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Octreotide

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Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of and developed by nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For HCSC members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of

American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated and coverage is not required for non-formulary drugs.

Coverage

NOTE 1: This medical policy does **NOT** address oncologic indications. This medical policy **IS NOT TO BE USED** for oncologic indications. Refer to RX502.061 Oncology Medications for oncologic indications.

Sandostatin® (octreotide acetate)
Sandostatin® (octreotide acetate) **may be considered medically necessary** for the following indication:

- Acromegaly in patients who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses.

Sandostatin® LAR Depot (octreotide acetate)
Sandostatin® LAR Depot (octreotide acetate) **may be considered medically necessary** for the following indications:

- In patients in whom initial treatment with Sandostatin injection has been shown to be effective and tolerated.
- Long-term maintenance therapy in acromegalic patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy, is not an option.

Sandostatin® and Sandostatin® LAR Depot (octreotide acetate) are **considered experimental, investigational, and/or unproven** for all other non-Food and Drug Administration approved indications.

Policy Guidelines

Sandostatin® (octreotide acetate) may be administered subcutaneously or intravenously.

Sandostatin® LAR Depot should be administered intramuscularly by a trained healthcare provider.

Description

Acromegaly

Acromegaly is a rare hormonal disorder that occurs when the pituitary gland produces too much growth hormone (GH) during adulthood. The overproduction of GH in most cases is due to a pituitary adenoma, a benign pituitary gland tumor. When GH is released into the bloodstream, the liver manufactures a hormone called insulin-like growth factor-1 (IGF-1). An excessive amount of IGF-1 can lead to atypical growth of skeletal and soft tissue. Physical changes can include enlargement of hands, feet, and face (protruding lower jaw and brow). Other symptoms may include headache, fatigue, and vision impairment. Symptoms of acromegaly vary and may be gradual. Due to the insidious onset; the condition may not be diagnosed immediately. Acromegaly could lead to serious life-threatening complications, therefore early diagnosis and treatment is important. (3)

Tests used to help diagnose and monitor this disorder may include but are not limited to such tests as magnetic resonance imaging (MRI) of the brain, IGF-1 levels, prolactin, and growth hormone levels. Treatment may consist of surgical, medical and radiotherapeutic options or a combination of these therapies. Surgery to remove the pituitary tumor may be the initial treatment in patients with microadenomas. There are situations in which the tumor is unable to be removed completely; radiation or medical therapy may be used as adjunct to surgery. (3)

<u>Treatment Options</u>

Treatment options for acromegaly include:

- Transsphenoidal surgery with the goal to remove as much of the tumor as possible going through the nasal passages, using intraoperative fluoroscopy (which gives real-time localization relative to the bone anatomy) or neuronavigation devices which provide computed localization referenced to a three-dimensional (3D) space calculated from preoperative imaging. (4)
- Radiation therapy:
    - Stereotactic radiosurgery – the delivery of a single high dose of radiation therapy using a high-precision localization system to treat a small target;
    - Fractionated radiation therapy – the delivery of radiation therapy in multiple, small, daily doses, usually five days a week for five to six weeks. (5)
- Medical therapy:
    - Dopamine agonists which may inhibit growth hormone (GH) secretion in some patients;
    - Somatostatin analogs inhibit GH secretion more effectively than native somatostatin because of their greater potency and longer plasma half-life. (5)

Regulatory Status

Sandostatin® is a man-made protein similar to a hormone in the body called somatostatin. It lowers many substances in the body such as insulin and glucagon (involved in regulating blood sugar), growth hormone and chemicals that affect digestion. The U.S. Food and Drug Administration (FDA) approved Sandostatin in 1988. Sandostatin® LAR Depot was approved in 1998. They are approved to treat acromegaly in patients who are unresponsive to or cannot be treated with surgery, pituitary irradiation, or bromocriptine mesylate, to reduce flushing episodes and watery diarrhea associated with carcinoid syndrome, and to treat profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors. (5, 6)

This policy does not address oncologic indications and is not to be used for oncologic indications. Refer to RX502.061 Oncology Medications for oncologic indications.

Rationale

This policy is based on the U.S. Food and Drug Administration (FDA) labeled indications for Sandostatin® (octreotide acetate) and Sandostatin® LAR Depot (octreotide acetate).

Acromegaly

Sandostatin® (6)

A randomized, double-blind, placebo-controlled, multicenter trial involving 115 acromegalic patients demonstrated the efficacy of octreotide 100 mcg subcutaneously every 8 hours for a 6-month period. About half of the patients experienced effective reduction in growth hormone concentration and about two-thirds an effective reduction of somatomedin C concentration. A higher dose of 250 mcg was also evaluated; although there was an increase in the frequency of tumor shrinkage with the higher dose, there was no clinical benefit associated with this increase.

Octreotide significantly reduces circulating levels of growth hormone releasing factor (GHRF) and growth hormone (GH). In a short-term study, growth hormone levels decreased by 50 to 90 percent following single 25 mcg doses of subcutaneous octreotide.

Long-term efficacy and tolerability of octreotide therapy were evaluated in 10 acromegaly patients for a period of 6 years. The conclusions regarding comparison with baseline were: 1) continuous subcutaneous infusion was the most effective route; 2) oral carbohydrate tolerance was unaffected by octreotide; 3) a transient reduction in iodothyronine deiodination was rapidly compensated for by a persistent slight elevation in TSH; 4) fat absorption was unaffected by octreotide; 5) foot volume was unaffected; and 6) sellar volume on CT scan decreased during therapy. Octreotide antibodies were noted in 2 patients but were not of any clinical consequence.

The efficacy of octreotide in the treatment of acromegaly was reported. With doses of 200 to 300 mcg daily given subcutaneously for 16 to 108 weeks, clinical improvement was observed in all 10 patients treated, which was evident within the first 6 weeks (disappearance of excessive perspiration, paresthesias, headache). Mean 24-hour serum growth hormone concentrations decreased significantly, even after 1 year of therapy; normalization of somatomedin-C serum levels was observed in 5 of the 10 patients. Both somatomedin-C and growth hormone levels decreased continuously during long-term therapy, with concentrations at 1.5 to 2 years of treatment being significantly lower than those observed after 6 to 12 months of therapy. Significant side effects were not observed during treatment. It is felt that octreotide should be used selectively in patients not benefiting from surgical therapy, in patients subjected to the effects of radiotherapy, and in untreated patients where surgery is hazardous.

Sandostatin® LAR Depot (1)

The clinical trials of Sandostatin LAR Depot were performed in patients who had been receiving Sandostatin Injection for a period of weeks to as long as 10 years. The acromegaly studies with Sandostatin LAR Depot described below were performed in patients who achieved GH levels of < 10 ng/mL (and, in most cases < 5 ng/mL) while on subcutaneous Sandostatin Injection. However, some patients enrolled were partial responders to subcutaneous Sandostatin Injection, i.e., GH levels were reduced by > 50% on subcutaneous Sandostatin Injection compared to the untreated state, although not suppressed to < 5 ng/mL.

Sandostatin LAR Depot was evaluated in three clinical trials in acromegalic patients.

In 2 of the clinical trials, a total of 101 patients were entered who had, in most cases, achieved a GH level < 5 ng/mL on Sandostatin Injection given in doses of 100 mcg or 200 mcg three times daily. Most patients were switched to 20 mg or 30 mg doses of Sandostatin LAR Depot given once every 4 weeks for up to 27 to 28 injections. A few patients received doses of 10 mg and a few required doses of 40 mg. Growth hormone and IGF-1 levels were at least as well controlled with Sandostatin LAR Depot as they had been on Sandostatin Injection and this level of control remained for the entire duration of the trials.

A third trial was a 12-month study that enrolled 151 patients who had a GH level < 10 ng/mL after treatment with Sandostatin Injection (most had levels < 5 ng/mL). The starting dose of Sandostatin LAR Depot was 20 mg every 4 weeks for 3 doses. Thereafter, patients received 10 mg, 20 mg, or 30 mg every 4 weeks, depending upon the degree of GH suppression. Growth hormone and IGF-1 were at least as well controlled on Sandostatin LAR Depot as they had been on Sandostatin Injection.

Table 1 summarizes the data on hormonal control for GH and insulin growth factor-1 (IGF-1) for those patients in the first two clinical trials who received all 27 to 28 injections of Sandostatin LAR Depot.

Table 1. Hormonal Response in Acromegalic Patients Receiving 27 to 28 Injections During[1] Treatment with Sandostatin LAR Depot

Mean Hormone Level	Sandostatin Injection (subcutaneously)		Sandostatin LAR Depot	
	N	%	N	%
GH < 5.0 ng/mL	69/88	78	73/88	83
< 2.5 ng/mL	44/88	50	41/88	47
< 1.0 ng/mL	6/88	7	10/88	11
IGF-1 normalized	36/88	41	45/88	51
GH < 5.0 ng/mL + IGF-1 normalized	36/88	41	45/88	51
< 2.5 ng/mL + IGF-1 normalized	30/88	34	37/88	42

< 1.0 ng/mL + IGF-1 normalized	5/88	6	10/88	11

GH: growth hormone; IGF-1: insulin growth factor-1; ng: nanogram; mL: milliliter.
[1] Average of monthly levels of growth hormone and insulin growth factor-1 over the course of the trials.

For the 88 patients in Table 1, a mean GH level of < 2.5 ng/mL was observed in 47% receiving Sandostatin LAR Depot. Over the course of the trials, 42% of patients maintained mean growth hormone levels of < 2.5 ng/mL and mean normal IGF-1 levels.

Table 2 summarizes the data on hormonal control (GH and IGF-1) for those patients in the third clinical trial who received all 12 injections of Sandostatin LAR Depot.

Table 2. Hormonal Response in Acromegalic Patients Receiving 12 Injections During[1] Treatment with Sandostatin LAR Depot

Mean Hormone Level	Sandostatin Injection (subcutaneously)		Sandostatin LAR Depot	
	N	%	N	%
GH < 5.0 ng/mL	116/122	95	118/122	97
< 2.5 ng/mL	84/122	69	80/122	66
< 1.0 ng/mL	25/122	21	28/122	23
IGF-1 normalized	82/122	67	82/122	67
GH < 5.0 ng/mL + IGF-1 normalized	80/122	66	82/122	67
< 2.5 ng/mL + IGF-1 normalized	65/122	53	70/122	57
< 1.0 ng/mL + IGF-1 normalized	23/122	19	27/122	22

GH: growth hormone; IGF-1: insulin growth factor-1; ng: nanogram; mL: milliliter; N: number.
[1] Average of monthly levels of growth hormone and insulin growth factor-1 over the course of the trial.

For the 122 patients in Table 2, who received all 12 injections in the third trial, a mean GH level of < 2.5 ng/mL was observed in 66% receiving Sandostatin LAR Depot. Over the course of the trial, 57% of patients maintained mean growth hormone levels of < 2.5 ng/mL and mean normal IGF-1 levels. In comparing the hormonal response in these trials, note that a higher percentage of patients in the third trial suppressed their mean GH to < 5 ng/mL on subcutaneous Sandostatin Injection, 95%, compared to 78% across the 2 previous trials.

In all 3 trials, GH, IGF-1, and clinical symptoms were similarly controlled on Sandostatin LAR Depot as they had been on Sandostatin Injection.

Of the 25 patients who completed the trials and were partial responders to Sandostatin Injection (GH > 5.0 ng/mL but reduced by > 50% relative to untreated levels), 1 patient (4%) responded to Sandostatin LAR Depot with a reduction of GH to < 2.5 ng/mL and 8 patients (32%) responded with a reduction of GH to < 5.0 ng/mL.

Two open-label clinical studies investigated a 48-week treatment with Sandostatin LAR Depot in 143 untreated (de novo) acromegalic patients. The median reduction in tumor volume was

20.6% in Study 1 (49 patients) at 24 weeks and 24.5% in Study 2 (94 patients) at 24 weeks and 36.2% at 48 weeks.

Summary of Evidence

Based on the review of studies provided to the U.S. Food and Drug Administration for approval, Sandostatin® (octreotide acetate) may be considered medically necessary for treatment of acromegaly in patients who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses. Sandostatin® LAR Depot (octreotide acetate) may be considered medically necessary for patients in whom initial treatment with Sandostatin Injection has been shown to be effective and tolerated and for long-term maintenance therapy in acromegalic patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option. Sandostatin® and Sandostatin® LAR Depot (octreotide acetate) are considered experimental, investigational, and/or unproven for all other non-FDA approved indications.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J2353, J2354

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

U.S. Food and Drug Administration Labels:

1. U.S. Food and Drug Administration, Drugs@FDA. Highlights of Prescribing Information: Sandostatin® LAR Depot (octreotide acetate). (revised July 2024). Available at: <https://www.accessdata.fda.gov> (accessed May 30, 2025).
2. U.S. Food and Drug Administration, Drugs@FDA. Highlights of Prescribing Information: Sandostatin® (octreotide acetate). (revised July 2024). Available at: <https://www.accessdata.fda.gov> (accessed May 30, 2025).

Other:

3. Acromegaly-Mayo Clinic. Diseases and Conditions. Available at <https://www.mayoclinic.org> (accessed July 14, 2025).

4. Swearingen B. Transsphenoidal surgery for pituitary adenomas and other sellar masses. In: UpToDate, Snyder PJ (Ed), UpToDate, Waltham, MA. Available at <https://www.uptodate.com> (accessed June 2, 2025).
5. Melmed S, Katznelson L. Treatment of acromegaly. In: UpToDate, Snyder PJ (Ed), UpToDate, Waltham, MA. Available at <https://www.uptodate.com> (accessed June 2, 2025).
6. Octreotide. In: Merative™ Micromedex® DRUGDEX® (electronic version). Merative, Ann Arbor, Michigan, USA. Available at <https://www.micromedexsolutions.com> (cited: June 2, 2025).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
12/15/2025	Document updated with literature review. The following changes were made to Coverage: 1) Revised coverage to be in alignment with the current Food and Drug Administration label for both Sandostatin® (octreotide acetate) and Sandostatin® LAR Depot (octreotide acetate); and 2) Added "non-Food and Drug Administration approved" to existing experimental, investigational and/or unproven statement. Added reference 2; others updated.
10/15/2024	Reviewed. No changes.
04/01/2024	New medical document. Sandostatin® (octreotide acetate) may be considered medically necessary for the following indication: Acromegaly in patients who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, or dopamine agonist (e.g., bromocriptine mesylate or cabergoline) at maximally tolerated doses. Sandostatin® LAR Depot (octreotide acetate) may be considered medically necessary for the following indication: Long-term maintenance therapy in acromegalic patients for whom medical treatment is appropriate and who have been shown to respond to and can tolerate octreotide acetate injection. Sandostatin® and Sandostatin® LAR Depot (octreotide acetate) are considered experimental, investigational, and/or unproven for all other indications. NOTE 1: This medical policy does NOT address oncologic

	indications. This medical policy IS NOT TO BE USED for oncologic indications. Refer to RX502.061 Oncology Medications for oncologic indications