



**POLICY:** Somatostatin Analogs – Somatuline® Depot (lanreotide injectable – Ipsen)

**DATE REVIEWED:** 07/31/2019

## OVERVIEW

Somatuline Depot is 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.<sup>1</sup> The goal of treatment in acromegaly is to reduce growth hormone (GH) and insulin-like growth factor-1 (IGF-1) levels to normal. Somatuline Depot is also indicated in patients with gastroenteropancreatic neuroendocrine tumors (GEP-NETs) with unresectable, well or moderately differentiated, locally advanced or metastatic tumors to improve progression-free survival. In addition, Somatuline Depot is indicated for the treatment of adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy.

Somatuline Depot is intended for administration by a healthcare provider. For acromegaly, the recommended starting dose is 90 mg given via deep subcutaneous (SC) route, at 4-week intervals for 3 months. After 3 months the dosage can be adjusted based on GH and IGF-1 levels. Patients who are controlled on Somatuline Depot 60 or 90 mg may be considered for an extended dosing interval of Somatuline Depot 120 mg every 6 or 8 weeks. GH and IGF-1 levels should be obtained 6 weeks after this change in dosing regimen to evaluate persistence of patient response.

For GEP-NETs and carcinoid syndrome, the recommended dosage is 120 mg SC every 4 weeks. If patients are already being treated with Somatuline Depot for GEP-NETs, an additional dose is not needed for carcinoid syndrome.

Somatuline Depot is available as 60 mg/0.2 mL, 90 mg/0.3 mL, and 120 mg/0.5 mL semi-solid formulation in a single, sterile, prefilled, ready-to-use syringe.

## Guidelines

### *Acromegaly Guidelines*

The Endocrine Society Clinical Practice Guidelines for Acromegaly (2014) recommend transsphenoidal surgery as the primary therapy in most patients; repeat surgery may be considered in patients with residual intrasellar disease after initial surgery.<sup>2</sup> Although routine preoperative medical therapy is not recommended, patients with severe pharyngeal thickness and sleep apnea or high-output heart failure may receive therapy with a somatostatin analog preoperatively to reduce surgical risk from severe comorbidities. A somatostatin analog may be used as primary therapy in patients who cannot be cured by surgery; have extensive cavernous sinus invasion; do not have chiasmal compression; or are poor surgical candidates. For patients with persistent disease after surgery, Somatuline Depot, along with other somatostatin analogs, is recommended as an effective therapy. In some cases, additional medical therapy and/or radiotherapy may be needed.

### *NET Guidelines*

According to the National Comprehensive Cancer Network (NCCN) guidelines for neuroendocrine and adrenal tumors (version 1.2019 – March 5, 2019), Somatuline Depot, as well as other somatostatin analogs, are recommended for the management of carcinoid syndrome (category 2A).<sup>3</sup> Additionally, patients with tumors of the gastrointestinal (GI) tract, lung, and thymus who have unresectable disease and/or distant metastases should be started on therapy with a somatostatin analog to potentially control tumor growth

(category 2A). The somatostatin analogs are also recommended as a primary treatment for unresected primary gastrinoma (category 2A). In some patients with adrenal NETs, Somatuline Depot is effective for symptom control, if somatostatin receptor scintigraphy is positive (category 2A). Somatostatin analog therapy may be used in patients with non-adrenocorticotrophic hormone (ACTH)-dependent Cushing's syndrome with tumors < 4 centimeters, benign characteristics on imaging, and abnormal contralateral gland and symmetric cortisol production. The somatostatin analogs are also recommended for treatment of symptoms related to hormone hypersecretion from pancreatic NETs (e.g., glucagonomas, VIPomas, gastrinomas) as well as for tumor control in these patients with unresectable and/or metastatic disease and clinically significant tumor burden or progression (category 2A).

The North American Neuroendocrine Tumor Society (NANETS) consensus guidelines for the surveillance and medical management of midgut NETs (2017) also recommend Sandostatin LAR Depot and Somatuline Depot as first-line initial therapy options in most patients with metastatic midgut NETs for control of carcinoid syndrome and inhibition of tumor growth.<sup>4</sup>

### *Pheochromocytoma/Paraganglioma Guidelines*

The NCCN guidelines on neuroendocrine and adrenal tumors (version 1.2019 – March 5, 2019), recommend octreotide or lanreotide as a second-line therapy for symptom control of local, unresectable pheochromocytomas or paragangliomas.<sup>3</sup>

## **POLICY STATEMENT**

Prior authorization is recommended for medical benefit coverage of Somatuline Depot. Because of the specialized skills required for evaluation and diagnosis of patients treated with Somatuline Depot as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Somatuline Depot to be prescribed by or in consultation with a physician who specializes in the condition being treated. Refer to criteria below for approval durations. In cases where the approval is authorized in months, 1 month is equal to 30 days.

## **RECOMMENDED AUTHORIZATION CRITERIA**

### **FDA-Approved Indications**

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- 1. Acromegaly.** Approve for 1 year if the patient meets the following criteria (A, B, and C):
  - A)** The medication is prescribed by or in consultation with an endocrinologist; **AND**
  - B)** The patient meets **ONE** of the following (i, ii, or iii):
    - i.** The patient has had an inadequate response to surgery and/or radiotherapy; **OR**
    - ii.** The patient is **NOT** an appropriate candidate for surgery and/or radiotherapy; **OR**
    - iii.** The patient is experiencing negative effects due to tumor size (e.g., optic nerve compression); **AND**
  - C)** The patient has (or had) a pre-treatment (baseline) insulin-like growth factor-1 (IGF-1) level above the upper limit of normal (ULN) based on age and gender for the reporting laboratory.

Note: Pre-treatment (baseline) refers to the IGF-1 level prior to the initiation of any somatostatin analog (e.g., octreotide acetate injection, Signifor<sup>®</sup> LAR [pasireotide for injectable suspension], Sandostatin<sup>®</sup> LAR Depot, Somatuline Depot), dopamine agonist (e.g., cabergoline, bromocriptine), or Somavert<sup>®</sup> (pegvisomant for injection). Reference ranges for IGF-1 vary among laboratories.

**Dosing.** Approve if the dose meets the following (A and B):

- A)** Each dose is  $\leq$  120 mg; **AND**
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B) Each dose is given no more frequently than once every 4 weeks.

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**2. Neuroendocrine Tumors (NETs) of the Gastrointestinal Tract, Lung, Thymus (Carcinoid Tumors), and Pancreas (including glucagonomas, gastrinomas, VIPomas, insulinomas).** Approve for 1 year if the medication is prescribed by or in consultation with an oncologist, endocrinologist, or gastroenterologist.

**Dosing.** Approve if the dose meets the following (A and B):

A) Each dose is  $\leq 120$  mg; AND

B) Each dose is given no more frequently than once every 4 weeks.

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**3. Carcinoid Syndrome.** Approve for 1 year if the medication is prescribed by or in consultation with an oncologist, endocrinologist, or gastroenterologist.

**Dosing.** Approve if the dose meets the following (A and B):

A) Each dose is  $\leq 120$  mg; AND

B) Each dose is given no more frequently than once every 4 weeks.

Note: If the patient is already being treated with Somatuline Depot for neuroendocrine tumors, an additional dose for carcinoid syndrome should not be administered.

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#### Other Uses with Supportive Evidence

**4. Pheochromocytoma/Paraganglioma:** Approve for 1 year if the medication is prescribed by or in consultation with an endocrinologist, oncologist, radiologist, neurologist, or neurosurgeon.

**Dosing.** Approve if the dose meets the following (A and B):

A) Each dose is  $\leq 120$  mg; AND

B) Each dose is given no more frequently than once every 4 weeks.

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#### CONDITIONS NOT RECOMMENDED FOR APPROVAL

Somatuline Depot has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

#### REFERENCES

1. Somatuline<sup>®</sup> Depot for injection [prescribing information]. Basking Ridge, NJ: Ipsen Biopharmaceuticals, Inc.; September 2017.
  2. Katznelson L, Laws ER Jr, Melmed S, et al; Endocrine Society. Acromegaly: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2014;99:3933-3951.
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3. The NCCN Neuroendocrine and Adrenal Tumors Clinical Practice Guidelines in Oncology (version 1.2019 – March 5, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed July 1, 2019.
4. Strosberg JR, Halfdanarson TR, Bellizzi AR, et al. The North American Neuroendocrine Tumor Society consensus guidelines for surveillance and medical management of midgut neuroendocrine Tumors. *Pancreas*. 2017;46(6):707-714.

## HISTORY

Type of Revision	Summary of Changes	Approval Date
New Policy	--	08/22/2018
Annual revision	<p>The following sections were removed throughout the policy; Initial Approval/Extended Approval, Duration of Therapy, Labs/Diagnostics, and Waste Management. In addition, the following was changed:</p> <ol style="list-style-type: none"> <li>1. <b>Acromegaly.</b> In criteria A., “Initial therapy” was removed and all of criteria B. was removed to match PA policy. Dosing was changed from specific regimens to a range utilizing criteria verbage of “each dose is ≤” and “each dose is given no more frequently than”. The route of administration was removed.</li> <li>2. <b>Neuroendocrine Tumors (NETs) of the Gastrointestinal Tract, Lung, Thymus (Carcinoid Tumors), and Pancreas (including glucagonomas, gastrinomas, vasoactive intestinal peptide-secreting tumors [VIPomas], insulinomas).</b> Dosing was changed from specific regimens to a range utilizing criteria verbage of “each dose is ≤” and “each dose is given no more frequently than”. The route of administration was removed.</li> <li>3. <b>Carcinoid Syndrome.</b> Dosing was changed from specific regimens to a range utilizing criteria verbage of “each dose is ≤” and “each dose is given no more frequently than”. The route of administration was removed.</li> <li>4. <b>Pheochromocytoma and Paraganglioma.</b> Addition of indication to approval criteria.</li> </ol>	07/31/2019