09-J0000-90

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Reviewed: 06/08/19

Revised: 07/15/19

Subject: Octreotide Acetate (Sandostatin LAR® Depot) Injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Octreotide acetate is a somatostatin analog that has similar effects in the body as those of the naturally occurring hormone. It inhibits the secretion of growth hormone, glucagon, insulin, gastrin, vasoactive intestinal peptide, secretin, motilin and pancreatic polypeptide. In addition, it suppresses the response of luteinizing hormone (LH) in response to gonadotropin releasing hormone (GnRH) and decreases splenic blood flow. Octreotide acetate is available as an immediate-release formulation, Sandostatin® (FDA-approved in 1988) and a long-acting formulation, Sandostatin LAR® Depot (FDA-approved in 1998). Octreotide acetate suppresses secretion of growth hormone (GH) and secondarily suppresses insulin-like growth factor-1 (IGF-1, somatomedin C) and is a treatment option for those with acromegaly. Studies have shown that after immediate-release octreotide acetate administration, growth hormone and IGF-1 levels are normalized in 50 to 60% of patients. Octreotide acetate also suppresses the release of the peptides and amines secreted from carcinoid tumors and vasoactive intestinal peptide tumors (VIPomas), which subsequently reduces the severe diarrhea and flushing associated with this disease. Sandostatin LAR was granted orphan designation by the FDA in 1998 for the treatment of severe diarrhea and flushing associated with malignant carcinoid tumors, acromegaly, and diarrhea associated with VIPoma; and, then in 2010, for the treatment of neuroendocrine tumors.

POSITION STATEMENT:

I. Initiation of octreotide acetate long-acting injection (Sandostatin LAR® Depot) **meets the definition of medical necessity** when administered for an indication listed in Table 1 below and **ALL** of the associated criteria are met:

Table 1

Indication	Specific Criteria
Acromegaly	**ALL** of the following: 1. Sandostatin LAR will be used as long-term therapy for the member's acromegaly 2. The dosage will not exceed 40 mg per 28-day treatment cycle 3. **EITHER** of the following are met: a. Member has had an inadequate response to surgery and/or radiotherapy. b. Member is not a candidate for surgery and/or radiotherapy.
Carcinoid Tumors (neuroendocrine tumors of the GI tract, lung, and thymus)	**ALL** of the following: 1. Treatment for **ONE** of the following: a. Metastatic or locoregional advanced disease b. Carcinoid syndrome c. Unresected primary gastrinoma d. Locoregional bronchopulmonary or thymic disease that is unresectable 2. The dosage will not exceed 30 mg per 28-day treatment cycle.
Meningioma	**ALL** of the following: 1. The tumor is somatostatin-receptor positive - documentation must be provided 2. The meningioma is surgically inaccessible (e.g., base-of-skull meningiomas) 3. The meningioma is refractory to radiation therapy or the member is unable to receive radiation therapy 4. The dosage does not exceed 30 mg per 28-day treatment cycle.
Pancreatic neuroendocrine tumor	**ALL** of the following: 1. Use is for **ONE** of the following: a. To treat symptoms associated with **ONE** of the following: i. Gastrinoma ii. Glucagonoma iii. Vasoactive intestinal peptide tumors (VIPomas) iv. Insulinoma **AND** tumor is somatostatin-

	receptor positive– documentation must be provided b. For tumor control in member's with unresectable disease, locoregional advanced disease, or metastatic disease 2. The dosage will not exceed 30 mg per 28-day treatment cycle.
Pheochromocytoma or paraganglioma	**ALL** of the following: 1. When used for symptomatic disease that is metastatic or locally unresectable 2. The tumor is somatostatin-receptor positive – documentation must be provided 3. The dosage will not exceed 30 mg per 28-day treatment cycle
Thymomas and Thymic carcinomas	**ALL** of the following: 1. Sandostatin LAR is used as second-line therapy with or without prednisone 2. The dosage will not exceed 20 mg every two weeks
Well-differentiated neuroendocrine tumors of unknown primary	**ALL** of the following: 1. Treatment of metastatic or unresectable locoregional disease 2. The dosage will not exceed 30 mg per 28-day treatment cycle.
Well-differentiated, high-grade neuroendocrine tumors (extrapulmonary)	**ALL** of the following: 1. Treatment of metastatic or unresectable locoregional disease 2. The dosage will not exceed 30 mg per 28-day treatment cycle.
Other FDA-approved or NCCN supported diagnosis (not previously listed above)	When **ALL** of the following are met: 1. **ONE** of the following is met: a. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) AND member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert) b. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation 2. The dose does not exceed the maximum FDA-approved dose

Approval duration: 1 year

II. Continuation of octreotide acetate long-acting injection (Sandostatin LAR Depot) **meets the definition of medical necessity** for members treated for an indication from Table 1 when the following criteria are met:

1. The member has been previously approved by Florida Blue or another healthplan in the past 2 years, **OR** the member has previously met all indication-specific criteria for coverage
2. Member has experienced a beneficial response to octreotide acetate long-acting injection
3. Dose does not exceed indication-specific dosing in Table 1

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

Members not currently receiving octreotide acetate injection subcutaneously:

- Acromegaly: To determine tolerance and efficacy, an initial dosage of octreotide acetate injection 50 mcg three times daily should be administered subcutaneously for 2 weeks (may be titrated up to 500 mcg three times daily if needed for maximum effect). Patients who are considered to be "responders" to the drug, based on GH and IGF-1 levels and who tolerate the drug can then be switched to Sandostatin LAR Depot 20 mg every 4 weeks for 3 months.
- Carcinoid Tumors: octreotide acetate injection subcutaneously 100 to 600 mcg/day in 2 to 4 divided dose (mean daily dosage is 300 mcg) for 2 weeks followed by Sandostatin LAR 20 mg every 4 weeks for 2 months.
- VIPomas: octreotide acetate injection subcutaneously 100 to 600 mcg/day in 2 to 4 divided dose (mean daily dosage is 300 mcg) for 2 weeks followed by Sandostatin LAR 20 mg every 4 weeks for 2 months.

Members currently receiving of octreotide acetate injection subcutaneously:

- Acromegaly: 20 mg every 4 weeks for 3 months. After 3 months, the dosage should be adjusted based on response as follows:
  - GH ≤2.5 ng/mL, IGF-1 normal, and clinical symptoms controlled: maintain Sandostatin LAR Depot dosage at 20 mg every 4 weeks.
  - GH >2.5 ng/mL, IGF-1 elevated, and/or clinical symptoms uncontrolled, increase Sandostatin LAR Depot dosage to 30 mg every 4 weeks.
  - GH ≤1 ng/mL, IGF-1 normal, and clinical symptoms controlled, reduce Sandostatin LAR Depot dosage to 10 mg every 4 weeks.

    - If GH, IGF-1, or symptoms are not adequately controlled at a dose of 30 mg, the dose may be increased to 40 mg every 4 weeks. Doses higher than 40 mg are not recommended.
- Carcinoid Tumors and VIPomas: 20 mg every 4 weeks for 2 months. After 2 months, the dosage should be adjusted as follows:
    - If symptoms are adequately controlled, consider a dose reduction to 10 mg for a trial period. If symptoms recur, dosage should then be increased to 20 mg every 4 weeks. Many patients can, however, be satisfactorily maintained at a 10-mg dose every 4 weeks.
    - If symptoms are not adequately controlled, increase Sandostatin LAR Depot to 30 mg every 4 weeks. Dosages higher than 30 mg are not recommended.

Dosage Adjustments:

- **Hepatic Impairment** - In patients with established liver cirrhosis, the starting dose should be 10 mg and titrated up based on clinical response.
- **Renal Impairment** - In patients with renal failure requiring dialysis, the starting dose should be 10 mg and titrated up based on clinical response.

Product Availability: single-use kits containing a 6-mL vial of 10 mg, 20 mg or 30 mg strength; a syringe containing 2 mL of diluent; one vial adapter; and one sterile 1½" 20 gauge safety injection needle. For prolonged storage, stored at refrigerated temperatures between 2°C to 8°C (36°F to 46°F) and protected from light until the time of use.

PRECAUTIONS:

Contraindications:

None

Warnings:

Cholelithiasis and Gallbladder sludge: Gallbladder abnormalities may occur. Monitor periodically and discontinue if complications are suspected.

Blood glucose effects: hypoglycemia or hyperglycemia may occur. Glucose monitoring is recommended and antidiabetic treatment may need adjustment.

Thyroid effects: hypothyroidism may occur. Monitor thyroid levels periodically.

Cardiovascular effects: bradycardia, arrhythmia or conduction abnormalities may occur. Use with caution in at-risk members.

Monitoring: Lab tests that may be helpful as biomarkers vary based on tumor type (e.g. Acromegaly measure GH and IGF-1; Carcinoid measure urinary 5-hydroxyindole acetic acid, plasma serotonin, plasma Substance P; VIPoma measure plasma vasoactive intestinal peptide and free T4)

Nutritional effects: Octreotide may alter absorption of dietary fats. Depressed vitamin B12 levels and abnormal Schilling tests have been observed in some persons receiving octreotide therapy, and monitoring of vitamin B12 levels is recommended during therapy with octreotide.

Renal function impairment: In members with severe renal failure requiring dialysis, the half-life of octreotide may be increased, necessitating adjustment of the maintenance dosage.

Hepatic function impairment: In members with established liver cirrhosis, the starting dose of octreotide suspension should be 10 mg. Up-titrate the dose based on clinical response and speed of response as deemed necessary by the health care provider. Once at a higher dose, maintain the member or adjust the dose based on response and tolerability as in any noncirrhotic members.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J2353	Injection, octreotide, depot form for intramuscular injection, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity:

C74.10 – C74.92	Malignant neoplasm of medulla and unspecified part of adrenal gland
C75.5	Malignant neoplasm of aortic body and other paraganglia
C7A.00	Malignant carcinoid tumor of unspecified site
C7A.010	Malignant carcinoid tumor of the duodenum
C7A.011	Malignant carcinoid tumor of the jejunum
C7A.012	Malignant carcinoid tumor of the ileum
C7A.019	Malignant carcinoid tumor of the small intestine, unspecified portion
C7A.020	Malignant carcinoid tumor of the appendix
C7A.021	Malignant carcinoid tumor of the cecum
C7A.022	Malignant carcinoid tumor of the ascending colon
C7A.023	Malignant carcinoid tumor of the transverse colon
C7A.024	Malignant carcinoid tumor of the descending colon
C7A.025	Malignant carcinoid tumor of the sigmoid colon
C7A.026	Malignant carcinoid tumor of the rectum
C7A.029	Malignant carcinoid tumor of the large intestine, unspecified portion
C7A.090	Malignant carcinoid tumor of the bronchus and lung
C7A.091	Malignant carcinoid tumor of the thymus
C7A.092	Malignant carcinoid tumor of the stomach
C7A.093	Malignant carcinoid tumor of the kidney
C7A.094	Malignant carcinoid tumor of the foregut, unspecified
C7A.095	Malignant carcinoid tumor of the midgut, unspecified
C7A.096	Malignant carcinoid tumor of the hindgut, unspecified
C7A.098	Malignant carcinoid tumors of other sites
C7A.1	Malignant poorly differentiated neuroendocrine tumors
C7A.8	Other malignant neuroendocrine tumors
C7B.00 – C7B.04	Secondary carcinoid tumors of distant lymph nodes, liver, bone, peritoneum
C7B.09	Secondary carcinoid tumors of other sites
C7B.8	Other secondary neuroendocrine tumors
C25.0 – C25.9	Malignant neoplasm of pancreas
C37	Malignant neoplasm of thymus
C70.0 – C70.9	Malignant neoplasm of meninges
D3A.00	Benign carcinoid tumor of unspecified site
D3A.010 – D3A.012	Benign carcinoid tumor of the duodenum, jejunum, ileum
D3A.019 – D3A.029	Benign carcinoid tumor of the large intestine, unspecified portion, appendix, cecum,

	ascending colon, transverse colon, descending colon, sigmoid colon, rectum
D3A.090 – D3A.098	Benign carcinoid tumor of the bronchus and lung, thymus, stomach
D3A.8	Other benign neuroendocrine tumors
D13.7	Benign neoplasm of endocrine pancreas
D15.0	Benign neoplasm of thymus
D32.0	Benign neoplasm of cerebral meninges
D32.1	Benign neoplasm of spinal meninges
D32.9	Benign neoplasm of meninges, unspecified
D35.2	Benign neoplasm of pituitary gland
D35.3	Benign neoplasm of craniopharyngeal duct
D37.9	Neoplasm of uncertain behavior of digestive organ, unspecified
D42.0	Neoplasm of uncertain behavior of cerebral meninges
D42.1	Neoplasm of uncertain behavior of spinal meninges
D42.9	Neoplasm of uncertain behavior of meninges, unspecified
D43.0 – D43.9	Neoplasm of uncertain behavior of brain and central nervous system
E16.1	Other hypoglycemia
E16.3	Increased secretion of glucagon
E16.4	Abnormality of secretion of gastrin
E16.8	Other specified disorders of pancreatic internal secretion
E22.0	Acromegaly and pituitary gigantism
E34.0	Carcinoid syndrome

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: No National Coverage Determination (NCD) or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

DEFINITIONS:

No guideline specific definitions apply.

RELATED GUIDELINES:

Capecitabine (Xeloda®) Tablets, 09-J1000-42

Docetaxel (Taxotere®) IV, 09-J0000-95

Interferon alfa-n3 (Alferon N Injection®), 09-J0000-33

Lanreotide (Somatuline® Depot) Injection, 09-J1000-20

Paraplatin (Carboplatin®) IV, 09-J0000-93

Pasireotide (Signifor, Signifor LAR) Injection - 09-J1000-94

Temozolomide (Temodar®) Capsule and Injection, 09-J1000-52

OTHER:

None applicable.

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 06/12/19.

GUIDELINE UPDATE INFORMATION:

03/15/09	New Medical Coverage Guideline.
10/15/09	Revision to guideline; consisting of adding compendia supported indication and updating coding.
01/15/10	Revision to guideline; consisting of updating coding.
11/15/10	Review and revision to guideline; consisting of updating coding and references.
11/15/11	Review and revision to guideline; consisting of updating precautions, coding and references.
12/15/12	Review and revision to guideline; consisting of reformatting position statement, updating coding and references.
06/15/13	Review and revision to guideline; consisting of revising the position statement to include treatment of meningioma and approval duration; reformatting precautions section; updating references, coding, and program exceptions;
02/15/14	Revision to guideline; consisting of adding codes for neuroendocrine tumors.
06/15/14	Review and revision to guideline; consisting of revising position statement, updating references and coding.
06/15/15	Review and revision to guideline; consisting of updating position statement, dosage/administration section, and references.
10/01/15	Revision to guideline consisting of coding updates.
11/01/15	Revision: ICD-9 Codes deleted.
06/15/16	Review and revision to guideline consisting of updating position statement, coding and references.
10/01/16	Update to ICD-10 codes.
06/15/17	Review and revision to guideline consisting of updating position statement and references.
11/15/17	Revision to guideline consisting of updating position statement and references.
06/15/18	Review and revision to guideline consisting of updating position statement, warnings, coding and references.
07/15/19	Review and revision to guideline consisting of updating position statement, coding and references.