Drug Coverage Policy

Effective Date……5/1/2026
Coverage Policy Number……IP0490
Policy Title……Octreotide Immediate Release Products

Somatostatin Analogs – Octreotide Immediate-Release Products

- Bynfezia Pen™ (octreotide acetate immediate-release subcutaneous injection – Sun Pharmaceutical)
- 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 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 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.[4] NCCN also notes that everolimus and octreotide may be useful for patients with recurrent meningiomas.
- **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

- **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 and Grade 2 diarrhea is an increase of 4 to 6 stools daily over baseline, intravenous (IV) fluids may be needed, and it is not interfering with activities of daily living. Grade 3 diarrhea is ≥ 7 stools daily over baseline, incontinence, IV fluids needed for > 24 hours, interfering with activities of daily living, and patients are hospitalized. 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.[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]
- **Small bowel bleeds/angiodysplasia related bleeding:** The American College of Gastroenterology guidelines for diagnosis and management of small bowel bleeding (2015) recommend somatostatin analogs; lanreotide or octreotide long-acting or immediate-release; for the treatment of chronic bleeding due to vascular abnormalities of the gastrointestinal tract.[14] Long-acting somatostatin analogs has been shown as a beneficial rescue therapy to control angiodysplasia bleeding. The OCEAN study, which is a multicenter randomized trial that compared standard of care to octreotide LAR in angiodysplasia-related bleeding, showed that octreotide reduced the total number of transfusions required compared to standard of care (11.0 transfusions vs. 21.2 transfusions, respectively).[15]

Coverage Policy

POLICY STATEMENT

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

Certain indications and/or approval conditions that are delegated to EviCore by Evernorth will follow Oncology Medications (1403) coverage policy for prior authorization medical necessity criteria. Note: Any listed preferred product requirements in this coverage policy, inclusive of oncology and/or oncology-related uses, are applicable as noted.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, prescription receipts and/or other information. All documentation must include patient-specific identifying information.

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; AND

D) Preferred product criteria is met for the product as listed in the below table

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; AND
   B) Preferred product criteria is met for the product as listed in the below table

Other Uses with Supportive Evidence

3. **Diarrhea Associated with Chemotherapy.** Approve for 3 months if the patients meets ALL of the following (A, B, C, and D):
   A) Patient has Grade 3 or Grade 4 diarrhea; AND
   Note: Examples of Grade 3 or Grade 4 diarrhea include more than 6 bowel movements above baseline per day, colitis symptoms, interference with activities of daily living, hemodynamic instability, hospitalization, serious complications (e.g., ischemic bowel, perforation, toxic mega-colon), or other colitis-related life-threatening conditions.
   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; AND
   D) Preferred product criteria is met for the product as listed in the below table

4. **Enterocutaneous Fistulas.** Approve for 3 months if the patient meets the following:
   A) Preferred product criteria is met for the product as listed in the below table

5. **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; AND
   B) Preferred product criteria is met for the product as listed in the below table

6. **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; AND
   B) Preferred product criteria is met for the product as listed in the below table

7. **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

8. **Small bowel bleeds/angiodysplasia related bleeding:** Approve for 6 months if the patient meets ALL of the following: (A, B and C):

A) Patient has chronic, recurrent gastrointestinal bleeds lasting ≥ 3 months; AND

B) The medication is prescribed by or in consultation with gastroenterologist.
C) Preferred product criteria is met for the product as listed in the below table

9. **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; AND
   B) Preferred product criteria is met for the product as listed in the below table

Employer Plans:

Product	Criteria
Bynfezia Pen™ Bynfezia Pen™ (octreotide acetate immediate-release)	The patient has tried **octreotide acetate immediate release (generic for Sandostatin),** AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between Bynfezia and **octreotide acetate immediate release (generic for Sandostatin)** which would result in a significant allergy or serious adverse reaction **[documentation required]**.

Individual and Family Plans:

Product	Criteria
Bynfezia Pen™ Bynfezia Pen™ (octreotide acetate immediate-release)	The patient has tried **octreotide acetate immediate release (generic for Sandostatin),** AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between Bynfezia and **octreotide acetate immediate release (generic for Sandostatin)** which would result in a significant allergy or serious adverse reaction **[documentation required]**.
Sandostatin (octreotide acetate immediate-release)	The 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.

Conditions Not Covered

Octreotide immediate-release products 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

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

References

1. Bynfezia Pen™ subcutaneous injection [prescribing information]. Cranbury, NJ: Sun Pharmaceutical; September 2024.
2. Sandostatin® subcutaneous injection [prescribing information]. East Hanover, NJ: Novartis; July 2024.
3. Octreotide subcutaneous injection [prescribing information]. Mahwah, NJ: Glenmark; October 2023.
4. 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.
5. 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.
6. The NCCN Thymomas and Thymic Carcinomas Clinical Practice Guidelines in Oncology (version 1.2025 – October 30, 2024). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 27, 2025.
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.
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.
14. Gerson LB, Fidler JL, Cave DR, Leighton JA. ACG clinical guideline: diagnosis and management of small bowel bleeding. *Am J Gastroenterol*. 2015;110(9):1265-1288.
15. Goltstein LCMJ, Grooteman KV, Bernts LHP, et al. Standard of care versus octreotide in angiodysplasia-related bleeding (the OCEAN Study): a multicenter randomized controlled trial. *Gastroenterology*. 2024;166(4):690-703.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Removed** criteria for: (1) Gastroesophageal variceal hemorrhage, acute, (2) Diarrhea	8/15/2024

	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).	
Selected Revision	**Policy Name.** **Updated from** "Somatostatin Analogs – Octreotide Immediate-Release Products (for Non-Oncology Uses)" to "Somatostatin Analogs – Octreotide Immediate-Release Products" **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 for NETs **Meningioma.** **Added** criteria for Meningioma **Pheochromocytoma and Paraganglioma.** **Added** criteria for Pheochromocytoma and Paraganglioma. **Thymoma and Thymic Carcinoma.** **Added** criteria for Thymoma and Thymic Carcinoma **Preferred Product Requirement Table.** **Sandostatin.** **Added** criteria for Sandostatin (octreotide acetate immediate-release), for Individual and Family Plans	10/15/2024
Annual Revision	**Diarrhea Associated with Chemotherapy:** This condition and criteria for approval was added under "Other Uses with Supportive Evidence." **Preferred Product Table - Individual and Family Plans:** **Updated from** "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,	5/15/2025

	preservatives] between the Brand and the bioequivalent generic product which would result, per the prescriber, in a significant allergy or serious adverse reaction" **to** "The 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."	
Selected Revision	**Diarrhea Associated with Chemotherapy:** A note was added to provide examples of Grade 3 or Grade 4 diarrhea.	07/15/2025
Selected Revision	**Small bowel bleeds/angiodysplasia related bleeding:** The condition small bowel bleeds/angiodysplasia related bleeding was added under "Other Uses with Supportive Evidence".	11/1/2025
Selected Revision	**Preferred Product Table - Individual and Family Plans:** **Added** step through octreotide acetate generic requirement for Bynfezia.	2/1/2026
Selected Revision	**Added** Documentation Instructions. **Preferred Product Table.** **Added** Preferred Product Table for Employer Plans for Bynfezia Pen **Added [documentation required]** for Bynfezia Pen	5/1/2026

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