Clinical Policy: Octreotide (Sandostatin Injection, Sandostatin LAR Depot)
Reference Number: ERX.SPMN.109
Effective Date: 03/14
Last Review Date: 09/16

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

Policy/Criteria
It is the policy of health plans affiliated with Envolve Pharmacy Solutions® that the following octreotide acetate formulations: Sandostatin® Injection, its generic, “octreotide acetate injection”, and Sandostatin® LAR Depot are medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Acromegaly (must meet all):
      1. Age ≥ 18 years;
      2. Diagnosis of acromegaly with inadequate response* to, or when treatment is not appropriate with, either of the following:
         a. Surgical resection;
         b. Pituitary irradiation;

      *Inadequate response is defined as unable to achieve normalization of GH and/or IGF-I levels or unable to adequately control tumor mass.

      3. Request is for one of the following formulations:
         a. Sandostatin Injection/octreotide acetate injection (subcutaneous or intravenous use):
            i. For the brand formulation, member has a contraindication to, or has tried and has an intolerance to, the generic formulation (“octreotide acetate injection”);
            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, immediately prior to the request, with demonstration of tolerance and efficacy (reduction in GH and/or IGF-I levels or increased control of tumor mass);
            ii. The starting dose of Sandostatin LAR Depot does not exceed 20 mg given IM intragluteally at 4-week intervals for 3 months (after 3 months, dosage may be adjusted based on GH and IGF-I levels, and symptoms, not to exceed 40 mg every 4 weeks);
            iii. If member has received pituitary irradiation, Sandostatin LAR Depot will be withdrawn early for approximately 8 weeks to assess disease activity (if GH or IGF-1 levels increase and signs and symptoms recur, Sandostatin LAR Depot therapy may be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).
Approval duration: 3 months

B. Carcinoid Tumors (neuroendocrine tumors of the gastrointestinal tract, lung, and thymus) (must meet all):
   1. Age ≥ 18 years;
   2. Diagnosis of severe diarrhea and flushing episodes associated with metastatic carcinoid tumors;
   3. Request is for one of the following formulations:
      a. Sandostatin Injection/octreotide acetate injection (subcutaneous or intravenous use):
         i. For the brand formulation, member has a contraindication to, or has tried and has an intolerance to, the generic formulation (“octreotide acetate injection”);
         ii. Upward dose titration does not exceed 1500 mcg/day in divided doses;
         iii. Sandostatin Injection/octreotide acetate injection may be used alone or with Sandostatin LAR Depot for periodic exacerbation of symptoms;
      b. Sandostatin LAR Depot (intramuscular use):
         i. Member has been adherent to octreotide acetate injection (brand or generic) for two weeks, immediately prior to the request, with demonstration of tolerance and efficacy (reduction in number or severity of diarrhea and/or flushing episodes);
         ii. The starting dose of Sandostatin LAR Depot does not exceed 20 mg given IM intraglutely 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: 3 months

C. Vasoactive Intestinal Peptide Tumors (neuroendocrine tumors – pancreatic or extrapancreatic – that secrete vasoactive intestinal polypeptide) (must meet all):
   1. Age ≥ 18 years;
   2. Diagnosis of profuse watery diarrhea associated with vasoactive intestinal peptide secreting tumor;
   3. Sandostatin Injection/octreotide acetate injection (subcutaneous or intravenous use):
      a. If request is for the brand formulation, member has a contraindication to, or has tried and has an intolerance to, the generic formulation (“octreotide acetate injection”);
      b. Upward dose titration does not exceed 750 mcg/day in divided doses;
      c. Sandostatin Injection/octreotide acetate injection may be used alone or with Sandostatin LAR Depot for periodic exacerbation of symptoms;
   4. Sandostatin LAR Depot (intramuscular use):
a. Member has been adherent to octreotide acetate injection (brand or generic) for two weeks, immediately prior to the request, with demonstration of tolerance and efficacy (reduction in diarrhea);
b. 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: 3 months

D. Other diagnoses/indications: Refer to ERX.SPMN.16 - Global Biopharm Policy

II. Continued Approval
A. Acromegaly (must meet all):
   1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
   2. Member’s GH and/or IGF-1 levels have improved or normalized, or there is improved control of tumor mass.

Approval duration: 6 months

B. Carcinoid Tumors (neuroendocrine tumors of the gastrointestinal tract, lung, and thymus) (must meet all):
   1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
   2. Member has experienced a decrease in number or severity of diarrhea and/or flushing episodes.

Approval duration: 6 months

C. Vasoactive Intestinal Peptide Tumors (neuroendocrine tumors – pancreatic or extrapancreatic – that secrete vasoactive intestinal polypeptide) (must meet all):
   1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
   2. Member has experienced a decrease in diarrhea.

Approval duration: 6 months

D. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy; or
   2. Refer to ERX.SPMN.16 - Global Biopharm Policy.
Background

Description/Mechanism of Action:
Octreotide is the acetate salt of a long-acting cyclic octapeptide with pharmacologic properties mimicking those of the natural hormone somatostatin. It is a more potent inhibitor of growth hormone, glucagon, and insulin than somatostatin. Like somatostatin, it also suppresses LH response to GnRH, decreases splanchnic blood flow, and inhibits release of serotonin, gastrin, vasoactive intestinal peptide, secretin, motilin, and pancreatic polypeptide.

Sandostatin Injection (octreotide acetate injection) is prepared as a clear, sterile solution of octreotide acetate salt, in a buffered lactic acid solution for administration by deep subcutaneous (intrafat) or intravenous injection. Sandostatin Injection is available as: sterile 1-mL ampules in 3 strengths, containing 50, 100, or 500 mcg octreotide (as acetate), and sterile 5-mL multi-dose vials in 2 strengths, containing 200 and 1000 mcg/mL of octreotide (as acetate).*

*Generics available.

Sandostatin LAR Depot (octreotide acetate for injectable suspension) is available in a vial containing the sterile drug product, which when mixed with diluent, becomes a suspension that is given as a monthly intragluteal injection. Sandostatin LAR Depot is available as: sterile 6-mL vials in 3 strengths delivering 10 mg, 20 mg, or 30 mg octreotide-free peptide.*

*Generics not available.

FDA Approved Indications:
Sandostatin Injection (subcutaneous or intravenous use) and Sandostatin LAR Depot* (intramuscular use) are somatostatin analogues with the following indications:

- **Acromegaly:**
  - To reduce blood levels of growth hormone and 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. The goal is to achieve normalization of growth hormone and IGF-I (somatomedin C) levels.

- **Carcinoid tumors:**
  - For 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 treatment of the profuse watery diarrhea associated with VIP-secreting tumors.

*Sandostatin LAR Depot is indicated in patients in whom initial treatment with Sandostatin Injection has been shown to be effective and tolerated.
Limitations of use:
In patients with carcinoid syndrome and VIPomas, the effect of Sandostatin Injection and Sandostatin LAR Depot on tumor size, rate of growth and development of metastases, has not been determined.

Appendices
Appendix A: Abbreviation Key
GH: growth hormone
GnRH: gonadotropin-releasing hormone
IGF-1: insulin growth factor 1 (somatomedin C)
LH: luteinizing hormone
VIPomas: vasoactive intestinal peptide tumors

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.

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>J2353</td>
<td>Injection, octreotide, depot form for intramuscular injection, 1 mg</td>
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<tr>
<td>J2354</td>
<td>Injection, octreotide, nondepot form for subcutaneous or intravenous injection, 25 mcg</td>
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<tr>
<th>ICD-10 Codes</th>
<th>Description</th>
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<tr>
<td>T38</td>
<td>Poisoning by, adverse effect of and underdosing of hormones and their synthetic substitutes and antagonists, not elsewhere classified.</td>
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Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Policy created.</th>
<th>Date</th>
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<tbody>
<tr>
<td>Policy created.</td>
<td>02/14</td>
<td>03/14</td>
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<tr>
<td>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;</td>
<td>07/16</td>
<td>09/16</td>
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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.

References

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.

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