Prior Authorization Approval Criteria

**Sandostatin (octreotide)**

**Generic name:** octreotide

**Brand name:** Sandostatin, available in both depot and immediate-release forms

**Medication class:** somatostatin analog

**FDA approved uses:**
- **Immediate-release injection:** treatment of acromegaly in patients who have failed or are not candidates for surgery or radiation
- **Depot injection:** treatment of acromegaly in patients who have failed or are not candidates for surgery or radiation, and who have responded to and tolerated octreotide immediate-release injection
- Both forms also approved for:
  - Metastatic carcinoid tumors
  - Vasoactive intestinal peptide tumors (VIPomas)

**Available dosage forms:**
- **Immediate-release injection:**
  - 0.05 mg/mL, 0.1 mg/mL, 0.2 mg/mL, 0.5 mg/mL, 1 mg/mL injection solution
- **Depot injection:** kits for reconstitution containing extended release biodegradable polymer microspheres: 10 mg, 20 mg, 30 mg

**Usual dose:**
- **Immediate-release injection:**
  - **Acromegaly:** Initiate at 50 mcg TID and increase to 100-500 mcg TID as needed to control GH (growth hormone) and IGF-1 (insulin-like growth factor 1) levels; most patients are controlled on 100 mcg TID. Continue for at least 2 weeks to determine tolerance before transitioning to depot octreotide injection. May be given SQ or IV.
  - **Metastatic carcinoid tumors:** Initiate at 100-600 mcg/day in 2-4 divided doses. Continue for at least 2 weeks to determine tolerance before transitioning to depot octreotide injection. May be given SQ or IV.
  - **Vipomas:** Initiate at 200 to 300 mcg/day in 2 to 4 divided doses for 2 weeks (range 150 to 750 mcg). Continue for at least 2 weeks to determine tolerance before transitioning to depot octreotide injection. May be given SQ or IV.

- **Depot injection:**
  - **Acromegaly:** Initiate therapy with 20 mg deep gluteal IM injection every 4 weeks for 3 doses, then adjust dose based on patients’ GH and IGF-1 levels. At 3 months, adjust as follows:
    - GH > 2.5 ng/mL, IGF-1 elevated, and/or clinical symptoms are uncontrolled: 30 mg every 4 weeks
    - GH > 1 to ≤ 2.5 ng/mL, IGF-1 normal, and clinical symptoms are controlled: 20 mg every 4 weeks
    - GH ≤ 1 ng/mL, IGF-1 normal, and clinical symptoms are controlled: 10 mg every 4 weeks
  - **Metastatic carcinoid tumors and VIPomas:** Initiate at 20 mg IM intragluteally at 4-week intervals for 2 months; continue SUBQ octreotide acetate injections for at least 2 weeks during the switch to depot octreotide injection. At 2 months,
adjust as follows:
  - Increase dose to 30 mg IM intragluteally every 4 weeks if symptoms not adequately controlled.
  - Decrease dose to 10 mg IM intragluteally in patients who achieve good symptom control.
  - Increase dose to 20 mg IM every 4 weeks if symptoms recur.

Duration of therapy:
- **Immediate-release injection**: at least 2 weeks to determine response and tolerance; patient may then be converted to long-acting depot injection
- **Depot injection**: Indefinite; long-term

Approximate monthly cost (based on AWP 2012):
- **Immediate-release injection**: 100 mcg TID is $2080.00 per month
- **Depot injection**: 20 mg every 4 weeks is $2930.00

Criteria for use (bullet points below are all inclusive unless otherwise noted):
- **Immediate-release injection (original approval for 2 months)**:
  - Clinically diagnosed acromegaly
  - Failure to respond to surgery or radiation OR not a candidate for surgery or radiation
  - OR
  - Clinically diagnosed metastatic carcinoid tumors, associated severe diarrhea and flushing
  - OR
  - Clinically diagnosed VIPomas, associated profuse watery diarrhea
- **Depot injection (original approval for 6 months)**:
  - Meets criteria for immediate-release octreotide injection
  - Responded to and tolerated immediate-release octreotide injection

Criteria for continuation of therapy for **Immediate-release injection**:
- Patient is tolerating and responding to medication and there continues to be a medical need for the medication.
- Patient is unable to transition to long term IM injection (depot injection)
- Approval for 6 months

Criteria for continuation of therapy for **Depot injection**:
- Patient is tolerating and responding to medication and there continues to be a medical need for the medication.
- Approval for 6 months

Cautions:
- Can reduce gallbladder motility, leading to gallbladder sludge and cholelithiasis
- Can cause dysglycemias: hypoglycemia, hyperglycemia, diabetes
- Can cause hypothyroidism
- Can lower B₁₂ levels, possibly due to altered nutrient absorption
- Can cause bradycardia

Monitoring:
- Baseline and periodic thyroid function (TSH, T₄) and B₁₂ levels to monitor toxicity
- **Acromegaly**:
  - GH level, with goal GH level ≤ 2.5 ng/mL
  - IGF-1 level, with goal of age & gender normalization of IGF-1
- **Metastatic carcinoid tumors**: urinary 5-hydroxyindole acetic acid (5-HIAA), plasma serotonin, plasma substance P
- **VIPomas**: plasma vasoactive intestinal peptide (VIP)
Contraindications:
- Hypersensitivity to octreotide or any component of the injection suspension

Not approved if:
- Patient does not meet the above-stated criteria
- Patient has any contraindications to the use of octreotide

Special considerations:
Immediate-release injection:
- Store in refrigerator at 2C to 8C; may keep at room temperature for up to 14 days
- Not recommended in the American Association of Clinical Endocrinologists’ current acromegaly treatment guidelines.
- Immediate-release octreotide has a long history of use and many off-label indications, including variceal bleeding; GI and pancreatic fistulas; diarrhea related to many disease states, including AIDS, diabetes, short-bowel syndrome, and chemotherapy/radiation-related; and gastric dumping syndrome.

Depot injection:
- Store in refrigerator at 2C to 8C; warm at room temperature for 30-60 minutes before injection
- Depot somatostatin analogs are recommended as first line pharmacotherapy in the American Association of Clinical Endocrinologists’ current acromegaly treatment guidelines; the guidelines do not give preference to either octreotide or lanreotide.
- Kit must be reconstituted and administered by a healthcare professional
- Limited clinical comparisons to octreotide depot injection: no head-to-head comparisons, only cross-over studies with patients previously treated with octreotide depot.
- Cross-over studies show similar efficacy and similar degrees of GH and IGF-1 suppression between octreotide and lanreotide depot injections, but fewer injection site reactions with lanreotide depot.
- Intolerance (severe diarrhea or GI upset; rash) to octreotide does not necessarily mean intolerance to lanreotide.

<table>
<thead>
<tr>
<th>Somatostatin Analog</th>
<th>How supplied</th>
<th>How injected</th>
<th>Dosing interval</th>
<th>Monthly Dose</th>
<th>Price per Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lanreotide (Somatuline Depot)</td>
<td>Ready-to-use prefilled syringes of &lt; 0.5 mL</td>
<td>SQ injection</td>
<td>Q4 weeks</td>
<td>60 mg</td>
<td>$2437.20</td>
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<tr>
<td></td>
<td>Allows at-home administration</td>
<td>Short 20 mm needle</td>
<td></td>
<td>90 mg</td>
<td>$3427.20</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>120 mg</td>
<td>$4856.40</td>
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<tr>
<td>Octreotide (Sandostatin LAR Depot)</td>
<td>Kits for reconstitution of ~2.5 mL</td>
<td>IM injection</td>
<td>Q4 weeks</td>
<td>10 mg</td>
<td>$2236.10</td>
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<tr>
<td></td>
<td>Requires healthcare professional for injection</td>
<td>Longer 38 mm needle for muscle penetration</td>
<td></td>
<td>20 mg</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>30 mg</td>
<td>$4386.97</td>
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<table>
<thead>
<tr>
<th>Treatment</th>
<th>Timepoint</th>
<th>Percent of patients with...</th>
<th>GH ≤ 2.5 ng/mL</th>
<th>Normal IGF-1</th>
<th>GH ≤ 2.5 ng/mL + Normal IGF-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sandostatin LAR Depot</td>
<td>Trial 1 (n=88)</td>
<td>44 weeks</td>
<td>66%</td>
<td>67%</td>
<td>57%</td>
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<td></td>
<td>Trial 2 (n=122)</td>
<td>108 weeks</td>
<td>47%</td>
<td>51%</td>
<td>42%</td>
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<tr>
<td>Somatuline Depot</td>
<td>Trial 1 (n=107)</td>
<td>Baseline</td>
<td>0%</td>
<td>8%</td>
<td>0%</td>
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<tr>
<td></td>
<td>4 weeks</td>
<td>34%</td>
<td>25%</td>
<td>16%</td>
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<td></td>
<td>16 weeks</td>
<td>50%</td>
<td>55%</td>
<td>39%</td>
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<td>32 weeks</td>
<td>57%</td>
<td>55%</td>
<td>45%</td>
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<tr>
<td>52 weeks</td>
<td>54%</td>
<td>59%</td>
<td>43%</td>
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<tr>
<td><strong>Trial 2 (n=63)</strong></td>
<td>Baseline</td>
<td>33%</td>
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<td>0%</td>
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<td>12 weeks</td>
<td>75%</td>
<td>27%</td>
<td>22%</td>
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<td>28 weeks</td>
<td>80%</td>
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<td>48 weeks</td>
<td>86%</td>
<td>43%</td>
<td>38%</td>
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**Step Therapy Requirements (for depot octreotide injection):**
- Has tried immediate-release octreotide and demonstrated response and tolerance
  - Acromegaly: Initiate at 50 mcg TID and increase to 100-500 mcg TID as needed
  - Metastatic carcinoid tumors: Initiate at 100-600 mcg/day in 2-4 divided doses.
  - VIPomas: Initiate at 200 to 300 mcg/day in 2 to 4 divided doses for 2 weeks (range 150 to 750 mcg).
  - Continue for at least 2 weeks to determine tolerance before converting to depot octreotide