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.

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.

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.
• 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.
• 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.

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).

Table 1. Summary of the Design Changes Throughout the Formative Studies

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

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

- Plunger support covering the plunger rod for added sturdiness
- Larger finger flanges as added support for pushing down the plunger
- Protective thermoformed tray for handling
- Transparent syringe body
- Needle cap is ridged, opaque, and easier to remove

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
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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