Medication Policy Manual

Policy No: dru489

Topic: Sandostatin® LAR Depot, octreotide long-acting release

Date of Origin: February 17, 2017

Committee Approval Date: October 13, 2017

Next Review Date: October 2018

Effective Date: November 1, 2017

IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of Medication Policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Octreotide long-acting release (Sandostatin LAR Depot) is a somatostatin analog indicated for acromegaly, diarrhea or flushing associated with metastatic carcinoid tumors, and watery diarrhea associated with vasoactive intestinal peptide tumors (VIPomas). The long-acting release (LAR) formulation is given intramuscularly once every four weeks.

This policy and the coverage criteria below do not apply to octreotide (generic). Octreotide (generic) does not require prior authorization.
Policy/Criteria

I. Most contracts require prior authorization approval of octreotide LAR (Sandostatin LAR Depot) prior to coverage. Octreotide LAR (Sandostatin LAR Depot) may be considered medically necessary when criteria A or B below are met.

A. Octreotide (generic) subcutaneous injection has been tolerated and criterion 1 below is met:
   1. There is documentation that confirms the medication is being used for its FDA-approved indication. (as specified in Table 1).

<table>
<thead>
<tr>
<th>Table 1. FDA-approved Indications for octreotide LAR (Sandostatin LAR Depot)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Acromegaly</td>
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<tr>
<td>2. Severe diarrhea/flushing episodes associated with metastatic carcinoid tumors</td>
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<tr>
<td>3. Profuse watery diarrhea associated with vasoactive intestinal peptide tumors (VIPomas)</td>
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</table>

OR

B. There is a diagnosis of unresectable, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) [e.g. gastrointestinal tract, lung, thymus, or pancreatic neuroendocrine tumors].

II. Administration, Quantity Limitations, and Authorization Period

A. Regence Pharmacy Services does not consider octreotide LAR (Sandostatin LAR Depot) to be a self-administered medication.

B. When prior authorization is approved, octreotide LAR (Sandostatin LAR Depot) may be authorized in the following quantities:

1. Acromegaly
   a. Initial authorization: Up to #1 octreotide LAR (Sandostatin LAR Depot) 20-mg kit every 4 weeks for 3 months.
   b. Continued authorization: Up to #1 octreotide LAR (Sandostatin LAR Depot) 40 mg every 4 weeks.

2. Carcinoid tumors, VIPomas, or GEP-NET
   a. Initial authorization: Up to #1 octreotide LAR (Sandostatin LAR Depot) 20-mg kit every 4 weeks for 2 months.
   b. Continued authorization: Up to #1 octreotide LAR (Sandostatin LAR Depot) 30-mg every 4 weeks.

C. Authorization may be reviewed annually to confirm that current medical necessity criteria are met and that the medication is effective.
III. Octreotide LAR (Sandostatin LAR Depot) is considered investigational when used for all other conditions, including meningiomas, thymic malignancies, portal hypertension, and other cancer settings.

Position Statement

Summary

- Octreotide LAR (Sandostatin LAR Depot) is a somatostatin analog indicated for the treatment of acromegaly in patients who have had an inadequate response to surgery or for whom surgery is not an option. The LAR formulation should only be used in patients who have tolerated octreotide (generic) subcutaneous injection for at least 2 weeks.

- Somatostatin is a natural hormone that lowers excessive growth hormone (GH) levels. Somatostatin analogs, such as octreotide LAR (Sandostatin LAR Depot), work by binding to somatostatin receptors, thereby suppressing GH secretion. They also inhibit adrenocorticotropic hormone (ACTH) secretion, which leads to decreased cortisol secretion.

- The Endocrine Society clinical guidelines for acromegaly recommend transsphenoidal surgery as first-line treatment for most patients. [1]

  * Pharmacological treatment with a somatostatin analog or pegvisomant (Somavert) is recommended as the initial adjuvant medical therapy.

  * In patients with mild disease, a trial of a dopamine agonist, such as cabergoline, is recommended as the initial adjuvant medical therapy.

  * Patients with an inadequate response to a somatostatin analog should try adding cabergoline or pegvisomant (Somavert).

- Somatostatin analogs, such as octreotide (generic, Sandostatin LAR Depot), provide the best value for acromegaly.

- Octreotide LAR (Sandostatin LAR Depot) is also indicated for severe diarrhea and flushing episodes associated with metastatic carcinoid tumors, and profuse watery diarrhea associated with vasoactive intestinal peptide-secreting tumors (VIPomas).

- The recommended initial dosing for octreotide LAR (Sandostatin LAR Depot) for acromegaly or for symptomatic control in carcinoid tumors or VIPomas is 20 mg intramuscular injection given by a health care provider once every 4 weeks. Dosing adjustments should be made after two or three months, based on response and tolerability, up to a maximum dose of 40 mg every 4 weeks for acromegaly and 30 mg every 4 weeks for carcinoid tumors or VIPomas.

- The safety and efficacy of doses exceeding the maximum dosage in the FDA-approved labeling have not been established in clinical trials.

- Octreotide LAR (Sandostatin LAR Depot) is also used off-label for locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs). This is supported by the National Comprehensive Cancer Network (NCCN) guidelines.
Clinical Efficacy

ACROMEGALY

- A single, high quality meta-analysis found that in patients taking octreotide LAR (Sandostatin LAR Depot) who were not preselected for somatostatin analog responsiveness, 54% met GH efficacy criteria and 63% had IGF-I normalization. [2]

- A single, low quality meta-analysis evaluated head-to-head studies between octreotide LAR (Sandostatin LAR Depot) and lanreotide (Somatuline Depot). [3]
  * A GH level < 2.5 μg/L was achieved in 65.3% of patients on octreotide LAR (Sandostatin LAR Depot) versus 59.5% of patients on lanreotide (Somatuline Depot).
  * Normalization of IGF-I was achieved in 46.7% of patients on octreotide LAR (Sandostatin LAR Depot) versus 52.7% of patients on lanreotide (Somatuline Depot).
  * Biochemical control was achieved in 46% of patients on octreotide LAR (Sandostatin LAR Depot) versus 41.9% of patients on lanreotide (Somatuline Depot).

SYMPTOMATIC CONTROL IN CARCINOID TUMORS or VIPomas

- A 6-month, double-blind trial of malignant carcinoid syndrome evaluated the efficacy of octreotide LAR (Sandostatin LAR Depot) 10 mg, 20 mg, or 30 mg. [4]
  * Overall, mean daily stool frequency was decreased with octreotide LAR (Sandostatin LAR Depot). The average number of daily stools decreased from ~4.5 stools per day at baseline to ~2.5 stools per day.
  * Mean daily flushing episodes also decreased with octreotide LAR (Sandostatin LAR Depot). The average number of daily flushing episodes decreased from 3.0-6.1 episodes per day at baseline to 0.6-1.0 episodes per day.
  * The reductions observed with octreotide LAR (Sandostatin LAR Depot) are within the range reported in the published literature for patients treated with octreotide (generic) subcutaneous injection.

GASTROENTEROPANCREATIC NEUROENDOCRINE TUMORS (GEP-NETs)

- The PROMID trial showed an improvement in time to tumor progression in neuroendocrine tumors of the midgut with octreotide LAR (Sandostatin LAR Depot) compared to placebo (14.3 months vs. 6 months). [5]

- The National Comprehensive Cancer Network (NCCN) Neuroendocrine Tumors guideline list octreotide LAR (Sandostatin LAR Depot) as category 2A recommendation for gastrointestinal tract, lung, thymus, or pancreatic neuroendocrine tumors. [6]

- A single systematic review showed that dose escalation up to 120 mg every 4 weeks may be considered for symptom control and tumor progression in neuroendocrine tumors; however, there was a lack of quantitative measurements of symptom severity and mainly supported by expert opinion. [9]
Additional prospective randomized controlled studies are needed to establish the safety and efficacy of above label dosing for octreotide LAR (Sandostatin LAR Depot).

Investigational Uses
- Although there is interest in using octreotide LAR (Sandostatin LAR Depot) in a variety of cancer settings, there is currently no published randomized trials to support the efficacy and safety of octreotide LAR (Sandostatin LAR Depot) in these settings.
- The safety and efficacy of octreotide LAR (Sandostatin LAR Depot) has not been established in portal hypertension. [7]

Safety [8]
- The most common adverse reactions associated with octreotide LAR (Somatostatin LAR Depot) in acromegaly were diarrhea, cholelithiasis, abdominal pain, and flatulence.
- The most common adverse reactions associated with octreotide LAR (Somatostatin LAR Depot) in carcinoid tumors and VIPomas were back pain, fatigue, headache, abdominal pain, nausea, and dizziness.
- Similarly to other somatostatin analogs, when octreotide LAR (Somatostatin LAR Depot) treatment is initiated, blood glucose levels should be monitored and anti-diabetic therapies should be adjusted accordingly.

Dosing
- Patients should be maintained on octreotide (generic) subcutaneous injection for at least 2 weeks to determine tolerance prior to initiating octreotide LAR (Sandostatin LAR Depot).
- The recommended dosing for octreotide LAR (Sandostatin LAR Depot) in acromegaly is as follows: [8]
  * Octreotide LAR (Sandostatin LAR Depot) 20 mg intramuscularly once every 4 weeks.
  * After 3 months of treatment, the dose of octreotide LAR (Sandostatin LAR Depot) may be adjusted based on GH and IGF-1 levels.
  * The recommended dosage range is octreotide LAR (Sandostatin LAR Depot) 10 mg to 40 mg.
- The recommended dosing for octreotide LAR (Sandostatin LAR Depot) in diarrhea associated with carcinoid tumors or VIPomas is as follows: [8]
  * Octreotide LAR (Sandostatin LAR Depot) 20 mg intramuscularly once every 4 weeks.
  * After 2 months of treatment, the dose of octreotide LAR (Sandostatin LAR Depot) may be adjusted based on symptomatic control.
  * The recommended dosage range is octreotide LAR (Sandostatin LAR Depot) 10 mg to 30 mg.
- The recommended dosing for octreotide LAR (Sandostatin LAR Depot) in GEP-NETs is 20 mg to 30 mg intramuscularly once every 4 weeks. [6]
- Octreotide LAR (Sandostatin LAR Depot) should be administered by a trained health care professional.

### Cross References

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<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
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<tbody>
<tr>
<td>HCPCS</td>
<td>J2353</td>
<td>Injection, octreotide, depot form for intramuscular injection, 1 mg</td>
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### References


### Revision History

<table>
<thead>
<tr>
<th>Revision Date</th>
<th>Revision Summary</th>
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<tbody>
<tr>
<td>10/13/2017</td>
<td>Clarification of covered diagnoses. No changes to coverage criteria with this annual update.</td>
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<tr>
<td>02/17/2017</td>
<td>New policy (effective 7/1/17)</td>
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