Medical Drug Clinical Criteria

Subject:	Octreotide Agents		
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Overview

This document addresses the use of octreotide agents, Sandostatin and Sandostatin LAR.

Octreotide exerts pharmacologic actions similar to the natural hormone somatostatin, but is a more potent inhibitor of GH, glucagon, and insulin than somatostatin. Like somatostatin, it also suppresses luteinizing hormone (LH) response to gonadotropin-releasing hormone (GnRH), decreases splanchnic blood flow, and inhibits release of serotonin, gastrin, vasoactive intestinal peptide, secretin, motilin, and pancreatic polypeptide.

Acromegaly is a rare condition that occurs if a tumor causes excess growth hormone secretion, that in turn increases IGF-1 levels. The increase in the hormones causes the hands, feet, lips, nose, and tongue to become larger, bone changes, headaches, joint aches, and vision problems. Complications may develop such as type 2 diabetes, high blood pressure, heart disease, sleep apnea, and arthritis. Estimates are there are 3,000 new cases of acromegaly per year with a prevalence of about 25,000 patients in the US. Treatment includes surgery, radiation, and medications. Medications are used if surgery is impractical or not successful. Medications for acromegaly include somatostatin analogs, growth hormone receptor antagonist, and dopamine agonist. Dopamine agonist (e.g., cabergoline) has a limited role in the treatment of acromegaly for those with mild disease. The following table includes the somatostatin analogs and the growth hormone receptor antagonist.

Table 1: Somatostatin Analogs and Growth Hormone Receptor Antagonist for Acromegaly

Product	Indications	Route and frequency for Acromegaly
Somatostatin Analogs		
Mycapssa (octreotide) delayed-release capsules	**Long-term maintenance treatment of acromegaly patients who have responded to and tolerated octreotide or lanreotide.**	**Oral capsule used twice daily or daily; maximum daily dosage is 80 mg per day.**
Octreotide (injection; immediate-release)	**Acromegaly in those who have inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses.** **Other indications: carcinoid tumors, vasoactive intestinal peptide tumors**	**Subcutaneous or intravenous injection three times a day**
Sandostatin LAR depot (octreotide, injection; long-acting release)	**For patients in whom initial treatment with octreotide injection has been shown effective and tolerated.** **Long-term maintenance treatment of acromegaly patients who have had an inadequate response to surgery and/or radiotherapy or for whom surgery and/or radiotherapy is not an option** **Other indications: carcinoid tumors, vasoactive intestinal peptide tumors**	**Intramuscular injection every 4 weeks administered by a healthcare professional**
Signifor LAR (pasireotide, injection)	**For patients with acromegaly who have had an inadequate response to surgery and/or whom surgery is not an option.** **Other indication: Cushing's disease**	**Intramuscular injection every 4 weeks administered by a healthcare professional**

Product	Indications	Route and frequency for Acromegaly
Somatuline Depot (lanreotide, injection)	**For long-term treatment of acromegaly who have had an inadequate response to surgery and/or radiotherapy, or whom surgery and/or radiotherapy is not an option.** **Other indications: gastroenteropancreatic neuroendocrine tumors, carcinoid syndrome**	**Deep subcutaneous injection every 4 weeks administered by a healthcare professional**
Growth Hormone Receptor Antagonist		
Somavert (pegvisomant, injection)	**For treatment of acromegaly in patients who have had an inadequate response to surgery or radiation, or for whom these therapies are not appropriate.**	**Subcutaneous injection daily**

The safety and/or efficacy of octreotide acetate have not been established for treating the following conditions. The peer-reviewed published medical literature consists of case reports, small case series, RCTs of small sample sizes, and non-randomized or uncontrolled trials which precludes drawing reliable conclusions on the safety and net health benefit of octreotide acetate for other conditions, including but not limited to:

1. AIDs-related diarrhea (Panel 2018);
2. Chyle fistula management following neck dissection surgery (Swanson, 2015);
3. Chylothorax in adults (Fujita, 2014; Ismail, 2015) and neonates (Das and Shah, 2010; Testoni, 2015);
4. Graves' ophthalmopathy (thyroid eye disease) (Stan, 2006);
5. Hypothalamic obesity (insulin hypersecretion) (Lustig, 2003; Michalsky, 2012);
6. Other carcinomas, such as:
    - Advanced, metastatic breast cancer (Bajetta, 2002; Chapman, 2015);
    - Hepatocellular cancer (Jia, 2010);
    - Prostate cancer (including castration-resistant) (Friedlander, 2012);
7. Other GI tract conditions, such as:
    - bleeding from vascular malformations (such as, angiodysplasias, angioectasias, or/GI tract AVM (Brown, 2010; Junquera, 2007; Loyaga-Rendon, 2015, Szilagyi and Ghali, 2006);
    - gastroparesis (Edmunds, 1998);
    - non-variceal upper GI bleeding (Archimandritis, 2000);
    - pancreatitis (Xu, 2013);
    - short bowel syndrome (Nehra, 2001);
    - small intestinal dysmotility associated with systemic sclerosis (scleroderma) (Nikou, 2007; Perlemuter, 1999; Soudah, 1991, Verne, 1995);
8. Polycystic kidney or liver disease (Caroli, 2013; Hogan, 2010; Ruggenenti, 2005).

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

~~Bynfezia Pen,~~ Sandostatin, or Sandostatin LAR Depot (octreotide)

Requests for ~~Bynfezia Pen,~~ Sandostatin, or Sandostatin LAR Depot (octreotide) may be approved if the following criteria are met:

I. Individual has a diagnosis of acromegaly; **AND**

II. Diagnosis of acromegaly has been ~~confirmed~~ verified by, or in consultation with, a board-certified endocrinologist who has reviewed and verified the test results (including, but not limited to: Insulin-like Growth Factor 1 levels; Oral Glucose Tolerance Test with associated Growth Hormone (GH) levels) that are indicative of a positive test; **AND**

III. Individual has had an inadequate response to any of the following:
    A. Surgical resection; **OR**
    B. Pituitary irradiation; **OR**
    C. Bromocriptine mesylate at maximally tolerated doses;

OR

IV. Surgery and/or radiotherapy is not an option;

OR

V. Individual has a diagnosis of carcinoid tumors and is using for any of the following:
   A. Metastatic carcinoid tumor to suppress or inhibit severe diarrhea and flushing episodes associated with the disease;

OR

VI. Individual has a diagnosis of neuroendocrine and adrenal tumors and is using for any of the following:
   A. For the management of unresectable locoregional disease or distant metastasis (NCCN 2A); **OR**
   B. For the treatment of profuse watery diarrhea associated with VIPomas; **OR**
   C. Prophylactic treatment prior to surgery for gastrinoma (AHFS);

OR

VII. Individual is using for bleeding Gastroesophagel (GE) varices and the following criteria are met:
   A. Gastroesophageal varices are associated with liver disease (Banares 2002, Corley 2001); **AND**
   B. Octreotide acetate is used in combination with endoscopic therapy or alone if endoscopic therapy is not immediately available (Garcia-Tsao 2007);

OR

VIII. Individual is using for malignant bowel obstruction to manage gastrointestinal symptoms (e.g. nausea, pain or vomiting) (AHFS);

OR

IX. Individual is using for thymic carcinoma or thymoma with or without prednisone (NCCN 2A);

OR

X. Individual is requesting Sandostatin for rapid relief of symptoms or for breakthrough symptoms in individuals taking long-acting octreotide acetate when any of the criteria are met for the above uses (NCCN 2A).

Requests for ~~Bynfezia Pen,~~ Sandostatin, or Sandostatin LAR (octreotide) may not be approved for any of the following:

I. Individual is using for the treatment of chylothorax; **OR**
II. Individual is using for the treatment of diarrhea associated with acquired immunodeficiency disease; **OR**
III. Individual is using for the treatment of gastrointestinal diseases (e.g. bleeding from vascular malformations, gastroparesis, pancreatitis, prevention of postoperative complications following pancreatic surgery, short bowel syndrome, or upper GI bleeding); **OR**
IV. Individual is using for the treatment of Graves' ophthalmopathy; **OR**
V. Individual is using for the treatment of hypothalamic obesity; **OR**
VI. Individual is using for the treatment of other carcinomas (e.g. advanced breast cancer, hepatocellular cancer, or prostate cancer); **OR**
VII. Individual is using for the treatment of polycystic kidney disease; **OR**
VIII. When the above criteria are not met and for all other indications.

Quantity Limits

Quantity Limits

Drug	Limit
~~Bynfezia (octreotide acetate) Pen 2,500 mcg/ml*~~	~~1 pen per 14 days~~
Sandostatin LAR (octreotide) Depot Kit 20 mg*	2 kits per 28 days
Sandostatin LAR (octreotide) Depot Kit 10 mg, 30 mg	1 kit per 28 days

*Indicates FDA maximum recommended dose for specific drug and dosage strength.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J2353	Injection, octreotide, depot form for intramuscular injection, 1 mg
J2354	Injection, octreotide, nondepot form for subcutaneous or intravenous injection, 25 mcg [Sandostatin LAR]

ICD-10 Diagnosis

C18.0-C18.9	Malignant neoplasm of colon [associated bowel obstruction]
C25.0-C25.9	Malignant neoplasm of pancreas [related VIPoma syndrome]
C37	Malignant neoplasm of thymus
C48.1-C48.8	Malignant neoplasm of peritoneum [associated bowel obstruction]
C57.00-C57.4	Malignant neoplasm of other and unspecified female genital organs [associated bowel obstruction]
C70.0-C70.9	Malignant neoplasm of meninges
C75.1	Malignant neoplasm of pituitary gland
C7A.00-C7A.8	Malignant neuroendocrine tumors (carcinoid tumors)
C7B.00-C7B.8	Secondary neuroendocrine tumors
D01.7	Carcinoma in situ of other specified digestive organs [pancreas]
D13.7	Benign neoplasm of endocrine pancreas
D15.0	Benign neoplasm of thymus
D35.2	Benign neoplasm of pituitary gland
D3A.010-D3A.8	Benign neuroendocrine tumors
E05.80-E05.81	Other thyrotoxicosis
E22.0	Acromegaly and pituitary gigantism
E31.20-E31.23	Multiple endocrine neoplasia [MEN] syndrome
E34.0	Carcinoid syndrome
H47.49	Disorders of optic chiasm in (due to) other disorders
I85.11	Secondary esophageal varices with bleeding
K56.690-K56.699	Other intestinal obstruction
K59.1	Functional diarrhea
K70.0-K75.9	Disease of liver [related bleeding esophageal varices]
R19.7	Diarrhea, unspecified
Z85.841	Personal history of malignant neoplasm of brain
Z85.845	Personal history of malignant neoplasm of other parts of nervous tissue

Document History

Revised: 09/11/2023
Document History:

- 09/11/2023: Annual Review: Removed obsolete agent, Bynfezia. Wording and formatting changes. Coding Reviewed: Removed Bynfezia from HCPCS J2354.
- 08/19/2022: Annual Review: Added confirmation of diagnosis requirements by board-certified endocrinologist. Added language to end of may not be approved for section. Coding reviewed: No changes.
- 08/20/2021: Annual Review: No changes. Coding reviewed: No changes.
- 08/21/2020: Annual review. Remove criteria for use in meningiomas as NCCN changed category rating from 2A to 2B. Remove prophylactic use prior to biopsy, anesthesia, and perioperatively to a surgical procedure in those with a carcinoid tumor as a Category C rating in AHFS and no longer in NCCN compendia. Remove use in Zollinger-Ellison syndrome as a Category C rating in AHFS. Remove use in chemotherapy or radiation-induced diarrhea when convention medications are unresponsive as no longer in NCCN compendia. Coding Reviewed: Removed ICD-10-CM D32.0-D32.9, E16.0-E16.9, T66.XXXA-T66.XXXS
- 03/16/2020: Select Review. New agent Bynfezia (octreotide acetate) Pen was included with existing octreotide criteria. New quantity limit for Bynfezia Pen. Coding review: Added Byfezia to J2354.
- 09/23/2019 - Administrative update to add drug specific quantity limit.
- 09/09/2019: Annual Review. No changes. Coding Reviewed: No changes
- 03/18/2019: No changes. Administrative update. Coding Reviewed: No changes.
- 11/16/2018: Annual review. Initial review of Sandostatin, Sandostatin LAR (Octreotide Agents). Minor formatting and wording updates. Include references for off-label criteria. HCPCS and ICD-10 Coding review: No changes.

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Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.