Drug Coverage Policy

Effective Date 5/15/2025
Coverage Policy Number.....IP0489
Policy Title..... Octreotide Long-Acting Products

Somatostatin Analogs – Octreotide Long-Acting Products

- Sandostatin® LAR Depot (octreotide acetate intramuscular injection – Novartis, generic)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Octreotide intramuscular injection, a somatostatin analog, is indicated for the following uses:[1]

1. **Acromegaly**, in patients 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 and insulin-like growth factor-1 levels to normal.
2. **Carcinoid tumors**, in patients with severe diarrhea and flushing episodes associated with metastatic carcinoid tumors.
3. **Vasoactive intestinal peptide tumors (VIPomas)**, in patients with profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors.

Guidelines

National Comprehensive Cancer Network (NCCN) guidelines support use of octreotide intramuscular injection in multiple conditions:

- **Central Nervous System Cancers:** Guidelines (version 4.2024 – January 21, 2025) recommend octreotide intramuscular injection for the treatment of meningiomas that recur despite surgery and/or radiation therapy; or are not amenable to treatment with surgery or radiation therapy.[2]
- **Merkel cell carcinoma** (version 1.2025 – January 17, 2025) clinical practice guidelines recommend octreotide LAR as a treatment option for patients with primary and recurrent regional disease or disseminated disease M1 who have contraindications to checkpoint immunotherapy (Bavencio® [avelumab intravenous infusion], Keytruda® [pembrolizumab intravenous infusion], and Opdivo® [nivolumab intravenous infusion]); or have progressed on checkpoint immunotherapy (category 2A for primary and recurrent regional disease and category 2B for M1 disease).[12]
- **Neuroendocrine and Adrenal Tumors:** Guidelines (version 4.2024 – January 17, 2025) recommend octreotide intramuscular injection for the management of carcinoid syndrome; tumors of the gastrointestinal tract, lung, thymus (carcinoid tumors), and pancreas (including glucagonomas, gastrinomas, VIPomas, insulinomas); pheochromocytomas; and paragangliomas.[3] Patients who have local unresectable disease and/or distant metastases and clinically significant tumor burden or progression should be started on therapy with a somatostatin analog to potentially control tumor growth. The North American Neuroendocrine Tumor Society (NANETS) consensus guidelines for the surveillance and medical management of midgut NETs (2017) also recommend octreotide intramuscular injection as a first-line initial therapy in most patients with metastatic midgut NETs for control of carcinoid syndrome and inhibition of tumor growth.[4]
- **Thymomas and Thymic Carcinomas:** Guidelines (version 1.2025 – October 30, 2024) recommend octreotide intramuscular injection as a therapy option with or without concomitant prednisone therapy.[5] In patients with thymoma who have positive octreotide scan or symptoms of carcinoid syndrome, octreotide therapy may be useful.

Supportive Evidence

- **Diarrhea Associated with Chemotherapy:** The Canadian Working Group on chemotherapy-induced diarrhea (2007) recommend octreotide LAR and octreotide immediate-release for the treatment of grades 3 or 4 chemotherapy induced diarrhea.[13] Aggressive management with high-dose loperamide or octreotide may reduce the morbidity and mortality associated with chemotherapy induced diarrhea and improve patient outcomes. Grade 1 diarrhea is when the patients is experiencing < 4 stools daily over their baseline. Grade 2 diarrhea is an increase of 4 to 6 stools daily over baseline, IV fluids may be needed; however, it is not interfering with activities of daily living. Grade 3 diarrhea is characterized by ≥ 7 stools daily over baseline, incontinence, the need for IV fluids for > 24 hours, interference with activities of daily living, and may require hospitalization. Grade 4

diarrhea is when the patient is experiencing life threatening consequences such as hemodynamic collapse.

- **Enterocutaneous Fistulas:** In case series, octreotide has been effective in patients with enterocutaneous fistulas.[6] Octreotide when used with an acid inhibitor agent (omeprazole) reduced the output of enterocutaneous fistulas. The European Journal of Medical Research reported in a trial where 84 of 154 patients were divided into the somatostatin group.[7] This trial showed that postoperative use of somatostatin served as a protective factor for developing into high-output recurrent fistulas. The average time for fistula closure without surgical intervention ranges from 12 to 66 days.[11]
- **Pancreatic Fistulas:** In case studies and retrospective reviews, octreotide demonstrated reduction of output and fistula closure.[8-10] The use of octreotide also showed a reduced risk of postoperative pancreatic fistulae and hospital stay.[10] On average, pancreatic fistulas closed between 18 to 35 days.[9]

Coverage Policy

POLICY STATEMENT

Prior Authorization is required for prescription benefit coverage of octreotide intramuscular injection. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with octreotide intramuscular injection as well as the monitoring required for adverse events and long-term efficacy, approval requires octreotide intramuscular injection to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Octreotide intramuscular injection is considered medically necessary when ONE of the following is met:

FDA-Approved Indications

1. **Acromegaly.** Approve for 1 year if the patient meets ALL of the following (A, B, C and D):
   A) Patient meets ONE of the following (i, ii, or iii):
      i. Patient has had an inadequate response to surgery and/or radiotherapy; OR
      ii. Patient is NOT an appropriate candidate for surgery and/or radiotherapy; OR
      iii. Patient is experiencing negative effects due to tumor size (e.g., optic nerve compression); AND
   B) Patient has (or had) a pre-treatment (baseline) insulin-like growth factor-1 (IGF-1) level above the upper limit of normal based on age and gender for the reporting laboratory; AND
   Note: Pre-treatment (baseline) refers to the IGF-1 level prior to the initiation of any somatostatin analog (e.g., Mycapssa [octreotide delayed-release capsules], an octreotide acetate injection product [e.g., Bynfezia Pen, Sandostatin {generic}, Sandostatin LAR Depot], Signifor LAR [pasireotide injection], Somatuline Depot [lanreotide injection], dopamine agonist [e.g., cabergoline, bromocriptine], or Somavert [pegvisomant injection]). Reference ranges for IGF-1 vary among laboratories.
   C) The medication is prescribed by or in consultation with an endocrinologist; AND
   D) Preferred product criteria is met for the product as listed in the below table

   Dosing. Approve up to 40 mg administered intramuscularly no more frequently than once every 4 weeks.

2. **Neuroendocrine Tumor(s) [NETs] of the Gastrointestinal Tract, Lung, Thymus (Carcinoid Tumors), and Pancreas (including glucagonomas, gastrinomas, vasoactive intestinal peptides-secreting tumors [VIPomas], insulinomas).** Approve for 1 year if the patient meets ALL of the following (A and B):

A) The medication is prescribed by or in consultation with an oncologist, endocrinologist, or gastroenterologist; AND
B) Preferred product criteria is met for the product as listed in the below table

Dosing. Approve up to 30 mg administered intramuscularly no more frequently than once every 4 weeks.

Other Uses with Supportive Evidence

3. **Diarrhea Associated with Chemotherapy.** Approve for 3 months if the patients meets ALL of the following (A, B, and C):
   A) Patient has Grade 3 or Grade 4 diarrhea; AND
   B) Patient has tried at least one antimotility medication; AND
   Note: Examples of antimotility medications include loperamide and diphenoxylate.
   C) The medication is being prescribed by or in consultation with an oncologist or gastroenterologist.

   Dosing. Approve up to 40 mg administered intramuscularly no more frequently than once every 4 weeks.

4. **Enterocutaneous Fistulas.** Approve for three months.

   Dosing. Approve up to 40 mg administered intramuscularly no more frequently than once every 4 weeks.

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

   Dosing. Approve up to 40 mg administered intramuscularly no more frequently than once every 4 weeks.

6. **Merkel Cell Carcinoma**. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has regional or distant metastatic disease; AND
   C) Patient meets ONE of the following (i or ii):
      i. Patient has contraindications to checkpoint immunotherapy; OR
      Note: Checkpoint immunotherapy includes Bavencio (avelumab intravenous infusion), Keytruda (pembrolizumab intravenous infusion), and Opdivo (nivolumab intravenous infusion).
      ii. Patient has progressed on checkpoint immunotherapy; AND
      Note: Checkpoint immunotherapy includes Bavencio (avelumab intravenous infusion), Keytruda (pembrolizumab
   D) Medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 30 mg administered intramuscularly no more frequently than once every 4 weeks.

7. **Pancreatic Fistulas.** Approve for two months if the patient is being treated for operative trauma, pancreatic resection, acute or chronic pancreatitis, or pancreatic infection.

Dosing. Approve up to 40 mg administered intramuscularly no more frequently than once every 4 weeks.

8. **Pheochromocytoma and Paraganglioma.** Approve for 1 year if the patient meets ALL of the following (A and B):
   A) The medication is prescribed by or in consultation with an endocrinologist, oncologist, or neurologist; AND
   B) Preferred product criteria is met for the product as listed in the below table

   Dosing. Approve up to 40 mg administered intramuscularly no more frequently than once every 4 weeks.

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

   Dosing. Approve up to 40 mg administered intramuscularly no more frequently than once every 4 weeks.

Employer Plans:

Product	Criteria
Sandostatin LAR Depot (octreotide acetate for intramuscular injection)	**ONE of the following:** 1. Acromegaly: The patient has tried Somatuline Depot. 2. Patient with neuroendocrine tumors: The patient meets the ONE of the following (A or B): Note: This includes (but is not limited to) carcinoid tumors, vasoactive intestinal peptide tumors (VIPomas), glucagonomas, gastrinomas, insulinomas. A. The patient has tried one of Somatuline Depot subcutaneous injection; OR B. Patient has already been started on therapy with Sandostatin LAR. 3. Patient with pheochromocytoma/paraganglioma: The patient meets the following (A or B): A. The patient has tried Somatuline Depot; OR B. Patient has already been started on therapy with Sandostatin LAR 4. Patient with diarrhea associated with chemotherapy; enterocutaneous fistula; meningioma; pancreatic fistula; Merkel cell carcinoma; thymoma/thymic carcinoma

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Octreotide intramuscular injection for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J2353	Injection, octreotide, depot form for intramuscular injection, 1 mg

References

1. Sandostatin® LAR Depot intramuscular injection [prescribing information]. East Hanover, NJ: Novartis; July 2023.
2. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 4.2024 – January 21, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 27, 2025.
3. The NCCN Neuroendocrine and Adrenal Tumors Clinical Practice Guidelines in Oncology (version 4.2024 – January 17, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 27, 2025.
4. Strosberg JR, Halfdanarson TR, Bellizi 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 Thymomas and Thymic Carcinomas Clinical Practice Guidelines in Oncology (version 1.2025 – October 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 27, 2025.
6. Kong X, Cao Y, Yang D, Zhang X. Continuous irrigation and suction with a triple-cavity drainage tube in combination with sequential somatostatin-somatotropin administration for the management of postoperative high-output enterocutaneous fistulas: Three case reports and literature review. *Medicine*. 2019;98(46):e18010.
7. Tian W, Zhao R, Luo S, et al. Effect of postoperative utilization of somatostatin on clinical outcome after definitive surgery for duodenal fistula. *Eur J Med Res*. 2023;28(1):63.
8. Alghamdi AA, Jawas AM, Hart RS. Use of octreotide for the prevention of pancreatic fistula after elective pancreatic surgery: a systematic review and meta-analysis. *Can J Surg*. 2007;50(6):459-466.
9. Veillette G, Dominguez I, Ferrone C, et al. Implications and management of pancreatic fistulas following pancreaticoduodenectomy: the Massachusetts General Hospital experience. *Arch Surg*. 2008;143(5):476-481.
10. Sundaram S, Patra BR, Choksi D, et al. Outcomes and predictors of response to endotherapy in pancreatic ductal disruptions with refractory internal and high-output external fistulae. *Ann Hepatobiliary Pancreat Surg*. 2022;26(4):347-354.
11. Noori I. Postoperative enterocutaneous fistulas: Management outcomes in 23 consecutive patients. *Ann Med Surg.* 2021;66:102413.
12. The NCCN Merkel Cell Carcinoma Clinical Practice Guidelines (version 1.2025 – January 17, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 27, 2025.
13. Maroun JA, Anthony LB, Blais N, et al. Prevention and management of chemotherapy-induced diarrhea in patients with colorectal cancer: a consensus statement by the Canadian Working Group on Chemotherapy-Induced Diarrhea. *Curr Oncol*. 2007;14(1):13-20.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	**Removed** criteria for (1) Gastroesophageal variceal hemorrhage, acute, (2) Diarrhea associated with chemotherapy or radiation, (3) Enterocutaneous fistula, (4) Perioperative management of individuals undergoing pancreatic resection (including fistula), (5) Thyroid-stimulating hormone (TSH)-secreting pituitary adenoma, (6) Secretory diarrhea in acquired immune deficiency syndrome (AIDS). **Removed** 'Individual has previously started on or is currently receiving Sandostatin LAR Depot (octreotide acetate) injection' from preferencing table **Added** for Sandostatin LAR Depot: step through of Somatuline Depot for Individual and Family Plan **Updated** title from Sandostatin LAR Depot (Non-Oncology Indications)	8/15/2024
Selected Revision	**Policy Name.** **Updated from** "Somatostatin Analogs – Sandostatin LAR Depot (for Non-Oncology Uses) **to** "Somatostatin Analogs – Sandostatin LAR Depot" **Enterocutaneous Fistulas:** The condition enterocutaneous fistulas was added under "Other Uses with Supportive Evidence." **Pancreatic Fistulas:** The condition pancreatic fistulas was added under "Other Uses with Supportive Evidence." **Neuroendocrine Tumor(s) [NETs] of the Gastrointestinal Tract, Lung, Thymus (Carcinoid Tumors), and Pancreas (including glucagonomas, gastrinomas, vasoactive intestinal peptides-secreting tumors [VIPomas], insulinomas).** **Added** criteria and dosing for NETs **Meningioma.** **Added** criteria and dosing for Meningioma **Pheochromocytoma and Paraganglioma.** **Added** criteria and dosing for Pheochromocytoma and Paraganglioma **Thymoma and Thymic Carcinoma.** **Added** criteria and dosing for Thymoma and Thymic Carcinoma	10/15/2024

	Preferred Product Requirement Table. Sandostatin LAR Depot. **Updated from** "Documented failure, contraindication, or intolerance to Somatuline Depot (lanreotide acetate) injection" **to "**ONE of the following:1.Acromegaly: Documentation the patient has tried Somatuline Depot.2.Patient with neuroendocrine tumors: The patient meets the following (A or B):Note: This includes (but is not limited to) carcinoid tumors, vasoactive intestinal peptide tumors (VIPomas), glucagonomas, gastrinomas, insulinomas; A.Documentation the patient has tried one of Somatuline Depot subcutaneous injection; OR B.Patient has already been started on therapy with Sandostatin LAR. 3.Patient with pheochromocytoma/paraganglioma: The patient meets the following (A or B): A.Documentation the patient has tried Somatuline Depot; OR B.Patient has already been started on therapy with Sandostatin LAR; 4.Patient with enterocutaneous fistula; meningioma; pancreatic fistula; thymoma/thymic carcinoma."	
Selected Revision	Policy name changed from Somatostatin Analogs – Sandostatin LAR Depot to Somatostatin Analogs – Octreotide Long-Acting Products. The generic octreotide intramuscular injection was added, where relevant, throughout the policy.	2/15/2025
Selected Revision	**Removed** Individual and Family Plans preferred product requirements.	04/01/2025
Annual Revision	**Enterocutaneous Fistulas:** **Removed "**Preferred product criteria is met for the product as listed in the below table." **Meningioma:** **Removed** "Preferred product criteria is met for the product as listed in the below table." **Pancreatic Fistulas:** **Removed "**Preferred product criteria is met for the product as listed in the below table." **Thymoma and Thymic Carcinoma:** **Removed** "Preferred product criteria is met for the product as listed in the below table." **Merkel Cell Carcinoma:** The condition Merkel cell carcinoma was added under "Other Uses with Supportive Evidence." **Diarrhea Associated with Chemotherapy:** The condition diarrhea associated with chemotherapy was added under "Other Uses with Supportive Evidence."	5/15/2025

	Preferred Product Table – Employer Plans: **Added** Diarrhea Associated with Chemotherapy and Merkel Cell Carcinoma	

The policy effective date is in force until updated or retired.