BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

OCTREOTIDE ACETATE products, oral and injection:
MYCAPSSA® (octreotide acetate) oral
Octreotide Acetate injection
SANDOSTATIN® (octreotide acetate) injection
SANDOSTATIN LAR DEPOT® (octreotide) injection
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

MYCAPSSA® (octreotide acetate) oral

➢ **Criteria for initial therapy:** Mycapssa (octreotide acetate) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Endocrinologist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of acromegaly who is tolerating long-acting somatostatin analog injection therapy and is biochemically controlled

4. Evidence of biochemical control is documented by insulin-like growth factor 1 (IGF-1) level less than or equal to the upper limit of normal for the patient's age and gender while on a long-acting somatostatin analog injection therapy

5. Individual is using (for at least 6 months) **ONE** the following long-acting somatostatin analog injection therapy:
    a. Sandostatin LAR (octreotide acetate) injection
    b. Somatuline Depot (lanreotide) injection

6. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or not a candidate for a generic equivalent [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Mycapssa (octreotide) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy):**

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Endocrinologist

2. Individual's condition responded while on therapy with response defined as **ALL** of the following:
    a. No evidence of disease progression
    b. Achieved and maintains normalization of growth hormone and IGF-I levels for age and gender (must use the same laboratory assay that was used at baseline measurement, laboratory reference range must be provided)

3. Individual has been adherent with the medication and the requested dose is **NOT** greater than 80 mg daily

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or not a candidate for a generic equivalent [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
    a. Acute cholecystitis
    b. Acute intestinal obstruction
    c. Ascending cholangitis
    d. Biliary obstruction
    e. Cholelithiasis
    f. Cholestatic hepatitis

g. Pancreatitis

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
2. **Off-Label Use of Cancer Medications**

Octreotide acetate injection, generic
SANDOSTATIN® (octreotide acetate) injection
SANDOSTATIN LAR DEPOT® (octreotide acetate) injection

- **Criteria for initial therapy:** Octreotide acetate, Sandostatin (octreotide acetate), or Sandostatin LAR Depot (octreotide acetate) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Endocrinologist, Gastroenterologist, or Oncologist depending upon the diagnosis
2. Individual is 18 years of age or older
3. Individual has a confirmed diagnosis of **ONE** of the following:
   a. Acromegaly in a patient who has had an inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine **or** cabergoline at maximally tolerated doses
   b. Metastatic carcinoid tumor and has severe diarrhea/flushing episodes
   c. Vasoactive Intestinal Peptide (VIP) secreting tumor and has profuse watery diarrhea
   d. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A
4. Individual has received and completed a baseline thyroid function tests (TSH, total and/or free T4) before initiation of treatment with continued monitoring of the individual as clinically appropriate
5. **Additional criteria for Sandostatin (octreotide acetate)**: Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for generic octreotide acetate
6. **Additional criteria for Sandostatin LAR Depot (octreotide acetate)**: There is evidence of biochemical control through documentation of insulin-like growth factor 1 (IGF-1) level less than or equal to the upper

limit of normal for the patient's age and gender while on immediate release somatostatin analog injection therapy

7. **Additional criteria for Sandostatin LAR Depot (octreotide acetate): If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or not a candidate for a generic equivalent [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Octreotide acetate, Sandostatin (octreotide acetate), or Sandostatin LAR Depot (octreotide acetate) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met **(samples are not considered for continuation of therapy):**

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Endocrinologist, Gastroenterologist, or Oncologist depending upon the diagnosis

2. Individual's condition has responded while on therapy with response defined as:
    a. **For acromegaly**:
        i. No evidence of disease progression
        ii. Achieved and maintains normalization of growth hormone and IGF-I levels for age and gender **or** GH levels are less than 1 ng/mL or 1 mcg/L [**Note**: 1 nanogram / milliliter = 1 microgram / liter]
    b. **For Carcinoid tumor**:
        i. No evidence of disease progression
        ii. Achieved and maintains an improvement in severe diarrhea and flushing episodes associated with the disease
        iii. Urinary 5-hydroxyindole acetic acid (5-HIAA) levels are reduced or have normalized
    c. **For VIP-secreting tumor**:
        i. No evidence of disease progression
        ii. Achieved and maintains an improvement in the number of profuse watery diarrhea episodes
        iii. Plasma VIP levels are reduced or have normalized

3. Individual has been adherent with the medication

4. **ONE** of the following:
    a. **For Sandostatin (octreotide acetate)**: Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for generic octreotide acetate

    b. **For Sandostatin LAR Depot (octreotide acetate)**: **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or not a candidate for a generic equivalent [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any significant adverse drug effects that may exclude continued use such as:

a. Acute cholecystitis
b. Acute intestinal obstruction
c. Ascending cholangitis
d. Biliary obstruction
e. Cholelithiasis
f. Cholestatic hepatitis
g. Pancreatitis

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Mycapssa (octreotide acetate) is a somatostatin analog indicated for long-term maintenance treatment in acromegaly. Mycapssa contains octreotide acetate in a delayed release, enteric coated, capsule.

Octreotide acetate injection is indicated to reduce blood levels of growth hormone (GH) and insulin-like growth factor 1 (IGF-I, also known as 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. The goal is to achieve normalization of growth hormone (less than 5 ng/mL) and IGF-1 levels (less than 1.9 unit/mL in males and less than 2.2 unit/mL in females). Improvement in clinical signs and symptoms, or reduction in tumor size or rate of growth, were not shown in clinical trials performed with octreotide acetate injection; these trials were not optimally designed to detect such effects.

Octreotide acetate injection is also indicated for the symptomatic treatment of patients with metastatic carcinoid tumors where it suppresses or inhibits the severe diarrhea and flushing episodes associated with the disease. Octreotide acetate injection studies were not designed to show an effect on the size, rate of growth or development of metastases.

Octreotide acetate injection is also indicated for the treatment of the profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors. Octreotide acetate injection studies were not designed to show an effect on the size, rate of growth or development of metastases.

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

Acromegaly is a disease characterized by excessive release of GH. Increased levels of GH stimulate an increase in hepatic production of IGF-1. Excess IGF-1 causes increased growth of bones and soft-tissues while excess GH

can cause other conditions such as diabetes mellitus, hypertension, and an increase in cardiovascular risk. Both serum GH concentrations and IGF-1 concentrations are increased in virtually all patients with acromegaly.

The goals of therapy in patients with acromegaly are to lower the serum IGF-1 concentration to within the normal range for the patient's age and gender and to lower the serum GH concentration to < 1 mcg/L. The Endocrine Society guidelines suggest that an age-normalized serum IGF-1 and a random GH < 1 mcg/L should both be therapeutic goals as they correlate with control of acromegaly.

First-generation long-acting somatostatin injectable analog (e.g., lanreotide, octreotide) are considered first-line therapy in patients with persistent disease despite surgical resection or in whom surgery is not appropriate.

Alternative agents are suggested for patients with mild disease postoperatively.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Resources:

Mycapssa (octreotide acetate) delayed release capsule product information, revised by Amryt Pharmaceuticals Designated Activity Company 03-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 23, 2023.

Octreotide acetate injection product information, revised by Hikma Pharmaceuticals, USA, Inc 07-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 23, 2023.

Sandostatin (octreotide acetate) injection product information, revised by Novartis Pharmaceuticals Corporation 10-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 23, 2023.

Sandostatin LAR Depot (octreotide acetate) injection product information, revised by Novartis Pharmaceuticals Corporation 07-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 23, 2023.

Melmed S, Katznelson L. Diagnosis of acromegaly. In: UpToDate, Snyder PJ, Martin KA (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through September 2023. Topic last updated December 03, 2021. Accessed October 23, 2023.

Melmed S, Katznelson L. Treatment of acromegaly. In: UpToDate, Snyder PJ, Martin KA (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through September 2023. Topic last updated April 28, 2023. Accessed October 23, 2023.

Strosberg JS. Diagnosis of carcinoid syndrome and tumor localization. In: UpToDate, Tanabe KK, Whitcomb DC, Shah SM (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through September 2023. Topic last updated April 20, 2022. Accessed October 23, 2023.

Strosberg JS. Treatment of carcinoid syndrome. In: UpToDate, Tanabe KK, Whitcomb DC, Shah SM (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through September 2023. Topic last updated October 19, 2023. Accessed October 23, 2023.

Bergsland E. VIPoma: Clinical manifestations, diagnosis, and management. In: UpToDate, Tanabe KK, Whitcomb DC, Grover S (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through September 2023. Topic last updated November 02, 2021. Accessed October 23, 2023.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Neuroendocrine and Adrenal Tumors Version 1.2023 – Updated August 02, 2023. Available at https://www.nccn.org. Accessed October 23, 2023.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.