



Drug Coverage Policy

Effective Date 10/15/2024
Coverage Policy NumberIP0490
Policy Title.....Octreotide Immediate
Release Products

Somatostatin Analogs – Octreotide Immediate-Release Products

- Bynfezia Pen™ (octreotide acetate immediate-release subcutaneous injection – Sun Pharmaceutical [discontinued])
- Sandostatin® (octreotide acetate immediate-release subcutaneous or intravenous 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 and have discretion in making individual coverage determinations. 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.

Cigna Healthcare Coverage Policy

Octreotide acetate immediate-release injection products (Bynfezia Pen, Sandostatin [generic]), somatostatin analogs, are indicated for the following uses:¹⁻³

- **Acromegaly**, to reduce blood levels of growth hormone and insulin-like growth factor-1 in adults with acromegaly who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses.

- **Carcinoid tumors**, in adults with severe diarrhea and flushing episodes associated with metastatic carcinoid tumors. Studies were not designed to show an effect on the size, rate of growth, or development of metastases.
- **Vasoactive intestinal peptide (VIP) tumors**, in adults with profuse watery diarrhea associated with VIP-secreting tumors. Studies were not designed to show an effect on the size, rate of growth, or development of metastases.

Guidelines

National Comprehensive Cancer Network (NCCN) guidelines support use of octreotide in multiple conditions.

- **Central Nervous System Cancers:** Guidelines (version 1.2023 – March 24, 2023) note that an octreotide scan may be used to confirm magnetic resonance imaging findings. NCCN also notes that everolimus and octreotide may be useful for patients with recurrent meningiomas.⁴
- **Neuroendocrine and Adrenal Tumors:** Guidelines (version 1.2023 – August 2, 2023) recommend octreotide 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.⁵ 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.
- **Thymomas and Thymic Carcinomas:** Guidelines (version 1.2024 – November 21, 2023) note that in patients with thymoma who have positive octreotide scan or symptoms of carcinoid syndrome, octreotide therapy may be useful.⁶

Supportive Evidence

- **Enterocutaneous Fistulas:** In case series, octreotide has been effective in patients with enterocutaneous fistulas.⁷ Octreotide, when used with an acid inhibitor agent (omeprazole), reduced the output of enterocutaneous fistulas. The European Journal of Medical Research reported results from a trial where 84 of 154 patients with enterocutaneous fistulas received somatostatin; 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.¹²
- **Pancreatic Fistulas:** Octreotide demonstrated reduction of output and fistula closure in case studies and retrospective reviews.⁹⁻¹¹ The use of octreotide also showed a reduced risk of postoperative pancreatic fistulae and hospital stay.¹¹ On average, pancreatic fistulas closed between 18 to 35 days.¹⁰

Medical Necessity Criteria

Octreotide immediate-release products 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.
- D) Preferred product criteria is met for the product(s) as listed in the below table(s)

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 patients meets ALL of the following (A and B):

- A) This medication is prescribed by or in consultation with an oncologist, endocrinologist, or gastroenterologist.
- B) Preferred product criteria is met for the product(s) as listed in the below table(s)

Other Uses with Supportive Evidence

3. Enterocutaneous Fistulas. Approve for 3 months if the patient meets the following:

- A) Preferred product criteria is met for the product(s) as listed in the below table(s)

4. Meningioma. 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, radiologist, or neurosurgeon.
- B) Preferred product criteria is met for the product(s) as listed in the below table(s)

5. Pancreatic Fistulas. Approve for 2 months if the patient meets ALL of the following (A and B):

- A) Patient is being treated for operative trauma, pancreatic resection, acute or chronic pancreatitis, or pancreatic infection
- B) Preferred product criteria is met for the product(s) as listed in the below table(s)

6. 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.
- B) Preferred product criteria is met for the product(s) as listed in the below table(s)

7. Thymoma and Thymic Carcinoma. 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.
- B) Preferred product criteria is met for the product(s) as listed in the below table(s)

Individual and Family Plans:

Product	Criteria
Sandostatin (octreotide acetate immediate-release)	Documentation that patient has tried the bioequivalent generic product, octreotide acetate immediate release , AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which would result, per the prescriber, in a significant allergy or serious adverse reaction

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.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

Coding

- 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
J2354	Injection, octreotide, nondepot form for subcutaneous or intravenous injection, 25 mcg

References

1. Bynfezia Pen™ subcutaneous injection [prescribing information]. Cranbury, NJ: Sun Pharmaceutical; April 2020.
2. Sandostatin® subcutaneous injection [prescribing information]. East Hanover, NJ: Novartis; November 2023.
3. Octreotide subcutaneous injection [prescribing information]. Mahwah, NJ: Glenmark; October 2023.
4. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 1.2023 – March 24, 2023). © 2023 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed May 16, 2024.
5. The NCCN Neuroendocrine and Adrenal Tumors Clinical Practice Guidelines in Oncology (version 1.2023 – August 2, 2023). © 2023 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed May 16, 2024.
6. The NCCN Thymomas and Thymic Carcinomas Clinical Practice Guidelines in Oncology (version 1.2024 – November 21, 2023). © 2023 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed May 16, 2024.
7. 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.
8. 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.

9. 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.
10. 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.
11. 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.
12. Noori I. Postoperative enterocutaneous fistulas: Management outcomes in 23 consecutive patients. *Ann Med Surg.* 2021;66:102413.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	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).	8/15/2024
Selected Revision	<p>Policy Name. Updated from "Somatostatin Analogs – Octreotide Immediate-Release Products (for Non-Oncology Uses)" to "Somatostatin Analogs – Octreotide Immediate-Release Products"</p> <p>Enterocutaneous Fistulas: The condition enterocutaneous fistulas was added under "Other Uses with Supportive Evidence."</p> <p>Pancreatic Fistulas: The condition pancreatic fistulas was added under "Other Uses with Supportive Evidence."</p> <p>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 for NETs</p> <p>Meningioma. Added criteria for Meningioma</p> <p>Pheochromocytoma and Paraganglioma. Added criteria for Pheochromocytoma and Paraganglioma.</p>	10/15/2024

	<p>Thymoma and Thymic Carcinoma. Added criteria for Thymoma and Thymic Carcinoma</p> <p>Preferred Product Requirement Table. Sandostatin. Added criteria for Sandostatin (octreotide acetate immediate-release), for Individual and Family Plans</p>	
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The policy effective date is in force until updated or retired.

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