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

Reference Number: CP.PHAR.40
Effective Date: 03.01.10
Last Review Date: 11.22
Line of Business: Commercial, HIM*, Medicaid

Coding Implications
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.

**For Health Insurance Marketplace (HIM),* *if request is through pharmacy benefit, Sandostatin LAR Depot, Bynfezia, and Mycapssa are non-formulary and should not be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

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 (including such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® 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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's benefit renewal date, whichever is longer

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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's benefit renewal date, whichever is longer

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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's benefit renewal date, whichever is longer

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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's benefit renewal date, whichever is longer

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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's benefit renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's benefit renewal date, whichever is longer

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

1. Currently receiving medication via Centene benefit, 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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's benefit renewal date, whichever is longer

C. Meningioma, Thymoma and Thymic Carcinoma (off-label) (must meet all):
1. Currently receiving medication via Centene benefit, 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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's benefit renewal date, whichever is longer

D. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid 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

Drug Name	Indication	Dosing Regimen	Maximum Dose
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.
2. Bynfezia Pen Prescribing Information. Gurjarat, India. Sun Pharmaceuticals; January 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213224s000lbl.pdf. Accessed November 10, 2021.
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

5. Katznelson L, Laws Jr. ER, Melmed S, et al. Acromegaly: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2014;99:3933-3951.
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.
7. Fleseriu M, Biller BMK, Freda PU, et al. A Pituitary Society update to acromegaly management guidelines. Pituitary. 2021; 24: 1-13.
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

9. Octreotide acetate [Sandostatin, Bynfezia]. National Comprehensive Cancer Network Compendium. Available at: nccn.org. Accessed November 10, 2021.

10. Octreotide acetate (LAR) [Sandostatin LAR Depot]. National Comprehensive Cancer Network Compendium. Available at: nccn.org. Accessed November 10, 2021.
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.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2353	Injection, octreotide, depot form for intramuscular injection, 1 mg
J2354	Injection, octreotide, nondepot form for subcutaneous or intravenous injection, 25 mcg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: - Policies combined for Medicaid and Commercial lines of business -Specialist added for oncology indications -Requests for non-oncology off-label indications and any oncology off-label indications not outlined above are directed to the off-label use policies referenced in Section I.F. - Positive therapeutic response examples (diarrhea, flushing, disease progression, unacceptable toxicity) are removed as they are not amenable to objective measurement. -References updated. Updated approval duration to 6 months.	11.30.17	02.18
1Q 2019 annual review; HIM line of business added; off-label NCCN recommended uses added for tumor control of neuroendocrine tumors with or without symptoms; positive octreotide scan added for insulinoma and 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 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 to HIM.PHAR.21 revised to HIM.PA.154; 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. Template changes applied to other diagnoses/indications and continued therapy section.	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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to

recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.