0.2, and 0.5 mg/kg for 104 weeks. Increased cutaneous and subcutaneous tumors of fibrous connective tissues at the injection sites were observed at the dose of 0.5mg/kg/day resulting in exposures less than the clinical therapeutic exposure at 120 mg given by monthly subcutaneous injection. The increased incidence of injection site tumors in rodents is likely related to the increased dosing frequency (daily) in animals compared to monthly dosing in humans and therefore may not be clinically relevant.

Lanreotide was not genotoxic in tests for gene mutations in a bacterial mutagenicity (Ames) assay, or mouse lymphoma cell assay with or without metabolic activation. Lanreotide was not genotoxic in tests for the detection of chromosomal aberrations in a human lymphocyte and *in vivo* mouse micronucleus assay.

Subcutaneous dosing (30mg/kg/2 wks) before mating and continuing into gestation in rats at doses 5 times the human clinical exposure (120 mg every 4 weeks) based on mg/m^2 had reduced fertility. Gestation length was statistically significantly increased suggesting some delay in parturition at 3 times human exposure. The reduction in fertility in non-acromegalic animals is likely related to the pharmacologic activity (decreased growth hormone secretion) of lanreotide acetate.

14 CLINICAL STUDIES

The effect of Somatuline Depot on reducing GH and IGF-levels and control of symptoms in patients with acromegaly was studied in two long-term, multiple-dose, randomized multicenter studies.

Study 1

This one-year study included a 4-week double-blind, placebo-controlled phase, a 16-week single-blind, fixed-dose phase, and a 32-week open-label dose-titration phase. Patients with active acromegaly based on biochemical tests and medical history entered a 12-week washout period if there was previous treatment with a somatostatin analog or a dopaminergic agonist.

Upon entry, patients were randomly allocated to receive a single deep subcutaneous injection of Somatuline Depot 60, 90 or 120 mg or placebo. Four weeks later, patients entered a fixed-dose phase where they received 4 injections of Somatuline Depot followed by a dose-titration phase of 8 injections for a total of 13 injections over 52 weeks (including the placebo phase). Injections were given at 4-week intervals. During the dose-titration phase of the study, the dose was titrated twice (every fourth injection), as needed, according to individual GH and IGF-1 levels.

A total of 108 patients (51 males, 57 females) were enrolled in the initial placebo-controlled phase of the study. Half (54/108) of the patients had never been treated with a somatostatin analog or dopamine agonist, or had stopped treatment for at least 3 months prior to their participation in the study and were required to have a mean GH level > 5 ng/mL at their first visit. The other half of the patients had received prior treatment with a somatostatin analog or a dopamine agonist before study entry and at study entry were to have a mean GH concentration >3 ng/mL and at least a 100% increase in mean GH concentration after washout of medication.

One hundred and seven (107) patients completed the placebo-controlled phase, 105 patients completed the fixed-dose phase and 99 patients completed the dose-titration phase. Patients not completing withdrew due to adverse events (5) or lack of efficacy (4).

In the double-blind phase of study 1, a total of 52 (63%) of the 83 lanreotide-treated patients had a > 50% decrease in mean GH from baseline to Week 4 including 52%, 44% and 90% of patients in the 60, 90 and 120 mg groups, respectively, compared to placebo (0%, 0/25). In the fixed-dose phase at Week 16, 72% of all 107 lanreotide-treated patients had a decrease from baseline in mean GH of > 50% including 68% (23/34), 64% (23/36) and 84% (31/37) of patients in the 60, 90 and 120 mg lanreotide treatment groups, respectively. Efficacy achieved in the first 16 weeks was maintained for the duration of the study (see Table 3).

Table 3 Overall Efficacy Results Based on GH and IGF 1 Levels by Treatment Phase in Study 1

		Baseline N=107	Before Titration 1 (16 weeks) N=107	Before Titration 2 (32 weeks) N=105	Last Value Available* N=107
GH					
≤5.0 ng/mL	Number of Responders (%)	20 (19%)	72 (67%)	76 (72%)	74 (69%)
≤2.5 ng/mL	Number of Responders (%)	0 (0%)	52 (49%)	59 (56%)	55 (51%)
≤1.0 ng/mL	Number of Responders (%)	0 (0%)	15 (14%)	18 (17%)	17 (16%)
Median GH	ng/mL	10.27	2.53	2.20	2.43
GH Reduction	Median % Reduction	--	75.5	78.2	75.5
IGF-1					
Normal[3]	Number of Responders (%)	9 (8%)	58 (54%)	57 (54%)	62 (58%)
Median IGF-1	ng/mL	775.0	332.0[1]	316.5[2]	326.0
IGF-1 Reduction	Median % Reduction	--	52.3[1]	54.5[2]	55.4
IGF-1 Normal[3] + GH ≤2.5 ng/mL	Number of Responders (%)	0 (0%)	41 (38%)	46 (44%)	44 (41%)

[1] n=105, [2] n=102, [3] Age-adjusted, * Last Observation Carried Forward

Study 2

This was a 48-week, open-label, uncontrolled multicenter study which enrolled patients who had an IGF-1 concentration ≥ 1.3 times the upper limit of the age-adjusted normal range. Patients receiving treatment with a somatostatin analog (other than Somatuline Depot) or a dopaminergic agonist had to attain this IGF-1 concentration after a washout period of up to 3 months.

Patients were initially enrolled in a 4-month fixed-dose phase where they received four deep subcutaneous injections of Somatuline Depot, 90 mg, at 4-week intervals. Patients then entered a dose-titration phase where the dose of Somatuline Depot was adjusted based on GH and IGF-1 levels at the beginning of the dose-titration phase and, if necessary, again after another 4 injections. Patients titrated up to the maximum dose (120 mg) were not allowed to titrate down again.

A total of 63 patients (38 males, 25 females) entered the fixed-dose phase of the trial and 57 patients completed 48-weeks of treatment. Six patients withdrew due to adverse reactions (3), other reasons (2), or lack of efficacy (1).

After 48 weeks of treatment with Somatuline Depot at 4-week intervals, 43% (27/63) of the acromegalic patients in this study achieved normal age-adjusted IGF-1 concentrations. Mean IGF-1 concentrations after treatment completion were 1.3 ± 0.7 times the upper limit of normal compared to 2.5 ± 1.1 times the upper limit of normal at baseline.

The reduction in IGF-1 concentrations over time correlated with a corresponding marked decrease in mean GH concentrations. The proportion of patients with mean GH concentrations < 2.5 ng/mL increased significantly from 35% to 77% after the fixed-dose phase and 85% at the end of the study. At the end of treatment, 24/63 (38%) of patients had

both normal IGF-1 concentrations and a GH concentration of ≤ 2.5 ng/mL (see Table 4) and 17/63 patients (27%) had both normal IGF-1 concentrations and a GH concentration of <1 ng/mL.

Table 4 Overall Efficacy Results Based on GH and IGF-1 Levels by Treatment Phase in Study 2

		Baseline N=63	Before Titration 1 (12 wks) N=63	Before Titration 2 (28 wks) N=59	Last Value Available* N=63
IGF-1					
Normal[1]	Number of Responders (%)	0 (0%)	17 (27%)	22 (37%)	27 (43%)
Median IGF-1	ng/mL	689.0	382.0	334.0	317.0
IGF-1 Reduction	Median % Reduction	--	41.0	51.0	50.3
GH					
≤5.0 ng/mL	Number of Responders (%)	40 (64%)	59 (94%)	57 (97%)	62 (98%)
≤2.5 ng/mL	Number of Responders (%)	21 (33%)	47 (75%)	47 (80%)	54 (86 %)
≤1.0 ng/mL	Number of Responders (%)	8 (13%)	19 (30%)	18 (31%)	28 (44%)
Median GH	ng/mL	3.71	1.65	1.48	1.13
GH Reduction	Median % Reduction	--	63.2	66.7	78.6[2]
IGF-1 normal[1] **+ GH ≤2.5 ng/mL**	Number of Responders (%)	0 (0%)	14 (22%)	20 (34%)	24 (38%)

[1] Age-adjusted, [2] N= 62, * Last Observation Carried Forward

Examination of age and gender subgroups did not identify differences in response to Somatuline Depot among these subgroups. The limited number of patients in the different racial subgroups did not raise any concerns regarding efficacy of Somatuline Depot in these subgroups.

16 HOW SUPPLIED/STORAGE AND HANDLING

Somatuline Depot is supplied in strengths of 60 mg, 90 mg and 120 mg in a single, sterile, pre-filled, ready-to-use, polypropylene syringe fitted with a 20 mm needle covered by a dry natural rubber sheath. Each pre-filled syringe is sealed in a laminated pouch and packed in a carton.

NDC 15054-060-01 60-mg, sterile, pre-filled syringe
NDC 15054-090-01 90-mg, sterile, pre-filled syringe
NDC 15054-120-02 120-mg, sterile,pre-filled syringe

Storage and Handling

Somatuline Depot must be stored in a refrigerator at 2°C to 8°C (36°F to 46°F) and protected from light in its original package. Thirty (30) minutes prior to injection, remove sealed pouch

of Somatuline Depot from refrigerator and allow it to come to room temperature. Keep pouch sealed until injection.

Each syringe is intended for single use. Do not use beyond the expiration date on the packaging.

17 PATIENT COUNSELING INFORMATION

The physician should provide a copy of the FDA-Approved Patient Labeling and review the contents with the patient. Patients should be advised to inform their doctor or pharmacist if they develop any unusual symptoms, or if any known symptom persists or worsens.

Patients should be advised that response to Somatuline Depot should be monitored by periodic measurements of GH and IGF-1 levels, with a goal of decreasing these levels to the normal range.

Manufactured by:
Ipsen Pharma Biotech
83870 Signes, France

Distributed by:
Tercica Inc.
Brisbane, CA 94005 USA

Patient Labeling

Somatuline® Depot (So-mah-tu-leen Dee-Poh)
(lanreotide) Injection

Read the Patient Information that comes with Somatuline® Depot before you receive the first injection and before each monthly injection. There may be new information. This leaflet does not take the place of talking with your doctor about your medical condition or your treatment.

What is Somatuline® Depot?

Somatuline® Depot is an injectable medicine used for the long-term treatment of patients with acromegaly:

- when surgery or radiotherapy have not worked well enough
- who are not able to have surgery or radiotherapy

Somatuline® Depot contains the medicine lanreotide, which is similar to the hormone somatostatin (which is made in the body). Somatuline® Depot, like somatostatin, lowers the levels of certain hormones in the body such as growth hormone (GH) and insulin-like growth factor-1 (IGF-1). Lowering these hormone levels can help treat patients with acromegaly.

Somatuline Depot has not been studied in children.

What should I tell my doctor before receiving Somatuline® Depot?

Tell your doctor about all of your medical conditions, including if you:

- have diabetes.
- have liver or kidney problems.
- have ever had heart problems.
- are allergic to latex or natural dry rubber. The pre-filled syringe needle cover contains rubber.
- are pregnant or can become pregnant. It is not known if Somatuline Depot could harm your unborn baby.
- are breast-feeding or planning to breast-feed. It is not known if Somatuline® Depot passes into your breast milk. Talk to your doctor about the best way to feed your baby if you receive Somatuline® Depot.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins and herbal supplements. Somatuline® Depot and other medicines may affect each other causing side effects. Somatuline® Depot may affect the way other medicines work, and other medicines may affect how Somatuline® Depot works. The dose of Somatuline® Depot or your other medicines may need to be adjusted.

Especially tell your doctor if you take:

- insulin or other diabetes medicines
- medicines that lower your heart rate such as beta blockers
- Cyclosporine (Gengraf, Neoral, Sandimmune)
- Bromocriptine (Parlodel)

Know the medicines you take. Keep a list of your medicines and show it to your doctor..

How will I receive Somatuline® Depot?

- You will receive a Somatuline® Depot injection every 4 weeks as directed by your doctor. Your doctor will tell you how long you need to receive Somatuline Depot.
- Somatuline® Depot is injected deep under the skin of the upper outer area of your buttock.
- The injection site should change (alternate) between your right and left side each time you receive an injection of Somatuline® Depot.
- After 3 months, your doctor should check your levels of growth hormone (GH) and insulin-like growth factor-1 (IGF-1), talk to you about your symptoms, and adjust your dose of Somatuline® Depot as needed.
- If you miss an injection, talk with your doctor as soon as possible to advise on another injection.

What are the possible side effects of Somatuline® Depot?

Side effects include:

- **Stomach and Intestinal problems.** Diarrhea, stomach (abdominal) pain, nausea, gas, constipation and loose stools can occur. These side effects tend to diminish with continued treatment.
- **Gallbladder problems.** Gallstones can develop in the gallbladder. Tell your doctor if you get severe pain in the right upper area of your stomach (abdomen), along with nausea and vomiting. The pain may last for several hours.
- **Skin reactions.** Pain, itching or a lump may occur at the injection site.
- **Heart problems including a low heart rate, high blood pressure, and new or worse heart valve problems.**
- **Change in blood sugar levels.** Somatuline® Depot can cause low blood sugar (hypoglycemia) or high blood sugar (hyperglycemia) levels, especially when you first start receiving the injections or if the dose is changed. If you have diabetes, carefully follow your doctor's instructions for monitoring your blood sugar levels. Your diabetes medicines may need to be changed in order to control your blood sugar while you are receiving Somatuline® Depot.

Other side effects include: headache, joint pain, anemia (decreased red blood cells), tiredness, and weight loss.

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of Somatuline® Depot. Ask your doctor for more information.

General Information about Somatuline® Depot

Medicines are sometimes prescribed for conditions other than those listed in the patient leaflet. This Patient Information leaflet summarizes the most important information about Somatuline® Depot. If you would like more information about Somatuline® Depot talk with your doctor. You can ask your doctor or healthcare provider for information on Somatuline® Depot that is written for health professionals.

For more information call TERCICA at 1-866-837-2422 or visit the website at www.somatulinedepot.com.

Issued August 2007
Somatuline® Depot is manufactured by Ipsen Pharma Biotech SAS BP, 707 Signes, 83030 Toulon Cedex 9, France for Beaufour Ipsen Pharma SAS, 24 rue Erlanger, 75016 Paris France

Manufacturer: Ipsen Pharma
Biotech; Signes France

Warning: Needle Sheath
Contains Dry Natural Rubber

Somatuline® Depot
(lanreotide) Injection 60 mg

Exp: MM YYYY
Lot: XXXX

Manufacturer: Ipsen Pharma
Biotech; Signes France

Warning: Needle Sheath
Contains Dry Natural Rubber

Somatuline® Depot
(lanreotide) Injection 90 mg

Exp: MM YYYY
Lot: XXXX

Manufacturer: Ipsen Pharma
Biotech; Signes France

Warning: Needle Sheath
Contains Dry Natural Rubber

Somatuline® Depot
(lanreotide) Injection 120 mg

Exp: MM YYYY
Lot: XXXX

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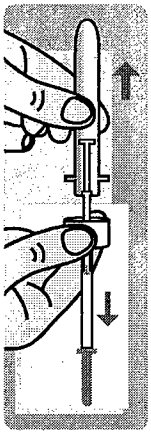
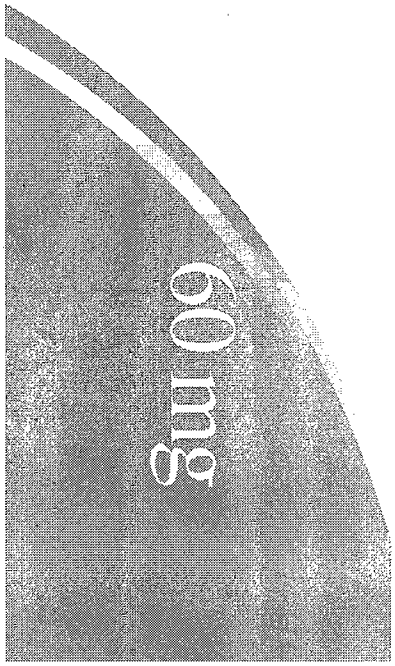




Somatuline® Depot
(lanreotide) Injection 60 mg

Rx only

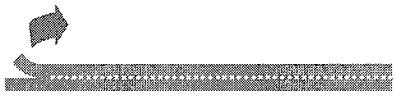
Manufactured by: Ipsen Pharma Biotech - Signes France

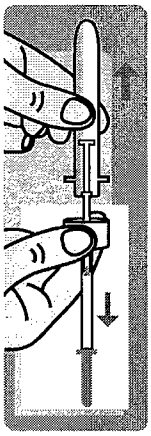
Warning: Needle Sheath Contains Dry Natural Rubber

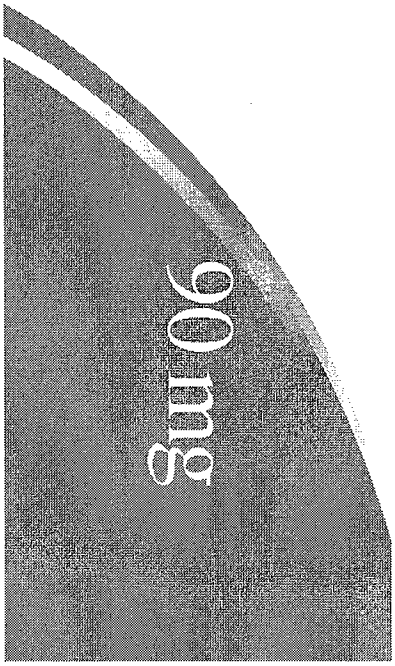
EXP: MM/YYYY

Lot:

Space for Bar Code







Somatuline® Depot
(lanreotide) Injection 90 mg

Rx only

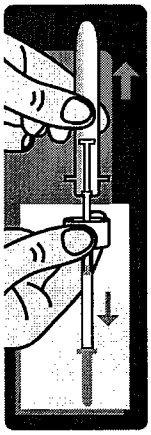
Manufactured by: Ipsen Pharma Biotech - Signes France

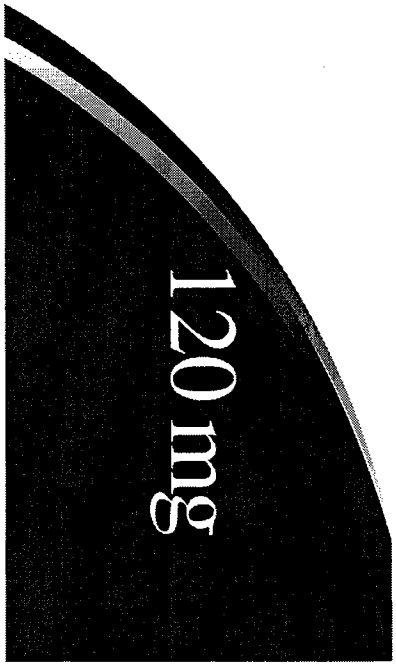
Warning: Needle Sheath Contains Dry Natural Rubber

EXP: MM/YYYY

Lot:

Space for Bar Code





Somatuline® Depot
(lanreotide) Injection 120 mg

Rx only

Manufactured by: Ipsen Pharma Biotech - Signes France

Warning: Needle Sheath Contains Dry Natural Rubber

EXP: MM/YYYY

Lot:

PHA209B-SC 17-AUG-07

Somatuline® Depot
(lanreotide) Injection 60 mg
Distributed by :
Tercica Inc. - Brisbane, CA 94005 - USA

60 mg

WARNING : NEEDLE SHEATH CONTAINS DRY NATURAL RUBBER
USE ONLY AS DIRECTED BY YOUR DOCTOR

IPSEN Tercica

Somatuline® Depot
(lanreotide) Injection 60 mg

For deep subcutaneous injection
Rx only. For single use only. Sterile.
Warning: Needle Sheath Contains Dry Natural Rubber

NDC 15054 060 01

IPSEN Tercica

Somatuline® Depot
(lanreotide) Injection 60 mg

60 mg

Somatuline® Depot
(lanreotide) Injection 60 mg

Manufactured by: Ipsen Pharma Biotech
83870 Signes
France

Distributed by: Tercica Inc.
Brisbane, CA 94005
USA

NDC 15054 060 01

If you have any questions about Somatuline® Depot, please call 1-866-837-2422

Rx only

STORAGE: Refrigerate at 2°C - 8°C
(36°F - 46°F) in its original package.

USUAL DOSAGE: see enclosed leaflet.

CONTENTS: This box contains one (1) pre-filled syringe.
Each pre-filled syringe contains a supersaturated solution of lanreotide acetate corresponding to 24.6mg of lanreotide base per 100mg solution, which ensures the injection of 60mg lanreotide.

5730.01

Black
decoupe foncee
278
542
non vernis

IPSEN PHARMA BIOTECH
Somatuline Depot 60 mg USA
5730.01
PHA209B - CA06-747
80 x 20 x 285

Somatuline® Depot
(lanreotide) Injection **90 mg**

Manufactured by: Ipsen Pharma Biotech
83870 Signes
France

Distributed by: Tercica Inc.
Brisbane, CA 94005
USA

NDC 15054 090 01

Rx only

If you have any questions about Somatuline® Depot, please call 1-866-837-2422

5740.01

STORAGE: Refrigerate at 2°C - 8°C (36°F - 46°F) in its original package.

USUAL DOSAGE: see enclosed leaflet.

CONTENTS: This box contains one (1) pre-filled syringe. Each pre-filled syringe contains a supersaturated solution of lanreotide acetate corresponding to 24.6mg of lanreotide base per 100mg solution, which ensures the injection of 90mg lanreotide.

Somatuline® Depot
(lanreotide) Injection **90 mg**

IPSEN Tercica

90 mg

Somatuline® Depot
(lanreotide) Injection **90 mg**
Distributed by :
Tercica Inc. - Brisbane, CA 94005 - USA

90 mg

NDC 15054 090 01

Somatuline® Depot
(lanreotide) Injection **90 mg**

For deep subcutaneous injection
Rx only. For single use only. Sterile.
Warning: Needle Sheath Contains Dry Natural Rubber

IPSEN Tercica

90 mg

Somatuline® Depot
(lanreotide) Injection **90 mg**

IPSEN Tercica

90 mg

WARNING: NEEDLE SHEATH CONTAINS DRY NATURAL RUBBER
USE ONLY AS DIRECTED BY YOUR DOCTOR

Somatuline® Depot
(lanreotide) Injection **90 mg**

IPSEN Tercica

90 mg

non vernis

Black

298

decoupe foncee

542

IPSEN PHARMA BIOTECH
Somatuline Depot 90 mg USA
5740.01
PHA210A - CA06-747-1
80 x 20 x 285

PHA210A-SC

17-AUG-07

17-AUG-07

Somatuline® Depot
(lanreotide) Injection **120 mg**

IPSEN Tercica

120 mg

Somatuline® Depot
(lanreotide) Injection **120 mg**

Manufactured by: Ipsen Pharma Biotech
83870 Signes
France

Distributed by: Tercica Inc.
Brisbane, CA 94005
USA

NDC 15054 120 02

Rx only

If you have any questions about Somatuline® Depot, please call 1-866-837-2422

5750.01

STORAGE: Refrigerate at 2°C - 8°C
(36°F - 46°F) in its original package.

USUAL DOSAGE: see enclosed leaflet.

CONTENTS: This box contains one (1) pre-filled syringe.
Each pre-filled syringe contains a supersaturated solution of
lanreotide acetate corresponding to 24.6mg of lanreotide base
per 100mg solution, which ensures the injection of 120mg lanreotide.

Somatuline® Depot
(lanreotide) Injection **120 mg**
Distributed by :
Tercica Inc. - Brisbane, CA 94005 - USA

120 mg

120 mg

Somatuline® Depot
(lanreotide) Injection **120 mg**

IPSEN Tercica

120 mg

Somatuline® Depot
(lanreotide) Injection **120 mg**

For deep subcutaneous injection
Rx only. For single use only. Sterile.
Warning: Needle Sheath Contains Dry Natural Rubber

NDC 15054 120 02

IPSEN Tercica

120 mg

WARNING: NEEDLE SHEATH CONTAINS DRY NATURAL RUBBER
USE ONLY AS DIRECTED BY YOUR DOCTOR

Somatuline® Depot
(lanreotide) Injection **120 mg**

IPSEN Tercica

120 mg

decoupe foncee

non vernis

Black

Blue 072

542

IPSEN PHARMA BIOTECH
Somatuline Depot 120 mg USA
5750.01
PHA207A - CA06-747-1
80 x 20 x 285

PHA207A-SC