Original Effective Date: 07/07/2017
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Last P&T Approval/Version: 07/26/2023
Next Review Due By: 07/2024
Policy Number: C8839-A

Octreotide

PRODUCTS AFFECTED

Sandostatin LAR, Sandostatin, octreotide, Bynfezia Pen, Mycapssa (octreotide DR caps)

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Acromegaly, Carcinoid Tumors, Neuroendrocrine Tumors, Vasoactive Intestinal Peptide Tumors, Congenital hyperinsulinism, Cushing's Syndrome, Chemotherapy-induced refractory diarrhea, Hyperglycemia from Islet cell adenoma or carcinoma, Malignant bowel obstruction, Short Bowel Syndrome, Thymoma

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review.

A. ACROMEGALY – ALL PRODUCTS:

1. Documented diagnosis of acromegaly
   AND
2. Documentation that member is not eligible for surgery or has had an inadequate response to pituitary surgery or radiation.
   AND
3. Documentation of unsuccessful treatment with cabergoline or bromocriptine mesylate at maximally tolerated doses for members with modest elevation of IGF-1 (defined as less than 1.4 mcg/L) and mild signs and symptoms of GH excess (2014 Guidelines) OR labeled contraindication to both cabergoline and bromocriptine.
   AND
4. FOR DEPOT INJECTION (SANDOSTATIN LAR) ONLY: Member must be stabilized on subcutaneous octreotide for at least 2 weeks before switching to the long-acting depot.
   AND
5. FOR BYNFEZIA REQUESTS: Trial and failure (30 days) or labeled contraindication to octreotide generic products
   AND
6. FOR MYCAPSSA REQUESTS: Member must be stabilized (stable dose for at least 3 months) on subcutaneous octreotide or lanreotide

B. CARCINOID TUMORS, NEUROENDOCRINE TUMORS, VASOACTIVE INTESTINAL PEPTIDE TUMORS (VIPomas) – INJECTABLE PRODUCTS ONLY:

1. Documentation that member has diagnosis of one of the following:
   a) A carcinoid/neuroendocrine tumor and has a diagnosis of carcinoid syndrome
      OR
   b) Neuroendocrine tumors [e.g., Islet cell tumors, gastrinomas, glucagonomas, insulinomas, lung tumors, somatostatinomas, tumors of the pancreas, GI tract, lung and thymus, adrenal glands, or Hormone-secreting poorly differentiated (high grade)/ large or small cell neuroendocrine tumor
      OR
   c) Vasoactive intestinal peptide tumor (VIPoma)

   AND
2. FOR BYNFEZIA REQUESTS: trial and failure (30 days) or labeled contraindication to octreotide generic products

C. CONGENITAL HYPERINSULINISM – IMMEDIATE RELEASE INJECTABLE PRODUCTS ONLY:

1. Documented diagnosis of congenital hyperinsulinism (congenital hyperinsulinemic hypoglycemia)
   AND
2. Documented unsuccessful treatment with diazoxide unless contraindicated by cardiac failure or pulmonary hypertension (Yorifuji et al., 2017)
   AND
3. FOR BYNFEZIA REQUESTS: Trial and failure (30 days), labeled contraindication to octreotide generic products

D. CUSHING'S SYNDROME – INJECTABLE PRODUCTS ONLY:

1. Documentation of hypercortisolism associated with the diagnosis of a neuroendocrine tumor and somatostatin scintigraphy-positive status (NCCN)
   AND
2. FOR BYNFEZIA REQUESTS: Trial and failure (30 days) or labeled contraindication to octreotide generic products

E. CHEMOTHERAPY–INDUCED REFRACTORY DIARRHEA – INJECTABLE PRODUCTS ONLY:

1. Documentation of National Cancer Institute (NCI) grade 3 or 4 diarrhea (7 or more stools per day baseline), or grade 2 diarrhea with documented trial and failure of loperamide AND diphenoxylate/atropine for 48 hours (Benson et al., 2004)

NOTE: Due to chemotherapy, not immunotherapy or CAR-T therapy
AND
2. FOR BYNFEZIA REQUESTS: Trial and failure (30 days) or labeled contraindication to octreotide generic products

F. HYPOGLYCEMIA DUE TO HYPERINSULINISM FROM ISLET CELL ADENOMA OR CARCINOMA – INJECTABLE PRODUCTS ONLY:
1. Documented diagnosis of hyperinsulinemic hypoglycemia due to Islet cell adenoma or carcinoma
AND
2. Documented trial and failure of or FDA labeled contraindication to diazoxide (FDA-approved indication of diazoxide)
AND
3. Documentation of somatostatin receptor positivity by scintigraphy.
AND
4. FOR BYNFEZIA REQUESTS: Trial and failure (30 days) or labeled contraindication to octreotide generic products

G. MALIGNANT BOWEL OBSTRUCTION – INJECTABLE PRODUCTS ONLY:
1. Documentation of inoperable malignant bowel obstruction. (Note: Continuation of approval is contingent upon documentation of continued symptomatic relief.)
AND
2. FOR BYNFEZIA REQUESTS: Trial and failure (30 days) or labeled contraindication to octreotide generic products

H. SHORT BOWEL SYNDROME – INJECTABLE PRODUCTS ONLY:
1. Documented diagnosis of short bowel syndrome
AND
2. Documented trial and failure of, or FDA labeled contraindication to, ALL of the following: high-dose H2 antagonists, proton- pump inhibitors, and anti-motility agents (loperamide, diphenoxylate/atropine, or other opioids established as treatment).
AND
3. Documentation of daily IV fluid requirements of 3 liters or greater per day due to gastrointestinal output, despite other current treatments (AGA guidelines 2022).
AND
4. FOR BYNFEZIA REQUESTS: Trial and failure (30 days) or labeled contraindication to octreotide generic products

I. THYMOMA - INJECTABLE PRODUCTS ONLY:
1. Documented diagnosis of thymoma
AND
2. Documentation of treatment failure with radiation or first line combination chemotherapy (for locally advanced, unresectable thymoma with evidence of extrathoracic metastases ONLY) per the members stage and disease per NCCN updated guidelines for Thymomas
AND
3. FOR BYNFEZIA REQUESTS: trial and failure (30 days), labeled contraindication to octreotide generic products

J. ALL OTHER INDICATIONS – INJECTABLE PRODUCTS ONLY:
1. Documented diagnosis of a compendial approved use listed below

CONTINUATION OF THERAPY:

A. FOR ALL INDICATIONS
1. Documented beneficial and clinically significant response to treatment (e.g., symptomatic relief of malignant bowel obstruction, etc.) [DOCUMENTATION REQUIRED]

AND

2. For dosage increase requests, supporting labs if applicable (for example, in Acromegaly, growth hormone and IGF-1 labs).
   AND
3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:
Initial authorization: 12 months for labeled uses, 3 months for off-label uses, Continuation of Therapy: for up to 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with an endocrinologist, oncologist/ hematologist, or Gastroenterologist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
No restrictions: The drug label information for both octreotide and octreotide depot include by way of precaution that formal controlled clinical trials have not been performed to evaluate the safety and efficacy of sandostatin in pediatric members under 6 years of age.

QUANTITY:
SANDOSTATIN LAR J2353 –
Acromegaly, chemo-induced diarrhea: 40 units (40 mg) every 4 weeks
NET, Carcinoid Syndrome, VIPomas, thymoma: 30 units (30 mg) every 4 weeks
All other supported uses: 40 units (40 mg) per date of service
No supported uses should be authorized more frequently than every 2 weeks. Waste of 10 units or more is medically unlikely.

Bynfezia (octreotide acetate)/octreotide:
Acromegaly: maximum of 300mcg/day
VIPoma: maximum of 450mcg/day
All other indications: maximum of 1,500mcg/day

Mycapssa: Max 80 mg/day

Dosage, frequency, and total treatment duration must be supported by FDA label or compendia supported dosing for prescribed indication

PLACE OF ADMINISTRATION:
Octreotide immediate release, Mycapssa (octreotide DR caps):
The recommendation is that the oral medications in this policy will be for pharmacy benefit coverage and patient self-administered

Octreotide—intravenous:
The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Octreotide—subcutaneous, octreotide depot – intramuscular:
The recommendation is that injectable medications in this policy will be for pharmacy benefit coverage and patient self-administered as per the Molina Health Care Site of Care program.

Site of Care Utilization Management Policy applies for Octreotide (intravenous, subcutaneous, octreotide depot and intramuscular). For information on site of care, see

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Octreotide – subcutaneous, intravenous
Octreotide depot – intramuscular
Mycapssa (octreotide DR caps)- oral

DRUG CLASS:
Somatostatic Agents

FDA-APPROVED USES:
SANDOSTATIN IMMEDIATE-RELEASE, SANDOSTATIN LAR DEPOT INJECTION, BYNFEZIA PEN:
Acromegaly: Indicated to reduce blood levels of growth hormone and IGF-I (somatomedin C) in acromegaly patients who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses. Carcinoid tumors: Long-term treatment of the severe diarrhea and flushing episodes associated with metastatic carcinoid tumors. Vasoactive Intestinal Peptide Tumors (VIPomas): Long-term treatment of the profuse watery diarrhea associated with VIP-secreting tumors.

Limitations of Use: In patients with acromegaly, the effect of BYNFEZIA Pen on improvement in clinical signs and symptoms, reduction in tumor size and rate of growth, has not been determined. In patients with carcinoid syndrome and VIPomas, the effect of BYNFEZIA Pen on size, rate of growth and development of metastases, has not been determined. In patients with carcinoid syndrome and VIPomas, the effect of Sandostatin Injection and SANDOSTATIN LAR DEPOT on tumor size, rate of growth and development of metastases, has also not been determined.

MYCAPSSA is a somatostatin analog indicated for long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide

COMPENDIAL APPROVED OFF-LABELED USES:
Carcinoid crisis (prevention); Diarrhea (refractory or persistent) associated with chemotherapy; Diarrhea associated with graft-versus-host disease (GVHD); Gastroenteropancreatic neuroendocrine tumors (metastatic); Gastroesophageal variceal hemorrhage; Hepatorenal syndrome; Malignant bowel obstruction; Sulfonylurea-induced hypoglycemia; Thymoma/thymic malignancies (advanced); Zollinger-Ellison syndrome; Cushing's syndrome (ectopic); Hypothalamic obesity; Post gastrectomy dumping syndrome; Small bowel fistulas

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
A. Acromegaly- -Recommended treatment for Acromegaly (Melmed and Katznelson) – Surgical removal of the pituitary growth hormone-secreting adenoma is recommended as first-line unless surgery is declined, the patient is a poor surgical candidate, or it is anticipated that the adenoma is not fully resectable. Surgical debulking for macroadenomas close to the chiasm and followed by medical therapy. Medical therapy options include bromocriptine, octreotide, lanreotide, pegvisomant, or cabergoline. In the setting of residual disease after surgery, medical therapy is indicated. Somatostatin

analogs are effective at normalizing GH and serum IGF-1 concentrations. than dopamine agonists, however, dopamine drugs such as cabergoline or bromocriptine may be suitable for treating mild to moderate elevations in IGF-1 concentration (mild signs and symptoms ofGH excess with IGF-1 elevations up to 1.3 mcg/L) that remain after surgical intervention. Radiation therapy is recommended if medical therapy has been ineffective or not, was tolerated. -
Recommended medical treatments and dosing--Octreotide – Acromegaly: SubQ, IV: Initial: 50 mcg 3 times/day; titrate to achieve growth hormone levels <5 ng/mL or IGF-I (somatomedin C) levels <1.9 units/mL in males and <2.2 units/mL in females. Usual effective dose: 100 mcg 3 times/day; range: 300 to 1,500 mcg/day. Doses above 300 mcg/day rarely result in additional benefit; if increased dose fails to provide additional benefit, the dose should be reduced. Note: Should be withdrawn yearly for a 4- week interval (8 weeks for depot injection) in patients who have received irradiation. Resume if levels increase and signs/symptoms recur. IM depot injection: Patients must be stabilized on subcutaneous octreotide for at least 2 weeks before switching to the long-acting depot. Upon switch: 20 mg IM intragluteally every 4 weeks for 3 months, then the dose may be modified based upon response. -- Bromocriptine - Acromegaly: Oral: Initial: 1.25 to 2.5 mg daily increasing by 1.25 to 2.5 mg daily as necessary every 3 to 7 days; usual dose: 20 to 30 mg daily (maximum: 100 mg/day) --Lanreotide – Acromegaly: SubQ: Initial dose: 90 mg once every 4 weeks for 3 months; after initial 3 months, continue monitoring and adjust dose as necessary based on clinical response of patient, growth hormone (GH) levels, and/or insulin-like growth factor 1 (IGF- 1) levels --Pegvisomant – Acromegaly: SubQ: Initial loading dose: 40 mg; maintenance dose: 10 mg once daily following initial loading dose; doses may be adjusted by 5 mg increments or decrements in 4- to 6- week intervals based on IGF-I concentrations (maximum maintenance dose: 30 mg daily)

--Cabergoline – Acromegaly (off-label use): The initial dose of cabergoline should be 0.5 mg once a week or 0.25 mg twice a week. The dose should be increased, if necessary, to 1 mg twice a week. Higher doses are not likely to decrease GH further. The presence of hyperprolactinemia does not consistently predict GH and IGF-1 response. --Endocrinology Society Guidelines – 5.1 We recommend medical therapy in a patient with persistent disease following surgery. (1|QQQQ) 5.2 Ina patient with significant disease (ie, with moderate-to-severe signs and symptoms of GH excess and without local mass effects), we suggest use of either an SRL or pegvisomant as the initial adjuvant medical therapy. (2|QQEE) 5.3 Ina patient with only modest elevations of serum IGF-1 and mild signs and symptoms of GH excess, we suggest a trial of a dopamine agonist, usually cabergoline, as the initial adjuvant medical therapy. (2|QQEE) B. Cushing's syndrome Cushing's syndrome is a manifestation of hypercortisolism, which can be secondary to a number of sources, chiefly, an ACTH-secreting pituitary tumor, a non- pituitary or "ectopic" ACTH-secreting tumor, or an adrenal adenoma or carcinoma that produces cortisol. Primary treatment is surgical, but when it is ineffective or cannot be performed, medical therapy is indicated.-The NCCN Guidelines Version 3.2018 - Neuroendocrine and Adrenal Tumors section Evaluation and Treatment of Cushing's Syndrome makes no mention for the use of pasireotide in Cushing's Syndrome caused by non- pituitary tumors. -"WMedical management of hypercortisolism is achieved with adrenostatic agents, including ketoconazole, mitotane, and/or mifepristone. Ketoconazole is most commonly used (at doses of 400-1200 mg/d) because of its easy availability and relatively tolerable toxicity profile. The data supporting use of other individual drugs for the management of Cushing's disease are limited. Octreotide or lanreotide can also be considered for ectopic Cushing's syndrome if the tumor is somatostatin scintography-positive, although it may be less effective in controlling ectopic ACTH secretion than it is in other contexts. Bilateral adrenalectomy is generally recommended when medical management of ectopic Cushing's syndrome fails." C. Short Bowel Syndrome From the 2003 American Gastroenterological Association Medical Position Statement on the Medical treatment of Short Bowel Syndrome -"High-dose H2 antagonists and proton pump inhibitors reduce gastric fluid secretion, and fluid losses during the first 6 months post-enterectomy. Fluid losses usually require long-term control with anti-

motility agents, such as loperamide hydrochloride or diphenoxylate (4–16 mg per day). If these are ineffective, especially in patients without colon in continuity or in patients with minimal residual jejunum or duodenum, use of codeine sulfate (15–60 mg two to three times a day) or tincture of opium may be necessary. Rarely, octreotide (100 mcg SQ,three times a day, 30 minutes before meals) is required. It should be used only if fluid intravenous requirements are greater than 3 L daily because post-resection intestinal adaptation may be impaired and the risk for cholelithiasis increased."

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Octreotide are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Mycapssa (octreotide delayed-release capsules) include: hypersensitivity to octreotide or any of the components of Mycapssa. Contraindications to Sandostatin LAR (octreotide) include: No labeled contraindications. Contraindications to Sandostatin (octreotide) include: sensitivity to this drug or any of its components. The following uses have been deemed to have insufficient or conflicting evidence to support use at the time of this review, or are not covered for other reasons: Breast Cancer, in combination with Tamoxifen, Chylothorax, Cystoid Macular Edema, Enterocutaneous fistula, Graves Ophthalmopathy, Hepatocellular Carcinoma, Idiopathic Tall Stature – cosmetic, not a medical condition, Pancreatitis and Polycystic Kidney or Liver Disease.

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING 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

HCPCS CODE	DESCRIPTION
J2353	Injection, octreotide, depot form for intramuscular injection, 1 mg
J2354	Injection, octreotide, non-depot form for subcutaneous or intravenous injection, 25 mcg

AVAILABLE DOSAGE FORMS:
SandoSTATIN LAR Depot: 10 mg, 20 mg, 30 mg
SandoSTATIN: 50 mcg/mL (1 mL); 100 mcg/mL (1 mL)
SandoSTATIN: 500 mcg/mL (1 mL),
octreotide 50 mcg/mL (1 mL); 100 mcg/mL (1 mL); 500 mcg/mL (1 mL); 200 mcg/mL (5 mL); 1000 mcg/mL (5 mL)
Bynfezia: Injection: 2,500 mcg/mL octreotide as a 2.8 mL single-patient-use pen
Mycapssa 20mg (28caps)

REFERENCES

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2. Sandostatin LAR Depot (octreotide injection suspension) [prescribing information]. East Hanover, NJ: Novartis; March 2021.
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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Diagnosis Required Medical Information Contiuation of Therapy Duration of Approval Prescriber Requirements Quantity Place of Administration Contraindications/Exclusions/Discontinuation Coding/Billing Information Available Dosage Forms References	Q3 2023
REVISION- Notable revisions: Required Medical Information References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file