Clinical Policy: Octreotide Acetate (Sandostatin Injection, Sandostatin LAR Depot, Bynfezia, Mycapssa)

Reference Number: ERX.SPA.67
Effective Date: 03.01.14
Last Review Date: 11.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Octreotide acetate (Sandostatin® Injection, Sandostatin® LAR Depot, Bynfezia Pen™, Mycapssa®) is a somatostatin analog.

FDA Approved Indication(s)
Sandostatin Injection and Bynfezia Pen are indicated for:
- Acromegaly
  - To reduce blood levels of growth hormone (GH) and insulin-like growth factor (IGF-I) (somatomedin C) in acromegaly patients who have had inadequate response or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses;
- Carcinoid tumors
  - 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
- Vasoactive intestinal peptide tumors (VIPomas)
  - For the treatment of the profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors

Sandostatin LAR Depot is indicated for treatment in patients who have responded to and tolerated Sandostatin Injection subcutaneous injection for:
- Acromegaly
- Carcinoid tumors
  - Severe diarrhea/flushing episodes associated with metastatic carcinoid tumors
- Vasoactive intestinal peptide tumors (VIPomas)
  - Profuse watery diarrhea associated with VIP-secreting tumors

Mycapssa is indicated for long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide.

Limitation(s) of use:
- In patients with carcinoid syndrome and VIPomas, the effect of Sandostatin Injection, Bynfezia Pen, and Sandostatin LAR Depot on tumor size, rate of growth and development of metastases, has not been determined.
- 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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Sandostatin Injection, Bynfezia Pen, Mycapssa, and Sandostatin LAR Depot are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acromegaly (must meet all)**:**

1. Diagnosis of acromegaly as evidenced by one of the following (a or b):
   a. Pre-treatment IGF-I level above the upper limit of normal based on age and gender for the reporting laboratory;
   b. Serum GH level ≥ 1 µg/mL after a 2-hour oral glucose tolerance test;
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 18 years or, if younger, epiphyseal growth plates have closed;
4. Inadequate response to surgical resection or pituitary irradiation (i.e., unable to achieve normalization of GH and/or IGF-I levels or unable to adequately control tumor mass), or member is not a candidate for such treatment;
5. Request meets one of the following *(Sandostatin Injection can be used with Sandostatin LAR Depot)* (a, b, or c):
   a. Sandostatin Injection and Bynfezia Pen: Dose does not exceed 1,500 mcg per day in divided doses;
   b. Sandostatin LAR Depot (i and ii):
      i. Dose does not exceed 40 mg every 4 weeks;
      ii. Member has received Sandostatin Injection for at least two weeks with improvement in GH or IGF-I levels, or tumor mass control;
   c. Mycapssa (i and ii):
      i. Dose does not exceed 80 mg (4 capsules) per day;
      ii. Member has responded to and tolerated treatment with octreotide or lanreotide.

Approval duration: 6 months

B. Carcinoid Tumor (Neuroendocrine Tumor of the Gastrointestinal Tract, Lung and Thymus) (must meet all)**:**

1. Diagnosis of a carcinoid tumor *(most commonly arising in the lungs and bronchi, small intestine, appendix, rectum, or thymus)* and one of the following (a or b):
   a. Request is for carcinoid syndrome (i.e., presence of diarrhea or flushing symptoms indicative of hormonal hypersecretion);
   b. Request is for advanced disease, with or without carcinoid syndrome;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request meets one of the following *(Sandostatin Injection can be used with Sandostatin LAR Depot)* (a, b, or c):
   a. Sandostatin Injection and Bynfezia Pen: Dose does not exceed 1,500 mcg per day in divided doses;
   b. Sandostatin LAR Depot (i and ii):
      i. Dose does not to exceed 30 mg every 4 weeks;
      ii. If request is for symptom management only, member has received Sandostatin Injection for at least two weeks with improvement in diarrhea or flushing episodes;
   c. Dose for Sandostatin Injection, Bynfezia Pen, or Sandostatin LAR Depot is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

C. Pancreatic Neuroendocrine Tumor (*including VIPoma*) and Adrenal Tumor (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. Pancreatic neuroendocrine tumor including but not limited to VIPoma, gastrinoma, insulinoma or glucagonoma, and one of the following (i, ii, iii, or iv):

i. Request is for management of symptoms indicative of hormonal hypersecretion (e.g., diarrhea);
ii. Request is for treatment of a gastrinoma with or without symptoms;
iii. For other pancreatic neuroendocrine tumors, request is for advanced disease, with or without symptoms;
iv. If request is for an insulinoma, tumor is somatostatin receptor positive on imaging;

b. Advanced adrenal pheochromocytoma/paraganglioma;

2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request meets one of the following *(Sandostatin Injection can be used with Sandostatin LAR Depot)* (a, b, or c):*
   a. Sandostatin Injection and Bynfezia Pen: Dose does not exceed 750 mcg per day in divided doses;
   b. Sandostatin LAR Depot (i and ii):
      i. Dose does not exceed 30 mg every 4 weeks;
      ii. If request is for symptom management only, member has received Sandostatin Injection for at least two weeks with improvement in symptoms prior to request for Sandostatin LAR Depot;
   c. Dose for Sandostatin Injection, Bynfezia Pen, or Sandostatin LAR Depot is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

D. Meningioma (off-label) (must meet all)**:**
1. Diagnosis of meningioma *(cancer of the central nervous system);*
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is not amenable to surgery or radiation;
5. Octreotide scan is positive;
6. Dose for Sandostatin Injection, Bynfezia Pen and/or Sandostatin LAR Depot is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

E. Thymoma and Thymic Carcinoma (off-label) (must meet all)**:**
1. Diagnosis of thymoma or thymic carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed as second-line therapy (first-line therapies include CAP [cisplatin, doxorubicin, cyclophosphamide], ADOC [cisplatin, doxorubicin, vincristine, cyclophosphamide], PE [cisplatin, etoposide], VIP [etoposide, ifosfamide, cisplatin], carboplatin/paclitaxel;
5. Dose for Sandostatin Injection, Bynfezia Pen and/or Sandostatin LAR Depot is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

F. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Acromegaly (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy (e.g., improvement in GH or IGF-1 serum concentrations, or in tumor mass control, since initiation of therapy);
3. If request is for a dose increase, request meets one of the following *(Sandostatin injection can be used with Sandostatin LAR Depot)* (a, b, or c):
   a. Sandostatin Injection and Bynfezia Pen: New dose does not exceed 1,500 mcg per day in divided doses;
   b. Sandostatin LAR Depot: New dose does not exceed 40 mg every 4 weeks;
   c. Mycapssa: New dose does not exceed 80 mg (4 capsules) per day.

Approval duration: 6 months

B. Carcinoid Tumor and Pancreatic/Adrenal Neuroendocrine Tumor (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Sandostatin Injection, Bynfezia, or Sandostatin LAR Depot for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following *(Sandostatin Injection can be used with Sandostatin LAR Depot)* (a, b, or c):
   a. Sandostatin Injection and Bynfezia Pen (i or ii):
      i. Carcinoid tumors: New dose does not exceed 1,500 mcg per day in divided doses;
      ii. VIPomas: New dose does not exceed 750 mcg per day in divided doses;
   b. Sandostatin LAR Depot: New dose does not exceed 30 mg every 4 weeks;
   c. New dose for Sandostatin Injection, Bynfezia Pen, or Sandostatin LAR Depot is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence).**

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

C. Meningioma, Thymoma and Thymic Carcinoma (off-label) (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Sandostatin Injection, Bynfezia, or Sandostatin LAR Depot for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose for Sandostatin Injection, Bynfezia Pen, and/or Sandostatin LAR Depot is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

D. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
GH: growth hormone
IGF-I: insulin growth factor I (somatomedin C)
NCCN: National Comprehensive Cancer Network
VIPoma: vasoactive intestinal peptide tumor

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Sandostatin Injection, Bynfezia Pen, Mycapssa:
  - Contraindication(s): sensitivity to this drug or any of its components
  - Boxed warning(s): none reported
- Sandostatin LAR Depot: none reported

Appendix D: General Information

Acromegaly: GH excess occurring in growing children/adolescents before epiphyseal growth plate closure (known as pituitary gigantism) is not included in the present policy given unique etiologic and management considerations.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Octreotide acetate (Sandostatin Injection) (SC or IV)	Acromegaly	Up to 1,500 mcg in 2 or more divided doses	1,500 mcg/day
	Carcinoid tumors	Up to 1,500 mcg in 2 or more divided doses	1,500 mcg/day
	VIPomas	Up to 750 mcg in 2 or more divided doses	750 mcg/day
Bynfezia Pen (Octreotide acetate) (SC)	Acromegaly	Up to 1,500 mcg in 3 divided doses	1,500 mcg/day
	Carcinoid tumors	Up to 1,500 mcg in 2 to 4 divided doses	1,500 mcg/day
	VIPomas	Up to 750 mcg in 2 to 4 divided doses	750 mcg/day
Octreotide acetate (Sandostatin LAR Depot) (IM)	Acromegaly	20-40 mg every 4 weeks	40 mg/4 weeks
	Carcinoid tumors	20-30 mg every 4 weeks	30 mg/4 weeks
	VIPomas	20-30 mg every 4 weeks	30 mg/4 weeks
Mycapssa (octreotide acetate)	Acromegaly	Initial: 20 mg PO BID. Titrate based on IGF-1 levels and patient's signs and symptoms. Increase dose in 20 mg increments to a maximum of 40 mg PO QD	80 mg/day

VI. Product Availability

Drug Name	Availability
Octreotide acetate (Sandostatin Injection)	Single-use ampules: 50 mcg/mL, 100 mcg/mL, 500 mcg/mL Multi-dose vials: 200 mcg/mL, 1,000 mcg/mL
Bynfezia Pen (octreotide acetate)	Single-patient-use pen: 2,500 mcg/mL octreotide as a 2.8 mL
Octreotide acetate (Sandostatin LAR Depot)	Single-use kit (vials): 10 mg, 20 mg, 30 mg
Mycapssa (octreotide acetate)	Delayed-release capsule: 20 mg

VII. References

1. Sandostatin Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2021. Available at http://www.pharma.us.novartis.com/product/pi/pdf/sandostatin_inj.pdf. Accessed November 10, 2021.
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3. Sandostatin LAR Depot prescribing information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2021. Available at http://www.pharma.us.novartis.com/product/pi/pdf/sandostatin_lar.pdf. Accessed November 10, 2021.
4. Mycapssa Prescribing Information. Scotland, UK: MW Encap LTD; June 2020. Available at: www.mycapssa.com. Accessed November 10, 2021.

Acromegaly

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6. Melmed S, Bronstein MD, Chanson P. A Consensus Statement on acromegaly therapeutic outcomes. Nat Rev Endocrinol. 2018 Sep;14(9):552-561. doi: 10.1038/s41574-018-0058-5.
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8. Guistina A, Barkhoudarian G, Beckers A, et al. Multidisciplinary management of acromegaly: A consensus. Rev Endocr Metab Disord. 2020; 21(4): 667-678.

Oncology

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11. National Comprehensive Cancer Network Guidelines. Neuroendocrine and Adrenal Tumors Version 3.2021. Available at nccn.org. Accessed November 10, 2021.
12. National Comprehensive Cancer Network Guidelines. Central Nervous System Cancers Version 2.2021. Available at nccn.org. Accessed November 10, 2021.
13. National Comprehensive Cancer Network Guidelines. Thymomas and Thymic Carcinomas Version 1.2021. Available at nccn.org. Accessed November 10, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: Age edited to include adolescents with closed epiphyseal plates. Specialist added for oncology indications. Examples of positive therapeutic response removed (diarrhea, flushing, disease progression, unacceptable toxicity) since not amenable to objective measurement. Off-label uses are added for meningioma and thymoma and thymic carcinoma. References updated.	11.30.17	02.18
1Q 2019 annual review: off-label NCCN recommended uses added for tumor control of neuroendocrine tumors with or without symptoms; positive octreotide scan added for meningioma per NCCN; references reviewed and updated.	11.13.18	02.19
1Q 2020 annual review: specialist added for acromegaly indication for alignment with other somatostatin analogs; references reviewed and updated.	11.06.19	02.20
Added Bynfezia Pen formulation to policy.	02.17.20	
RT4: added Mycapssa to policy.	07.14.20	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: advanced adrenal pheochromocytoma /paraganglioma added per NCCN; references reviewed and updated.	11.03.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	11.10.21	02.22
For acromegaly, added confirmatory diagnostic requirements (IGF-I or GH) per PS/ES practice guidelines.	08.01.22	11.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.