Clinical Policy: Octreotide (Sandostatin Injection, Sandostatin LAR Depot)
Reference Number: ERX.SPA.67
Effective Date: 03.01.14
Last Review Date: 08.17
Line of Business: Commercial [Prescription Drug Plan] Revision Log

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

Description
Octreotide (Sandostatin® LAR Depot, Sandostatin®) is a somatostatin analogue.

FDA approved indication
Sandostatin LAR is indicated:
- For the treatment of acromegaly in patients who have responded to and tolerated sandostatin injection subcutaneous injection
- For the treatment of severe diarrhea/flushing episodes associated with metastatic carcinoid tumors in patients who have responded to and tolerated sandostatin injection subcutaneous injection
- For the treatment of profuse watery diarrhea associated with vasoactive intestinal polypeptide (VIP)-secreting tumors in patients who have responded to and tolerated sandostatin injection subcutaneous injection

Sandostatin is indicated to reduce blood levels of growth hormone (GH) and insulin growth factor 1 (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.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

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

I. Initial Approval Criteria
A. Acromegaly (must meet all)**:**
1. Diagnosis of acromegaly with inadequate response to (i.e., unable to achieve normalization of GH and/or IGF-I levels or unable to adequately control tumor mass), or when treatment is not appropriate with, either of the following:
   a. Surgical resection;
   b. Pituitary irradiation;
2. Age ≥ 18 years;
3. Request is for one of the following formulations:
   a. Sandostatin Injection/octreotide acetate injection (subcutaneous or intravenous use):
      i. For the brand formulation, failure of generic formulation (octreotide acetate injection) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
      ii. Upward dose titration does not exceed 1500 mcg/day in divided doses;
   b. Sandostatin LAR Depot (intramuscular use):
      i. Member has been adherent to octreotide acetate injection (brand or generic) for at least two weeks with a reduction in GH or IGF-I levels or an increased control of tumor mass immediately prior to the request for Sandostatin LAR Depot;

ii. The starting dose of Sandostatin LAR Depot does not exceed 20 mg given IM at 4-week intervals for 3 months (after 3 months, dosage may be adjusted based on GH/IGF-1 levels, and symptoms, not to exceed 40 mg every 4 weeks).

Approval duration: 6 months

B. Carcinoid Tumors (neurodendocrine tumors of the gastrointestinal track, lung, and thymus) (must meet all)**:**

1. Diagnosis of severe diarrhea and flushing episodes associated with metastatic carcinoid tumors;
2. Age ≥ 18 years;
3. Request is for one or both of the following formulations (Sandostatin Injection/octreotide acetate injection may be used alone or with Sandostatin LAR Depot for periodic exacerbation of symptoms):
   a. Sandostatin Injection/octreotide acetate injection (subcutaneous or intravenous use):
      i. For the brand formulation, failure of generic formulation (octreotide acetate injection) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
      ii. Upward dose titration does not exceed 1500 mcg/day in divided doses;
   b. Sandostatin LAR Depot (intramuscular use):
      i. Member has been adherent to octreotide acetate injection (brand or generic) for two weeks with reduction in number or severity of diarrhea or flushing episodes immediately prior to the request for Sandostatin LAR Depot;
      ii. The starting dose of Sandostatin LAR Depot does not exceed 20 mg given IM intragluteally at 4-week intervals for 2 months with continued administration of octreotide acetate injection for up to 4 weeks (after 2 months, dosage of Sandostatin LAR Depot is adjusted based on symptoms, not to exceed 30 mg every 4 weeks).

Approval duration: 6 months

C. Vasoactive Intestinal Peptide Tumors (neuroendocrine tumors - pancreatic or extrapancreatic – that secrete VIP) (must meet all)**:**

1. Diagnosis of profuse watery diarrhea associated with VIP secreting tumor;
2. Age ≥ 18 years;
3. Request for one or both of the following formulations (Sandostatin Injection/octreotide acetate injection may be used alone or with Sandostatin LAR Depot for periodic exacerbation of symptoms):
   a. Sandostatin Injection/octreotide acetate injection (subcutaneous or intravenous use):
      i. If request is for the brand formulation, failure of generic formulation (octreotide acetate injection) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
      ii. Upward dose titration does not exceed 750 mcg/day in divided doses;
   b. Sandostatin LAR Depot (IM use):
      i. Member has been adherent to octreotide acetate injection (brand or generic) for two weeks with a reduction in diarrhea immediately prior to the request for Sandostatin LAR Depot;
      ii. The starting dose of Sandostatin LAR Depot does not exceed 20 mg given IM intragluteally at 4-week intervals for 2 months with continued administration of octreotide acetate solution for up to 4 weeks (after 2 months, dosage of Sandostatin LAR Depot is adjusted based on symptoms, not to exceed 30 mg every 4 weeks).

Approval duration: 6 months

D. 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., GH and/or IGF-1 levels have improved or normalized, or there is improved control of tumor mass);
3. If request is for a dose increase, new dose does not exceed 1500 mcg per day.

Approval duration: 12 months

B. Carcinoid Tumors (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., decrease in number or severity of diarrhea and/or flushing episodes);
3. If request is for a dose increase, new dose does not exceed 1500 mcg per day.

Approval duration: 12 months

C. Vasoactive Intestinal Peptide Tumors (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., decrease in diarrhea);
3. If request is for a dose increase, new dose does not 750 mcg per day.

Approval duration: 12 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
IM: intramuscular
IGF-1: insulin growth factor 1
NCCN: National Comprehensive Cancer Network
VIP: vasoactive intestinal peptide

Appendix B: General Information

Sandostatin LAR Depot is used for long-term maintenance therapy after the patient has successfully been titrated on Sandostatin for a minimum of 2 weeks.

- Two open label clinical studies investigated a 48-week treatment with Sandostatin LAR Depot in 143 untreated (de novo) acromegalic patients. The median reduction in tumor volume was 20.6 % in Study 1 (49 patients) at 24 weeks and 24.5% in Study 2 (94 patients) at 24 weeks and 36.2% at 48 weeks.
- Use of Sandostatin to manage persons with short bowel syndrome if daily intravenous fluid requirements are greater than 3 liters is not supported by literature. Sandostatin reduces fluid losses but also diminishes splanchnic protein synthesis, which can interfere with the process of adaptation. Sandostatin increases small bowel transit time but tachyphylaxis often develops. In addition, Sandostatin predisposes patients to the development of gallstones for which they are already at high risk.
- The American Hospital Formulary Service states Sandostatin is effective for the acute management of potentially life threatening hypotension associated with carcinoid crisis or to

prevent carcinoid crisis that might be precipitated by anesthesia, surgery, initiation of chemotherapy, or infection.
- The National Comprehensive Cancer Network (NCCN) practice compendium guidelines recommend Sandostatin and Sandostatin LAR with a category 2A for unresectable malignant thymoma that is refractory to standard chemotherapy
- The NCCN practice compendium guidelines recommend Sandostatin and Sandostatin LAR with a category 2A for recurrent of progressive meningiomas when further radiation is not possible.
  - Gastrinoma and Zollinger-Ellison syndrome
  - Insulinoma

Appendix C: Therapeutic Alternatives

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
(Sandostatin®) Octreotide	Acromegaly 100 mcg three times per day Carcinoid Tumors 100-600 mcg per day in 2-4 divided doses VIP Tumors 200-300 mcg in 2-4 divided doses	Acromegaly 500 mcg three times per day Carcinoid Tumors 750 mcg per day VIP Tumors 450 mcg per day

V. Dosage and Administration

Indication	Dosing Regimen		Maximum Dose
	Currently receiving Sandostatin Injection subcutaneously	*Not currently receiving Sandostatin Injection subcutaneously*	
Acromegaly	20 mg every 4 weeks for 3 months	50 mcg three times daily Sandostatin Injection subcutaneously for 2 weeks, then Sandostatin LAR 20 mg intragluteally every 4 weeks for 3 months	1500 mcg per day
Carcinoid tumors	20 mg every 4 weeks for 2 months	Sandostatin Injection subcutaneously 100-600 mcg/day in 2-4 divided doses for 2 weeks, then Sandostatin LAR 20 mg every 4 weeks for 2 months	1500 mcg per day
VIP tumors	20 mg every 4 weeks for 2 months	Sandostatin Injection subcutaneously 100-600 mcg/day in 2-4 divided doses for 2 weeks, then Sandostatin LAR 20 mg every 4 weeks for 2 months	750 mcg per day

VI. Product Availability

Injectable suspension in vials: 10 mg per 6 mL, 20 mg per 6 mL, or 30 mg per 6 mL

VII. References

1. Sandostatin Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2012. Available at http://www.pharma.us.novartis.com/product/pi/pdf/sandostatin_inj.pdf. Accessed July 13, 2017.
2. Sandostatin LAR Depot Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2017. Available at http://www.pharma.us.novartis.com/product/pi/pdf/sandostatin_lar.pdf. Accessed July 13, 2017.
3. Melmed S, Colao A, Barkan A, et al. Guidelines for acromegaly management: an update. J Clin Endocrinol Metab. May 2009; 94(5): 1509-1517.

4. Neuroendodrine tumors (Version 3.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed July 13, 2017.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	02/14	03/14
Policy converted to new template. For all three indications: age and dosing parameters added per PI; safety criteria and documentation requests removed; initial approval period increased to 3 months. Acromegaly: removed prospective question regarding stopping therapy; removed bromocriptine/cabergoline requirements; edited monitoring parameters to include IGF-1, GH and tumor mass; removed requirement that member have clinical evidence of acromegaly per App B. Carcinoid tumors: clarified that carcinoid tumors are now known as neuroendocrine tumors of the GI tract, lung, and thymus; removed requirement that member be experiencing carcinoid syndrome; removed question about whether member is a candidate for surgery as surgery can be used with octreotide to cure or control. VIPomas: as with carcinoid tumors, questions about surgery are removed.	07/16	09/16
Converted to new template. Updated approval durations from 3/6 months to 6/12 months. The following criteria in section A "acromegaly" is removed: "If member has received pituitary irradiation Sandostatin LAR Depot will be withdrawn yearly for approximately 8 weeks to assess disease activity (if GH or IGF-1 levels increase and signs and symptoms recur Sandostatin LAR Depot therapy may be resumed)." Added max dose to continued therapy. Added general info appendix.	07/17	08/17

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.