



**POLICY:** Somatostatin Analogs – Sandostatin® LAR Depot (octreotide acetate for injectable suspension – Novartis)

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

## OVERVIEW

Sandostatin LAR Depot, a somatostatin analog, is indicated as long-term maintenance therapy in 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> Sandostatin LAR Depot is only indicated in patients who tolerated and had an effective response to initial treatment with octreotide subcutaneous (SC) injection. The goal of treatment in acromegaly is to reduce growth hormone (GH) and insulin-like growth factor-1 (IGF-1) levels to normal. Sandostatin LAR Depot is also indicated in patients with metastatic carcinoid tumors for the long-term treatment of the severe diarrhea and flushing episodes associated with these tumors, as well as the long-term treatment of the profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors (VIPomas).

For acromegaly, patients currently receiving octreotide injection can be switched directly to Sandostatin LAR Depot 20 mg intramuscularly (IM) intragluteally at 4-week intervals for 3 months. After 3 months, the dose can be adjusted based on GH and IGF-1 levels, up to a maximum of 40 mg every 4 weeks. In patients who have received pituitary irradiation, Sandostatin LAR Depot should be withdrawn yearly for approximately 8 weeks to assess disease severity. If GH or IGF-1 levels increase and signs and symptoms recur, therapy can be resumed.

For carcinoid tumors and VIPomas, similar to acromegaly, patients should be receiving octreotide injection before switching to Sandostatin LAR Depot. The recommended Sandostatin LAR Depot dose is 20 mg IM intragluteally at 4-week intervals for 2 months. Because of the need for serum octreotide to reach therapeutically effective levels following initial injection of Sandostatin LAR Depot, carcinoid tumor and VIPoma patients should continue to receive octreotide subcutaneous injection for at least 2 weeks in the same dosage they were taking before the switch. After 2 months, dosage may be adjusted; dosages higher than 30 mg are not recommended.

Sandostatin LAR Depot is available in single-use kits containing a 6 mL vial of 10 mg, 20 mg, or 30 mg strength, a syringe containing a 2 mL diluent, one vial adapter, and one sterile safety injection needle.

## 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, Sandostatin LAR Depot, along with other somatostatin analogs, is recommended as an effective therapy. In some cases, additional medical therapy and/or radiotherapy may be needed.

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### *NET Guidelines*

According to the National Comprehensive Cancer Network (NCCN) guidelines for neuroendocrine and adrenal tumors (version 1.2019 – March 5, 2019), Sandostatin LAR 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, Sandostatin LAR 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 as a first-line initial therapy in most patients with metastatic midgut NETs for control of carcinoid syndrome and inhibition of tumor growth.<sup>4</sup>

### *Meningiomas Guidelines*

NCCN guidelines on central nervous system cancers (version 1.2019 – March 5, 2019) recommend Sandostatin LAR Depot or octreotide injection for the treatment of surgically inaccessible recurrent or progressive meningiomas when additional radiation is no longer possible.<sup>5</sup>

### *Thymomas and Thymic Carcinomas Guidelines*

The NCCN guidelines on thymomas and thymic carcinomas (version 2.2019 – March 11, 2019) recommend LAR Depot or short-acting octreotide injection as a second-line systemic therapy option with or without concomitant prednisone therapy. In patients with thymoma who have positive octreotide scan or symptoms of carcinoid syndrome, octreotide therapy may be useful.<sup>6</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>

## **Dosing Information**

Patients not currently receiving octreotide subcutaneous injection should begin therapy with that short-acting agent first. Patients should be maintained on octreotide subcutaneous injection for at least 2 weeks to determine tolerance to octreotide. Patients who are considered “responders” based on GH and IGF-1 levels can be switched to Sandostatin LAR Depot.

## **POLICY STATEMENT**

Prior authorization is recommended for medical benefit coverage of Sandostatin LAR Depot. Because of the specialized skills required for evaluation and diagnosis of patients treated with Sandostatin LAR Depot as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Sandostatin LAR Depot to be prescribed by or in consultation with a physician who specializes in the

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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 LAR Depot, Somatuline<sup>®</sup> Depot [lanreotide subcutaneous injection]), 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  $\leq 40$  mg; AND
- 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, vasoactive intestinal peptide-secreting tumors [VIPomas], insulinomas).**

**Criteria.** 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  $\leq 30$  mg; AND
- B) Each dose is given no more frequently than once every 4 weeks.

### Other Uses with Supportive Evidence

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3. **Meningioma.** Approve for 1 year if the medication is prescribed by or in consultation with an oncologist, radiologist, or neurosurgeon.

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

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- A) Each dose is  $\leq$  40 mg; AND
- B) Each dose is given no more frequently than once every 4 weeks.

**4. Thymoma and Thymic Carcinoma.** Approve for 1 year if the medication is prescribed by or in consultation with an oncologist.

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

- A) Each dose is  $\leq$  40 mg; AND
- B) Each dose is given no more frequently than once every 4 weeks.

**5. Pheochromocytoma and 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  $\leq$  40 mg; AND
- B) Each dose is given no more frequently than once every 4 weeks.

#### CONDITIONS NOT RECOMMENDED FOR APPROVAL

Sandostatin LAR 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. Sandostatin® LAR Depot for injectable suspension [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; April 2019.
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.
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 9, 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.
5. The NCCN Central Nervous System Cancers 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.
6. The NCCN Thymomas and Thymic Carcinomas Clinical Practice Guidelines in Oncology (Version 2.2019 – March 11, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed July 1, 2019.

#### HISTORY

Type of Revision	Summary of Changes	Approval Date
New Policy	--	08/22/2018
Annual Revision	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: <b>1. 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	07/31/2019

	<p>utilizing criteria verbage of “each dose is ≤” and “each dose is given no more frequently than”. The route of administration was removed.</p> <p><b>2. 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.</p> <p><b>3. Meningioma.</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.</p> <p><b>4. Thymoma and Thymic Carcinoma.</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.</p> <p><b>5. Pheochromocytoma and Paraganglioma.</b> Addition of indication to approval criteria.</p>	
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