Somatuline® Depot
(lanreotide) Injection 60 mg 90 mg 120 mg

Overview of Formative Studies Leading to the Redesigned Somatuline® Depot Delivery System:

Derived from "Co-Creation of a Lanreotide Autogel/Depot Syringe for the Treatment of Acromegaly and Neuroendocrine Tumours Through Collaborative Human Factor Studies"

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INDICATIONS

SOMATULINE® DEPOT (lanreotide) is a somatostatin analog indicated for:

- the long-term treatment of patients with acromegaly 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;
- the treatment of adult patients with unresectable, well- or moderately-differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival; and
- the treatment of adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy.

Note: Somatuline Depot is intended for healthcare provider administration.[1]

Objective

To develop and validate a redesigned delivery system for Somatuline Depot in collaboration with patients, caregivers, and HCPs at key stages in the developmental and testing process.[2]

Study Design

- The multicenter, international human factor studies consisted of 4 formative studies and 1 validation study. A total of 213 participants were enrolled, including 33 patients with acromegaly and 28 patients with GEP-NET[2]
- Four formative studies from 2015 to 2016 produced a final prototype of the delivery system based on feedback regarding the design and functionality from 145 participants, including patients with acromegaly and GEP-NET as well as caregivers and HCPs[2]
- One validation study in 2017 evaluated the final delivery system and IFU based on feedback from 68 participants, including 15 representatives of patients with acromegaly, 7 patients with GEP-NET, 11 representatives or caregivers of patients with GEP-NET, and 35 HCPs[2]

GEP-NET=gastroenteropancreatic neuroendocrine tumor; HCP=healthcare professional; IFU=instructions for use.

Formative Studies—Results Leading to the Development of the Current Delivery System

The design was progressively changed based on participants' feedback during the 4 formative studies to create the redesigned Somatuline Depot delivery system (Table 1)[2]

Table 1. Summary of the Design Changes Throughout the Formative Studies[2]

Participant feedback during the formative studies	Changes for the redesigned delivery system
Assessment of the previous device and new prototypes	
Needle cap should be small, with grips for removal	Rubber grid material for removal
Syringe body should be clear and relatively thin, with a comfortable grip	Transparent body with sturdier cover for visualization of complete dose administration
Flanges should be textured, with a more comfortable grip	Larger curved flanges for better finger placement and stability
In-use scenario	
One participant tried injecting without removing the plunger protector	Plunger protector was replaced with a tray
One participant accidentally pulled out the plunger support while trying to remove the cap	Improvement of the syringe body design and plunger support to prevent tear-off

IMPORTANT SAFETY INFORMATION

Contraindications

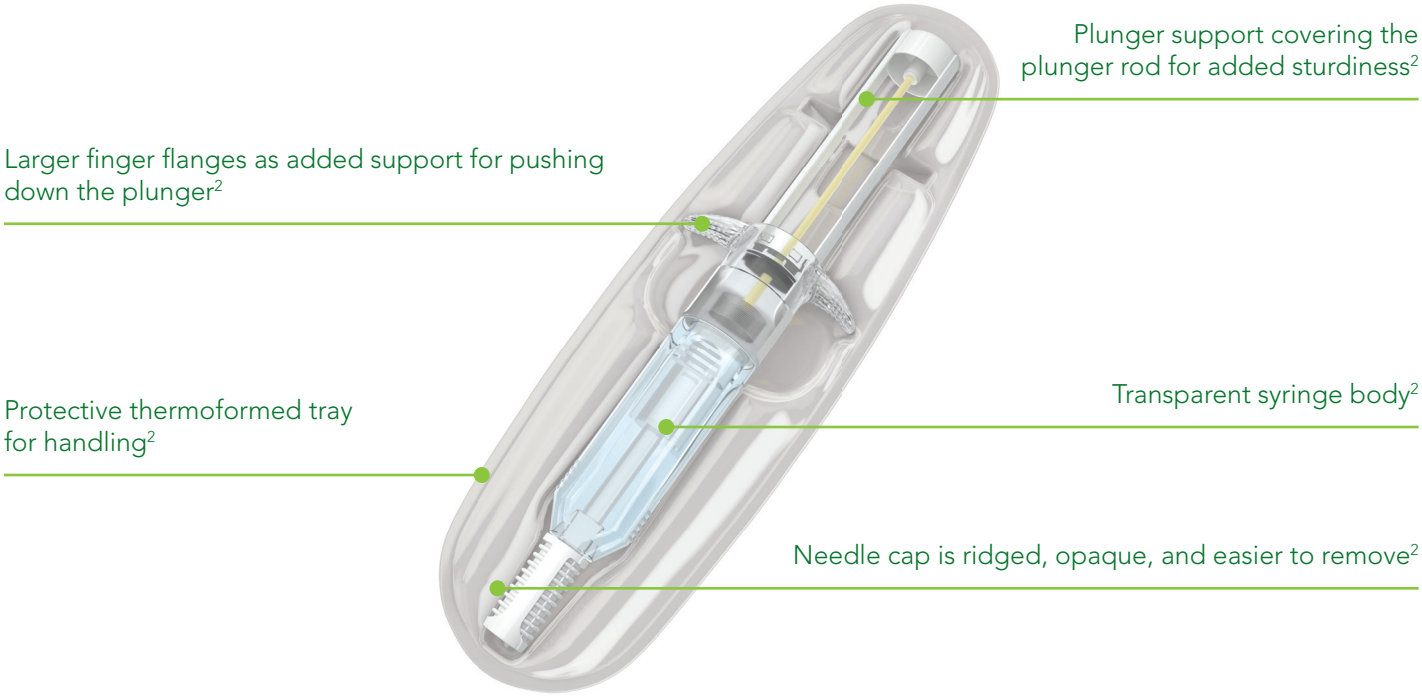
- SOMATULINE DEPOT is contraindicated in patients with hypersensitivity to lanreotide. Allergic reactions (including angioedema and anaphylaxis) have been reported following administration of lanreotide.

Warnings and Precautions

- **Cholelithiasis and Gallbladder Sludge**
  - SOMATULINE DEPOT may reduce gallbladder motility and lead to gallstone formation.
  - Periodic monitoring may be needed.
  - If complications of cholelithiasis are suspected, discontinue SOMATULINE DEPOT and treat appropriately

See additional Important Safety Information and accompanying Full Prescribing Information.

Current Somatuline® Depot Delivery System: Redesigned Features



Device not shown at actual size.

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IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions (continued)

- **Hypoglycemia or Hyperglycemia**
  - Patients treated with SOMATULINE DEPOT may experience hypoglycemia or hyperglycemia.
  - Blood glucose levels should be monitored when SOMATULINE DEPOT treatment is initiated, or when the dose is altered, and antidiabetic treatment should be adjusted accordingly.
- **Cardiovascular Abnormalities**
  - SOMATULINE DEPOT may decrease heart rate.
  - In cardiac studies with acromegalic patients, the most common cardiac adverse reactions were sinus bradycardia, bradycardia, and hypertension.
  - In patients without underlying cardiac disease, SOMATULINE DEPOT may lead to a decrease in heart rate without necessarily reaching the threshold of bradycardia.
  - In patients suffering from cardiac disorders prior to treatment, sinus bradycardia may occur. Care should be taken when initiating treatment in patients with bradycardia.
- **Thyroid Function Abnormalities**
  - Slight decreases in thyroid function have been seen during treatment with lanreotide in acromegalic patients.
  - Thyroid function tests are recommended where clinically appropriate.
- **Monitoring/Laboratory Tests:** In acromegaly, serum GH and IGF-1 levels are useful markers of the disease and effectiveness of treatment.

Adverse Reactions

- **Acromegaly:** Adverse reactions in >5% of patients who received SOMATULINE DEPOT were diarrhea (37%), cholelithiasis (20%), abdominal pain (19%), nausea (11%), injection-site reactions (9%), constipation (8%), flatulence (7%), vomiting (7%), arthralgia (7%), headache (7%), and loose stools (6%).
- **GEP-NETs:** Adverse reactions >10% of patients who received SOMATULINE DEPOT were abdominal pain (34%), musculoskeletal pain (19%), vomiting (19%), headache (16%), injection site reaction (15%), hyperglycemia (14%), hypertension (14%), and cholelithiasis (14%).
- **Carcinoid Syndrome:** Adverse reactions occurring in the carcinoid syndrome trial were generally similar to those in the GEP-NET trial. Adverse reactions occurring in ≥5% of patients who received SOMATULINE DEPOT and at least 5% greater than placebo were headache (12%), dizziness (7%), and muscle spasm (5%).

Drug Interactions: SOMATULINE DEPOT may decrease the absorption of cyclosporine (dosage adjustment may be needed); increase the absorption of bromocriptine; and require dosage adjustment for bradycardia-inducing drugs (e.g., beta-blockers).

Special Populations

- **Lactation:** Advise women not to breastfeed during treatment and for 6 months after the last dose.
- **Moderate to Severe Renal and Hepatic Impairment:** See full prescribing information for dosage adjustment in patients with acromegaly.

To report SUSPECTED ADVERSE REACTIONS, contact Ipsen Biopharmaceuticals, Inc. at 1-855-463-5127 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see accompanying Full Prescribing Information

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Summary and Conclusion

Summary

Feedback from collaborative studies involving patients, caregivers, and HCPs led to a redesign of the delivery system for Somatuline® Depot based on the participants' needs and requirements.[2]

Note: Somatuline Depot is intended for healthcare provider administration.[1]

Conclusion

These studies highlight the importance of addressing the concerns and needs of users during the development of the delivery system.

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions (continued)

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Special Populations

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See additional Important Safety Information and accompanying Full Prescribing Information.

References: 1. Somatuline Depot (lanreotide) Injection [US Prescribing Information]. Cambridge, MA: Ipsen Biopharmaceuticals, Inc.; June 2019.
2. Adelman DT, Van Genechten D, Megret CM, Truong Thanh XT, Hand P, Martin WA. Co-creation of a lanreotide autogel/depot syringe for the treatment of acromegaly and neuroendocrine tumours through collaborative human factor studies. *Adv Ther.* 2019;36(12):3409-3423.