Somatostatin Analogs Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Open, FlexRx Closed, GenRx Open, GenRx Closed, Health Insurance Marketplace, KeyRx and FocusRx formularies.

This is a FlexRx standard and GenRx standard prior authorization.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

**FDA APPROVED INDICATIONS AND DOSAGE**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indications</th>
<th>Dosing and Administration</th>
</tr>
</thead>
</table>
| **Sandostatin®** (octreotide acetate) subcutaneous injection | • To reduce blood levels of growth hormone and IGF-1 (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  
  
  • Symptomatic treatment of patients with metastatic carcinoid tumors by suppressing or inhibiting the severe diarrhea/flushing episodes associated with the disease  
  
  • Treatment of the profuse watery diarrhea associated with VIP-secreting tumors  
  
  Limitations of Use: In patients with carcinoid syndrome and VIPomas, the effect of Sandostatin Injection | **Acromegaly:** Initiate therapy at 50 mcg subcutaneously 3 times daily. Dose may be increased depending on IGF-1 and growth hormone levels. The most commonly effective dose is 100 mcg three times daily, but some patients may require up to 500 mcg three times daily for maximum effectiveness. Doses above 300 mcg/day seldom result in additional biochemical benefit, and if an increase in dose fails to provide additional benefit, the dose should be reduced.  
  **Carcinoid tumors:** 100–600 mcg/day subcutaneously in 2-4 divided doses for the first 2 weeks. Clinical and biochemical benefits were obtained in some patients with as little as 50 mcg, while others required doses up to 1500 mcg per day. Experience with doses above 750 mcg/day is limited.  
  **VIP-secreting tumors:** 200-300 mcg/day subcutaneously in 2-4 divided doses for the first 2 weeks. Dosage may be adjusted to achieve a therapeutic response, but typically, doses |
<table>
<thead>
<tr>
<th>Agent</th>
<th>Indications</th>
<th>Dosing and Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>and Sandostatin LAR Depot on tumor size, rate of growth and development of metastases, has not been determined</td>
<td>above 450 mcg/day are not required</td>
</tr>
<tr>
<td>Sandostatin® LAR (octreotide acetate) intragluteal injection</td>
<td>Patients should use Sandostatin subcutaneous injection for at least 2 weeks before initiating Sandostatin LAR (see Sandostatin for dosing for each indication) to determine tolerance and response to octreotide acetate</td>
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<tr>
<td><strong>● Acromegaly in patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option</strong></td>
<td><strong>Acromegaly:</strong> 20 mg intraglutentially every 4 weeks for 3 months. After 3 months, dosage may be adjusted depending on response to a maximum dose of 40 mg intraglutentially every 4 weeks. Doses higher than 40 mg are not recommended.</td>
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</tr>
<tr>
<td><strong>● Treatment of the severe diarrhea/flushing episodes associated with metastatic carcinoid tumors</strong></td>
<td><strong>Carcinoid tumors:</strong> 20 mg intraglutentially every 4 weeks for 2 months. If switching from Sandostatin subcutaneous injection to Sandostatin LAR patients should continue to use Sandostatin subcutaneous injection at the same dose used before the switch for at least 2 weeks after initial Sandostatin LAR injection. After 2 months, dose can be adjusted depending on symptom control up to a maximum of 30 mg intraglutentially every 4 weeks. Doses higher than 40 mg are not recommended.</td>
<td></td>
</tr>
<tr>
<td><strong>● Treatment of the profuse watery diarrhea associated with VIP-secreting tumors</strong></td>
<td><strong>VIP-secreting tumors:</strong> 20 mg intraglutentially every 4 weeks for 2 months. If switching from Sandostatin subcutaneous injection to Sandostatin LAR patients should continue to use Sandostatin subcutaneous injection at the same dose used before the switch for at least 2 weeks after initial Sandostatin LAR injection. After 2 months, dose can be adjusted depending on symptom control up to a maximum of 30 mg intraglutentially every 4 weeks. Doses higher than 40 mg are not recommended.</td>
<td></td>
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</tbody>
</table>

**Limitations of Use:**

Patients should use Sandostatin subcutaneous injection for at least 2 weeks before initiating Sandostatin LAR (see Sandostatin for dosing for each indication) to determine tolerance and response to octreotide acetate.
<table>
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<tr>
<th>Agent</th>
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</tr>
</thead>
<tbody>
<tr>
<td><em>Somatuline Depot</em>® (lanreotide) deep subcutaneous injection</td>
<td>• Long-term treatment of acromegalic patients who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy</td>
<td><strong>Acromegaly:</strong> The recommended starting dosage is 90 mg given via the deep subcutaneous route, at 4 week intervals for 3 months. After 3 months the dosage may be adjusted depending on response to a maximum of 120 mg given via the deep subcutaneous route every 4 weeks. <strong>GEP-NET:</strong> 120 mg by deep subcutaneous injection every 4 weeks <strong>Carcinoid syndrome:</strong> 120 mg by deep subcutaneous injection every 4 weeks. Do not administer an additional dose if the patient is already receiving Somatuline Depot for GEP-NETs.</td>
</tr>
<tr>
<td><em>Somavert</em>® (pegvisomant) subcutaneous injection</td>
<td>• Treatment of adult patients with unresectable, well- or moderately-differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NET) • Treatment of adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy • Acromegaly in patients with inadequate response to surgery and/or radiation therapy or for whom these therapies are inappropriate</td>
<td><strong>Acromegaly:</strong> 40 mg loading dose administered subcutaneously followed by 10 mg subcutaneously once daily starting the day after the loading dose. The dosage should be titrated to normalize the serum IGF-1 concentrations up to a maximum of 30 mg given subcutaneously once daily.</td>
</tr>
</tbody>
</table>

**CLINICAL RATIONALE**

**Acromegaly**

Acromegaly is the clinical syndrome that results from excessive secretion of growth hormone (GH). Excess GH stimulates hepatic secretion of insulin like growth factor – 1 (IGF-1), which causes most of the clinical manifestations of acromegaly. The most common cause of acromegaly is a
somatotroph (GH secreting) adenoma of the anterior pituitary. The clinical features of acromegaly are attributable to high serum concentrations of both GH and IGF-1. Excess GH and IGF-1 have both somatic and metabolic effects. Somatic effects include stimulation of growth of many tissues, such as skin, connective tissue, cartilage, bone, viscera, and many epithelial tissues. Metabolic effects include nitrogen retention, insulin antagonism, and lipolysis. Headache and vision loss can develop due to elevated serum GH concentration as well as tumor mass. Virtually all patients with acromegaly have acral and soft tissue overgrowth and skin thickening. The characteristic findings are an enlarged jaw (macroglossia) and enlarged, swollen hands and feet.\(^5\)

Manifestations of soft tissue overgrowth include macroglossia, deepening of the voice, and paresthesias of the hands (e.g. carpal tunnel syndrome in around 20%). Obstructive sleep apnea develops in approximately 50% of patients. When excess GH secretion occurs in children (before epiphyses of the long bones are fused) linear growth increases, resulting in pituitary gigantism. In contrast adults with acromegaly do not become taller. Diabetes and cardiovascular disease, such as hypertension, left ventricular hypertrophy and cardiomyopathy, may also develop. Mortality of patients with acromegaly is primarily from cardiovascular disease.\(^5\)

The goals of therapy in treatment of acromegaly are to lower the serum IGF-1 to within the reference range for the patient’s age and gender and to lower growth hormone (GH) concentration to less than 1.0 ng/mL. When the serum GH and IGF-1 concentrations decline to normal, the characteristic soft tissue overgrowth and related symptoms gradually recede and the metabolic abnormalities, such as diabetes mellitus, improve. In addition, life expectancy returns to that of the general population.\(^6\)

Diagnosis of acromegaly involves measurement of IGF-1 levels in patients with clinical manifestations of acromegaly, including sleep apnea syndrome, type 2 diabetes mellitus, debilitating arthritis, carpal tunnel syndrome, hyperhidrosis, and hypertension and low GH levels (<1 micrograms/L) following documented hyperglycemia during an oral glucose load.\(^6\)

Treatment of patients with acromegaly is aimed at normalizing GH and/or IGF1 levels to improve signs and symptoms of the disease and reduce excess mortality. Long-term biochemical control is achieved in fewer than 65% of patients following surgical resection of the tumor despite the use of novel surgical approaches, and only approximately half of patients treated with medical therapy achieve control of IGF1 levels. Radiation therapy remains an option in patients with persistently active disease, but rates of control and safety have only marginally improved with the use of stereotactic radiosurgery instead of conventional fractionated radiotherapy.\(^6\)

Initial treatment depends on the size and location of the adenoma, the presence of symptoms due to size (such as vision impairment), and the patient’s ability to undergo surgery. Surgical resection by an experienced neurosurgeon is recommended as initial therapy for most patients and represents the optimal opportunity for cure. Patients for whom a medication can be considered as primary therapy include those who have unacceptable surgical risk, refuse surgery, or have adenomas that are unlikely to be cured surgically.\(^6\)

After surgery biochemical control based on IGF-1 and/or GH levels should be assessed after 12 weeks. Recommendations. For patients with persistent disease after surgery, a first-generation long-acting somatostatin receptor ligand (SRL) either octreotide or lanreotide. The choice between octreotide LAR and lanreotide is determined by availability, convenience of administrations and patient preference. Cabergoline can be attempted as a first-line medical therapy in patients with acromegaly and mildly elevated levels of IGF-1 (< 2.5 times the upper limit of normal).\(^6\)

If first-line medical therapy is not successful in normalizing levels of IGF1 additional therapies are necessary. For patients who achieve partial response (a decrease in GH and/or IGF1 ≥ 50%) after using a long-acting first-generation SRL, the dose should be increased. If using lanreotide, both dose and/or frequency can be increased. The addition of cabergoline can be tried if the levels of IGF-1 remain modestly elevated during SRL treatment.\(^6\)
If biochemical control is not achieved after administering the maximal dose of first-generation SRL, treatment should be individualized on the basis of the presence or absence of clinically relevant residual tumor and impaired glucose tolerance. If a clinically relevant residual tumor that is unsuitable for resection is present, the patient should be switched from first-generation SRL to pasireotide LAR; if severe hyperglycemia occurs, patients should be switched to pegvisomant. However, if there is pre-existing clinically relevant impaired glucose metabolism, patients should be switched from first-generation SRL to pegvisomant. If there is clinically relevant residual tumor and pre-existing impaired glucose metabolism, maintaining first-generation SRL and adding pegvisomant is recommended. GH levels in patients receiving pegvisomant should not be measured due to levels remain elevated during treatment.6

If biochemical control is not achieved after second-line therapy, stereotactic radiosurgery or surgical intervention or reintervention should be reconsidered, as appropriate.6

Carcinoid syndrome
Carcinoid syndrome is caused by the secretion of serotonin and other bioactive amines into the systemic circulation and is manifested by flushing and diarrhea, fibrosis of the right-sided heart valves, and intestinal mesentery.7

Episodic flushing is the clinical hallmark of the carcinoid syndrome and occurs in 85 percent of patients. The typical flush associated with midgut neuroendocrine tumors (NETs) begins suddenly and lasts from 30 seconds to as long as 30 minutes. Flushing primarily involves the face, neck, and upper chest, which become red to violaceous or purple. Severe flushes are accompanied by a fall in blood pressure and rise in pulse rate. As the disease progresses, the episodes may last longer, and the flushing be more diffuse.7

Secretory diarrhea occurs in 80 percent of patients and is often the most debilitating component of the syndrome. Stools may vary from few to more than 30 per day, are typically watery and nonbloody, and can be explosive and accompanied by abdominal cramping.8

Somatostatin analogs (octreotide or lanreotide) are recommended as initial therapy in patients with carcinoid syndrome. Over time, patients with carcinoid syndrome may become refractory to somatostatin analogs. NET physicians often increase the dose and/or frequency of somatostatin analogs in an attempt to control refractory carcinoid syndrome.7

The National Comprehensive Cancer Network (NCCN) recommends that patients who have metastatic neuroendocrine tumors and carcinoid syndrome should be treated with octreotide or lanreotide. The long-acting release (LAR) formulation of octreotide is commonly used for the chronic management of symptoms and the Short-acting octreotide can be added for rapid relief or for breakthrough symptoms. Lanreotide has a similar mechanism of action as octreotide, but is administered as a deep subcutaneous injection.9

Vasoactive intestinal peptide tumors10
Vasoactive intestinal peptide tumors (VIPomas) are rare functioning neuroendocrine tumors that secrete vasoactive intestinal polypeptide (VIP). VIPomas are detected in 1 in 10 million people per year.15 95 percent of VIPomas arise within the pancreas, and are classified as functioning pancreatic neuroendocrine (islet cell) tumors. The other VIP-secreting tumors reported include lung cancer, colorectal cancer, ganglioneuroblastoma, pheochromocytoma, hepatoma, and adrenal tumors.

The majority of patients with VIPoma have VIPoma syndrome, which is also called the pancreatic cholera syndrome, Verner0morrison syndrome, and the watery diarrhea, hypokalemia, and hypochlorhydria or achlorhydria (WDHA) syndrome. VIPoma syndrome is characterized by watery diarrhea that persists with fasting. Stool volumes can exceed 3,000 mL/day in 70 percent of patients. Associated symptoms include flushing episodes in 20 percent of patients and symptoms
related to hypokalemia and dehydration, such as lethargy, nausea, vomiting, muscle weakness, and muscle cramps.

Treatment if a patient with a VIPoma begins with replacement of fluid losses and correction of electrolyte abnormalities. Many patients require more than 5 L of fluid and 350 mEq of potassium daily.

Somatostatin and its analogs (e.g., octreotide, lanreotide) inhibit the secretion of VIP and are the treatment of choice to control diarrhea in patient with VIPoma. Although somatostatin analogs are highly effective at controlling the symptoms of hormone hypersecretion, objective evidence of antitumor activity has not been clearly demonstrated.

**Gastroenteropancreatic neuroendocrine tumors**

Gastroenteropancreatic neuroendocrine tumors (GEP-NET) are a type of neuroendocrine tumors. Neuroendocrine cells are distributed widely throughout the body, and neuroendocrine neoplasms can arise at many sites. The 2010 World Health Organization (WHO) classification of neuroendocrine neoplasms arising the digestive system separates these tumors into two broad categories, well differentiated and poorly differentiated.

**Efficacy**

**Sandostatin**

Sandostatin reduces growth hormone to within normal ranges in 50% of patients and reduced IGF-1 to within normal ranges in 50-60% of patients. Since the effects of pituitary irradiation may not become maximal for several years, adjunctive therapy with Sandostatin to reduce blood levels of growth hormone and IGF-1 offers potential benefit before the effects of irradiation are manifested.

**Sandostatin LAR**

Sandostatin LAR depot was evaluated in three clinical trials in acromegalic patients. In two of the clinical trials, a total of 101 patients were entered who had, in most cases, achieved a growth hormone level <5 ng/mL while on subcutaneous Sandostatin injection. Growth hormone and IGF-1 levels were at least as well controlled with Sandostatin LAR depot as they had been on Sandostatin injection and this level of control remained for the entire duration of the trials.

A third trial was a 12-month study that enrolled 151 patients who had a growth hormone level <10 ng/mL after treatment with Sandostatin injection. Growth hormone and IGF-1 were at least as well controlled on Sandostatin LAR depot as they had been on Sandostatin injection.

**Somatuline**

Somatuline depot was studied in 2 long-term, multiple-dose, randomized, multicenter studies.

Study 1, as listed in the prescribing information, included a 4-week, double-blind, placebo-controlled phase; a 16-week single-blind, fixed-dose phase; and a 32-week, open-label, dose-titration phase. Upon entry, 108 patients were randomly allocated to receive a single, deep subcutaneous injection of Somatuline depot 60, 90, or 120 mg, or placebo. Four weeks later, patients entered a fixed-dose phase where they received 4 injections of Somatuline depot followed by a dose-titration phase of 8 injection for a total of 13 injections over 52 weeks (including the placebo phase).

A total of 52 of the 83 lanreotide-treated patients had a greater than 50% decrease in mean growth hormone from baseline to week 4. In the fixed-dose phase at week 16, 72 of all 107 lanreotide-treated patients had a decrease from baseline in mean growth hormone of greater than 50%. Efficacy achieved in the first 16 weeks was maintained for the duration of the study.

Study 2, as listed in the prescribing information, was a 48-week, open-label, uncontrolled, multicenter study that enrolled 63 patients who had an IGF-1 concentration 1.3 times or greater than the upper limit of the normal age-adjusted range. Patients were initially enrolled in a 4-
month, fixed-dose phase where they received 4 deep subcutaneous injections of Somatuline depot 90 mg, at 4-week intervals. Patients then entered a dose-titration phase where the dose was titrated depending on growth hormone and IGF-1 levels. 27 patients achieved normal age-adjusted IGF-1 concentrations at the end of this study.

The efficacy of Somatuline depot was established in a multicenter, randomized, double-blind, placebo-controlled trial of 204 patients with unresectable, well or moderately differentiated, metastatic or locally advanced, gastroenteropancreatic neuroendocrine tumors. 101 patients received Somatuline depot 120 mg and 103 patients received placebo. The major efficacy outcome measure was progression-free survival. Patients in the Somatuline depot arm had a statistically significant improvement in progression free survival than in the placebo arm.

Study 4, as listed in the prescribing information, was a multicenter, randomized, 16-week, double-blind, placebo-controlled trial in 115 patients with histopathologically-confirmed neuroendocrine tumors and a history of carcinoid syndrome. 59 patients received Somatuline depot and 56 patients received placebo. The primary efficacy outcome measure was the percentage of days in which patients administered at least one injection of rescue medication for symptom control. Patients in the Somatuline depot arm experienced 15% fewer days on rescue medication compared to the placebo arm.

Somavert®
A total of 112 patients with acromegaly participated in a 12-week, randomized, double-blind, multicenter study comparing placebo and Somavert. 26 patients received Somavert 10 mg daily, 26 patients received Somavert 15 mg daily, 28 patients received Somavert 20 mg daily and 31 patients received placebo. The primary efficacy endpoint was IGF-1 percent change in IGF-1 concentrations from baseline to week 12. The three groups that received Somavert showed statistically significant (p<0.01) reductions in serum levels of IGF-1 compared to the placebo group.

Safety

Sandostatin and Sandostatin LAR®
The most common adverse events of diarrhea, steatorrhea, vomiting and abdominal distention have occurred in 22-35% of patients. Biliary tract abnormalities occurred in 63% of patients. In clinical trials the incidence of gall stones or sludge in patients who received therapy for 12 months or longer was 52%. Octreotide is also associated with hypoglycemia and hyperglycemia (3-6% of acromegaly patients). Bradycardia developed in 25% and conduction abnormalities occurred in 10% of patients and arrhythmias in 9%. Monitoring vitamin B₁₂ levels is recommended during chronic therapy due to the risk of depressed vitamin B₁₂.

Somatuline®
The most common adverse events are diarrhea, cholelithiasis, abdominal pain, nausea and injection site reactions. In the post marketing environment, a small number of allergic reactions have been reported (including angioedema, anaphylaxis, and hypersensitivity); otherwise, the profile of reported adverse reactions are consistent with those that were observed in clinical studies.

Safety data was evaluated in 101 patients who received at least one dose of lanreotide for gastroenteropancreatic neuroendocrine tumors (GEP-NETS). The most commonly (greater than or equal to 10%) reported adverse reactions in lanreotide-treated patients were abdominal pain, musculoskeletal pain, vomiting, headache, injection site reaction, hyperglycemia, hypertension, and cholelithiasis. The most common serious adverse reaction of lanreotide observed in this trial was vomiting (4%).

Somavert®
The most common adverse events (>10% of patients) include infections, pain, diarrhea, nausea, flu syndrome, abnormal liver function tests, and injection site reactions.
Lipohypertrophy has been reported in <5% of patients following pegvisomant therapy. Asymptomatic, transient elevations in transaminases up to 15 times ULN have been reported in <2% of patients. Immunogenicity was reported in 17% of patients but the presence of these antibodies did not appear to impact the efficacy of pegvisomant.

For additional clinical information see Prime Therapeutics Formulary Chapter 4.9H: Somatostatic Agents and Chapter 4.9N: Somavert.

**Compendia supported diagnoses**

For the purposes of the criteria, diagnoses deemed appropriate are those that are supported in AHFS, NCCN 1 or 2A level of evidence, or DrugDex with 1 or 2A level of evidence.

**References**

### Somatostatin Analog with Prior Authorization with Quantity Limit

#### TARGET AGENTS
- Sandostatin® (octreotide acetate)\(^a\)
- Sandostatin LAR® (octreotide acetate)
- Somatuline® Depot (lanreotide acetate)
- Somavert® (pegvisomant)

\(^a\) – generic available

<table>
<thead>
<tr>
<th>Agents</th>
<th>GPI</th>
<th>Multisource Code</th>
<th>Quantity Limit</th>
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</thead>
<tbody>
<tr>
<td><strong>Sandostatin (octreotide acetate)</strong>(^a)</td>
<td></td>
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<tr>
<td>50 mcg/mL single use ampule</td>
<td>30170070102005</td>
<td>M, N, O, or Y</td>
<td>90 mL (90 ampules)/30 days</td>
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<td>100 mcg/mL single use ampule</td>
<td>30170070102010</td>
<td>M, N, O, or Y</td>
<td>90 mL (90 ampules)/30 days</td>
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<td>200 mcg/mL in a 5 mL multi-dose vial</td>
<td>30170070102015</td>
<td>M, N, O, or Y</td>
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<td>500 mcg/mL single use ampule</td>
<td>30170070102020</td>
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<td>M, N, O, or Y</td>
<td>30 mL (6 vials)/30 days</td>
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<td><strong>Sandostatin LAR (octreotide acetate suspension)</strong></td>
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<td>20 mg (10 mg/mL) kit</td>
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<td>60 mg (30 mg/mL) kit</td>
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<td>1 kit/28 days</td>
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<td><strong>Somatuline Depot (lanreotide acetate suspension)</strong></td>
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<td>60 mg pre-filled syringe</td>
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<td>M, N, O, or Y</td>
<td>1 vial/day</td>
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\(^a\) Generic available

#### PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

**Initial Authorization**

Sandostatin (octreotide) or Sandostatin LAR (octreotide) will be approved when ALL of the following are met:

1. ONE of the following:
   A. There is information that the patient is currently being treated with the requested agent
   **OR**
B. The prescriber states the patient is being treated with the requested agent
AND is at risk if therapy is changed
OR
c. The patient has a diagnosis of acromegaly AND BOTH of the following:
   i. ONE of the following:
      1. The patient had an inadequate response to surgical resection or pituitary radiation therapy as indicated by growth hormone and serum IGF-1 that are above the reference ranges
      OR
      2. The patient is not a candidate for surgical resection
      OR
      3. The requested agent will be used in combination with pituitary radiation therapy
   AND
   ii. ONE of the following:
      1. The patient is NOT currently being treated with Signifor LAR (pasireotide)
      OR
      2. The patient is currently being treated with Signifor LAR (pasireotide) AND will discontinue prior to initiating the requested agent
OR
D. The patient has flushing and/or diarrhea associated with metastatic carcinoid tumors
OR
E. The patient has profuse watery diarrhea associated with Vasoactive Intestinal Peptide (VIP) secreting tumors
OR
F. The patient has another FDA labeled diagnosis
OR
G. The patient has another diagnosis that is supported by compendia. (AHFS, NCCN level of evidence 1 or 2A, or DrugDex level of evidence 1 or 2A)
   AND
2. If the requested agent is Sandostatin, the patient has tried and had an inadequate response to octreotide
AND
3. If the request is for Sandostatin LAR, the patient has responded to and tolerated Sandostatin (octreotide) for a minimum of 2 weeks
AND
4. The prescriber is a specialist in the area of the patient’s diagnosis (e.g., endocrinologist, oncologist) or has consulted with a specialist in the area of the patient’s diagnosis
AND
5. The patient does NOT have any FDA labeled contraindications to the requested agent
AND
6. ONE of the following:
   A. The requested quantity (dose) does not exceed the program quantity limit
   OR
   B. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
      AND
ii. The requested quantity (dose) does not exceed the maximum FDA labeled dose or the dose supported by compendia for the requested diagnosis AND

iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit

OR

C. ALL of the following:
   i. The requested quantity (dose) is greater than the program quantity limit
      AND
   ii. The requested quantity (dose) is greater than the maximum FDA labeled dose or the dose supported by compendia for the requested indication
      AND
   iii. The prescriber has submitted information in support of therapy with a higher dose for the requested diagnosis

**Length of Approval:** 6 months

**Somatuline Depot** will be approved when ALL the following are met:

1. ONE of the following:
   A. There is information that the patient is currently being treated with the requested agent
   OR
   B. The prescriber states the patient is being treated with the requested agent AND is at risk if therapy is changed
   OR
   C. The patient has a diagnosis of acromegaly AND BOTH of the following:
      i. ONE of the following:
         1. The patient had an inadequate response to surgical resection or pituitary radiation therapy as indicated by growth hormone and serum IGF-1 that are above the reference ranges
         OR
         2. The patient is not a candidate for surgical resection
         OR
         3. The requested agent will be used in combination with pituitary radiation therapy
         AND
      ii. ONE of the following:
         1. The patient is NOT currently being treated with Signifor LAR (pasireotide)
         OR
         2. The patient is currently being treated with Signifor LAR (pasireotide) AND will discontinue prior to initiating the requested agent
      OR
   D. BOTH of the following:
      i. The patient has a diagnosis of gastroenteropancreatic neuroendocrine tumors (GEP-NETs)
      AND
      ii. The tumors are unresectable, locally advanced, well or moderately differentiated OR metastatic
OR
E. The patient has a diagnosis of carcinoid syndrome (i.e. flushing and/or diarrhea)
OR
F. The patient has another FDA approved diagnosis
OR
G. The patient has another diagnosis that is supported by compendia. (AHFS, NCCN level of evidence 1 or 2A, or DrugDex level of evidence 1 or 2A)

AND
2. The prescriber is a specialist in the area of the patient’s diagnosis (e.g., endocrinologist, oncologist) or has consulted with a specialist in the area of the patient’s diagnosis

AND
3. The patient does NOT have any FDA labeled contraindications to the requested agent

AND
4. ONE of the following:
   A. The requested quantity (dose) does not exceed the program quantity limit
   OR
   B. ALL of the following
      i. The requested quantity (dose) is greater than the program quantity limit
      AND
      ii. The requested quantity (dose) does not exceed the maximum FDA labeled dose or the dose supported by compendia for the requested diagnosis
      AND
      iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit
   OR
   C. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
      AND
      ii. The requested quantity (dose) is greater than the maximum FDA labeled dose or the dose supported by compendia for the requested diagnosis
      AND
      iii. The prescriber has submitted information in support of therapy with a higher dose for the requested diagnosis

Length of Approval: 6 months

Somavert (pegvisomant) will be approved when ALL the following are met:
1. ONE of the following:
   A. There is information that the patient is currently receiving the requested agent
   OR
   B. The prescriber states the patient is being treated with the requested agent AND is at risk if therapy is changed
   OR
   C. The patient has a diagnosis of acromegaly AND ALL of the following:
      i. ONE of the following:
1. The patient had an inadequate response to surgical resection or pituitary radiation therapy as indicated by growth hormone and serum IGF-1 that are above the reference ranges OR
2. The patient is not a candidate for surgical resection OR
3. The requested agent will be used in combination with pituitary radiation therapy

AND

ii. ONE of the following:
   1. The patient has tried and had an inadequate response to Sandostatin LAR (octreotide suspension), or Somatuline Depot (lanreotide) AND ONE of the following:
      a. The dose and/or frequency of Sandostatin LAR (octreotide suspension) or Somatuline Depot (lanreotide) has been increased to the maximally tolerated dose OR
      b. The patient has preexisting impaired glucose metabolism OR
   2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to BOTH Sandostatin LAR (octreotide suspension), AND Somatuline Depot (lanreotide) OR
   3. The patient is currently on a prerequisite agent (Sandostatin [octreotide], Sandostatin LAR [octreotide suspension], or Somatuline Depot [lanreotide] and will be using the requested agent as add on (adjunctive) therapy OR
   4. The prescriber has provided information in support of the requested agent over BOTH Sandostatin LAR (octreotide suspension) AND Somatuline Depot (lanreotide) OR
   5. The patient has tried Signifor LAR (pasireotide) AND had severe hyperglycemia

AND

iii. ONE of the following:
   1. The patient is NOT currently being treated with Signifor LAR (pasireotide) OR
   2. The patient is currently being treated with Signifor LAR (pasireotide) AND will discontinue prior to initiating the requested agent

OR
D. The patient has another FDA approved diagnosis OR
E. The patient has another diagnosis that is supported by compendia. (AHFS, NCCN level of evidence 1 or 2A, or DrugDex level of evidence 1 or 2A)

AND
2. The prescriber is a specialist in the area of the patient’s diagnosis (e.g., endocrinologist, oncologist) or has consulted with a specialist in the area of the patient’s diagnosis AND
3. The patient does NOT have any FDA labeled contraindications to the requested agent
4. ONE of the following:
   A. The requested quantity (dose) does not exceed the program quantity limit
   OR
   B. ALL of the following
      i. The requested quantity (dose) is greater than the program quantity limit
      AND
      ii. The requested quantity (dose) does not exceed the maximum FDA labeled dose or the dose supported by compendia for the requested diagnosis
      AND
      iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit
   OR
   C. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
      AND
      ii. The requested quantity (dose) is greater than the maximum FDA labeled dose or the dose supported by compendia for the requested diagnosis
      AND
      iii. The prescriber has submitted information in support of therapy with a higher dose for the requested diagnosis

Length of Approval:  6 months

Renewal Evaluation
Targeted agents will be renewed when ALL of the following are met:
1. The patient has been previously approved for the requested agent through the plan’s Prior Authorization process
   AND
2. The patient has shown clinical improvement (e.g. decrease in symptom severity/frequency, reduction in tumor size, normalized IGF-1 and/or growth hormone levels)
   AND
3. The prescriber is a specialist in the area of the patient’s diagnosis (e.g., endocrinologist, oncologist) or has consulted with a specialist in the area of the patient’s diagnosis
   AND
4. The patient does NOT have any FDA labeled contraindications to the requested agent
   AND
5. ONE of the following:
   A. The requested quantity (dose) does not exceed the program quantity limit
   OR
   B. ALL of the following
      i. The requested quantity (dose) is greater than the program quantity limit
      AND
      ii. The requested quantity (dose) does not exceed the maximum FDA labeled dose or the dose supported by compendia for the requested diagnosis
iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit

**OR**

C. ALL of the following:

i. The requested quantity (dose) is greater than the program quantity limit

**AND**

ii. The requested quantity (dose) is greater than the maximum FDA labeled dose or the dose supported by compendia for the requested diagnosis

**AND**

iii. The prescriber has submitted information in support of therapy with a higher dose for the requested diagnosis

**Length of Approval:** 12 months
Step Therapy Supplement

This program applies to FlexRx Closed, FlexRx Open, GenRx Closed, GenRx Open, Health Insurance Marketplace, FocusRx and KeyRx formularies.

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT

OBJECTIVE

The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL

The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
   a. A statement by the prescriber that the patient is currently taking the requested agent
      AND
   b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
      AND
   c. The prescriber states that a change in therapy is expected to be ineffective or cause harm

   OR

2. The patient’s medication history include the required prerequisite/preferred agent(s) as indicated by:
   a. Evidence of a paid claim(s) within the past 999 days
      OR
   b. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days AND the required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event

   OR

3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: As per program specific criteria