Somatostatin Analogs Prior Authorization with Quantity Limit Program Summary

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

This is a FlexRx Standard and GenRx Standard program.

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

POLICY REVIEW CYCLE

Effective Date	Date of Origin
2/1/2024	7/1/2019

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Lanreotide Deep subcutaneous injection	• Long Term treatment of acromegalic patients who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy • Treatment of adult patients with unresectable, well-or moderately-differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NRTs) to improve progression-free survival		12
Mycapssa® (octreotide) Delayed-release capsules, for oral use	• Long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide		2
Sandostatin® LAR (octreotide acetate) Gluteal intramuscular injection	Treatment in patients who have responded to and tolerated Sandostatin injection subcutaneous injection for: • Long-term maintenance therapy of 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. The goal of treatment in acromegaly is to reduce GH and IGF-1 levels to normal. • Treatment of the severe diarrhea/flushing episodes associated with metastatic carcinoid tumors • 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 and Sandostatin LAR Depot on tumor size, rate of growth and development of metastases, has not been determined		4

Agent(s)	FDA Indication(s)	Notes	Ref#
Sandostatin®, Octreotide 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. The goal is to achieve normalization of GH and IGF-1 levels. • 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	*Generic available	3,11
Somatuline Depot® (lanreotide) Subcutaneous injection	• Long-term treatment of acromegalic patients who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy • Treatment of adult patients with unresectable, well- or moderately- differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NET) to improve progression-free survival. • Treatment of adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy		5
Somavert® (pegvisomant) Subcutaneous injection	• Treatment of acromegaly in patients who have had an inadequate response to surgery or radiation therapy, or for whom these therapies are inappropriate. The goal of treatment is to normalize serum insulin-like growth factor-1 (IGF-1) levels.		6

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Acromegaly	Acromegaly is caused by excess circulating levels of growth hormone (GH) and insulin-like growth factor-1 (IGF-1), which typically result from a GH-secreting pituitary adenoma. The clinical features of acromegaly are attributable to high serum concentrations of both GH and IGF-1. Patients exhibit characteristic acral and soft tissue overgrowth (particularly in the face and hands), arthritis, jaw overbite, respiratory obstruction, hypertension and headache, as well as visual disturbances and cranial nerve palsy from tumor mass effects. Metabolic dysfunction, including insulin resistance and elevated HbA_{1c}, increases the risk of diabetes mellitus and cardiovascular-related morbidity and mortality.(7) 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 GH concentration to less than 1 microgram/L. 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.(7) 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 IGF-1 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.(7) 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.(7,13) For patients with persistent disease after surgery, a first-generation long-acting somatostatin receptor ligand (SRL; octreotide LAR or lanreotide) is recommended as first-line therapy. 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 (less than 2.5 times the upper limit of normal).(7,13) 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. If biochemical control is not achieved after second-line therapy, stereotactic radiosurgery or surgical intervention or reintervention should be reconsidered, as appropriate.(7,13)
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.(8) Approximately 30-40% of patients with well-differentiated neuroendocrine tumors present with carcinoid syndrome. The main symptoms of carcinoid syndrome are episodic facial flushing, that may be accompanied by hypotension and tachycardia, diarrhea, bronchoconstriction, venous telangiectasia, dyspnea, and ultimately fibrotic complications such as mesenteric and retroperitoneal fibroses and carcinoid heart disease. In over 90% of cases, flushing is the clinical hallmark of the carcinoid syndrome and is often episodic.(10) Secretory diarrhea occurs in 60–80% of patients, is intermittent and sporadic, and is often accompanied by abdominal cramping.(10) 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.(8,10) 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 tumors(9)	Vasoactive intestinal peptide tumors (VIPomas) are rare functioning neuroendocrine tumors that secrete vasoactive intestinal polypeptide (VIP). 95% 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.

	VIPomas are characterized by watery diarrhea, hypokalemia, and achlorhydria (WDHA syndrome) from secretion of VIP. Treatment in a patient with a VIPoma begins with replacement of fluid losses and correction of electrolyte abnormalities. 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.
Gastroenteropancreatic neuroendocrine tumors	Neuroendocrine tumors (NETs) are heterogeneous neoplasms arising in secretory cells of the diffuse neuroendocrine system. They are characterized by a relatively indolent rate of growth and the ability to secrete a variety of peptide hormones and biogenic amines. Gastroenteropancreatic neuroendocrine tumors (GEP-NET) are a type of neuroendocrine tumor. Gastroenteropancreatic NETs (GEP-NETs) include carcinoid tumors of the gastrointestinal tract and pancreatic NETs (pNETs). GEP-NETs represent the second most common digestive cancer in terms of prevalence. GEP-NETs may present as hormonally functioning or nonfunctioning tumors and may have distinct clinical features based on their site of origin. Tumor grade and differentiation are crucial determinants of the clinical behavior of GEP-NETs. Whereas grade refers to the proliferative activity of neoplastic cells, differentiation refers to the extent to which tumor cells resemble their normal counterparts. The World Health Organization (WHO) classification of neuroendocrine neoplasms arising in the digestive system separates these tumors into two broad categories, well differentiated and poorly differentiated. Well-differentiated NETs consist of small, monomorphic cells arranged in islets or trabeculae with a "salt-and-pepper" chromatin pattern. Conversely, poorly differentiated tumors are often characterized as sheets of pleomorphic cells with extensive necrosis. Surgery is the mainstay for the treatment of local or locoregional GEP-NETs. Both octreotide and lanreotide are active at controlling hormonal symptoms associated with functioning advanced metastatic pNETs. First-line somatostatin analogs (SSAs) are generally used for patients with somatostatin receptor (SSTR)-positive disease.(1,9) Patients who have locoregional advanced and/or metastatic gastrointestinal tract (well-differentiated) NETs and carcinoid syndrome should be treated with octreotide or lanreotide. For symptomatic patients with unresectable locoregional pancreatic endocrine tumors (well-differentiated), those who initially present with clinically significant tumor burden, or those with clinically significant disease progression, octreotide or lanreotide should be considered if patients are not already receiving treatment with these options.(9)
Efficacy	**Mycapssa(2)** The efficacy of Mycapssa was established in a 9 month, randomized, double-blind, placebo-controlled study that enrolled 56 patients with acromegaly. In this study, patients initiated Mycapssa treatment twice daily 1 month after their last injection of somatostatin analogs. The starting dose was 40 mg (20 mg in the morning and 20 mg in the evening). Dose increase was allowed during dose titration to 60 mg (40 mg in the morning and 20 mg in the evening) and to a maximal dose of 80 mg daily (40 mg in the morning and 40 mg in the evening) until patients were deemed adequately controlled based on biochemical results and/or clinical judgement. Patients then maintained their target dose until end of treatment. The primary efficacy endpoint was somatostatin dose-adjusted proportion of patients who maintain their biochemical response, defined as an IGF-1 level less than or equal to the upper limit of normal at the end of 9 months of treatment. 58% of patients treated with Mycapssa vs 19% of patients treated with placebo maintained their biochemical response. **Sandostatin/Octreotide(3,11)** 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/octreotide to reduce blood levels of growth hormone and IGF-1 offers potential benefit before the effects of irradiation are manifested. **Sandostatin LAR(4)**

	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 less than 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 less than 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. A 6-month clinical trial of malignant carcinoid syndrome was performed in 93 patients who had previously been shown to be responsive to Sandostatin Injection. Sixty-seven patients were randomized at baseline to receive double-blind doses of 10 mg, 20 mg, or 30 mg Sandostatin LAR Depot every 28 days and 26 patients continued, unblinded, on their previous Sandostatin Injection regimen (100 to 300 mcg three times daily). Overall, mean daily stool frequency was as well controlled on Sandostatin LAR Depot as on Sandostatin Injection (approximately 2 to 2.5 stools/day). Seventy-eight patients with malignant carcinoid syndrome who had participated in this 6-month trial, subsequently participated in a 12-month extension study in which they received 12 injections of Sandostatin LAR Depot at 4-week intervals. For those who remained in the extension trial, diarrhea and flushing were as well controlled as during the 6-month trial. **Somatuline/Lanreotide(5,12)** 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, to 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. Twenty-seven 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. Fifty-nine 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(6)** A total of 112 patients with acromegaly participated in a 12-week, randomized, double-blind, multi-center study comparing placebo and Somavert. Twenty-six patients received Somavert 10 mg daily, 26 patients received Somavert 15 mg daily, 28 patients received Somavert 20 mg daily and 32 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 (2-6,11-12)	• **Mycapssa** (octreotide) is contraindicated in patients with a hypersensitivity to octreotide or any of the components of Mycapssa • **Sandostatin** (octreotide)**/Octreotide** is contraindicated in patients with a hypersensitivity to the drug or any of its components • **Sandostatin LAR** (octreotide) has no FDA labeled contraindications • **Somatuline Depot** (lanreotide)**/Lanreotide** is contraindicated in patients with a hypersensitivity to lanreotide • **Somavert** (pegvisomant) has no FDA labeled contraindications
Compendia supported diagnoses	For the purposes of the criteria, diagnoses deemed appropriate are those that are supported in AHFS, NCCN 1 or 2A recommended use, or DrugDex 1 or 2A level of evidence.

REFERENCES

Number	Reference
1	Cives, M., Strosberg, J. Gastroenteropancreatic Neuroendocrine Tumors. CA Cancer J Clin, November 2018; 68 (6) 471-487. https://doi.org/10.3322/caac.21493
2	Mycapssa prescribing information. MW Encap Ltd. March 2022.
3	Sandostatin prescribing information. Novartis. October 2022.
4	Sandostatin LAR prescribing information. Novartis. March 2021.
5	Somatuline Depot prescribing information. Ipsen Biopharmaceuticals, Inc. February 2023.
6	Somavert prescribing information. Pharmacia and Upjohn Company LLC. August 2021.
7	Melmed S, Bronstein MD, Chanson P, et al. A Consensus Statement on Acromegaly Therapeutic Outcomes. Nat Rev Endocrinol. 2018 Jul;14:552-561.
8	Kunz PL, Reidy-Lagunes D, Anthony LB, et al. Consensus Guidelines for the Management and Treatment of Neuroendocrine Tumors. Pancreas. 2013 May;42(4):557-577.
9	National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors. Version 2.2022 - December 2022.
10	Anezka C Rubin de Celis Ferrari, João Glassberg, Rachel P Riechelmann. Carcinoid Syndrome: Update on the Pathophysiology and Treatment. Clinics (Sao Paulo). 2018 Aug;73(1):e490s.
11	Octreotide prescribing information. Mylan Institutional LLC. November 2022.
12	Lanreotide prescribing information. Cipla USA Inc. December 2021.
13	Fleseriu M, Biller BMK, Freda PU, et al. A Pituitary Society Update to Acromegaly Management Guidelines. Pituitary. 2020 Oct;24:1-13.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Somatuline depot	lanreotide acetate extended release inj	120 MG/0.5ML ; 60 MG/0.2ML ; 90 MG/0.3ML	M ; N ; O ; Y	N		
Mycapssa	octreotide acetate cap delayed release	20 MG	M ; N ; O ; Y	N		
Sandostatin lar depot	octreotide acetate for im inj kit	10 MG ; 20 MG ; 30 MG	M ; N ; O ; Y	N		
Sandostatin	octreotide acetate inj	100 MCG/ML ; 1000 MCG/5ML ; 1000 MCG/ML ; 200 MCG/ML ; 50 MCG/ML ; 500 MCG/ML	M ; N ; O ; Y	O ; Y		
	octreotide acetate subcutaneous soln pref syr	100 MCG/ML ; 50 MCG/ML ; 500 MCG/ML	M ; N ; O ; Y	N		
Somavert	pegvisomant for inj	10 MG ; 15 MG ; 20 MG ; 25 MG ; 30 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
	Octreotide Acetate Inj 1000 MCG/ML (1 MG/ML)	1000 MCG/ML	6	Vials	30	DAYS			
	Octreotide Acetate Inj 200 MCG/ML (0.2 MG/ML)	1000 MCG/5ML ; 200 MCG/ML	18	Vials	30	DAYS			
	Octreotide Acetate Subcutaneous Soln Pref Syr	50 MCG/ML	90	Syringes	30	DAYS			
	Octreotide Acetate Subcutaneous Soln Pref Syr	100 MCG/ML	90	Syringes	30	DAYS			
	Octreotide Acetate Subcutaneous Soln Pref Syr	500 MCG/ML	90	Syringes	30	DAYS			
Mycapssa	Octreotide Acetate Cap Delayed Release 20 MG	20 MG	120	Capsules	30	DAYS			
Sandostatin	Octreotide Acetate Inj 100 MCG/ML (0.1 MG/ML)	100 MCG/ML	90	Ampules	30	DAYS			
Sandostatin	Octreotide Acetate Inj 50 MCG/ML (0.05 MG/ML)	50 MCG/ML	90	Ampules	30	DAYS			
Sandostatin	Octreotide Acetate Inj 500 MCG/ML (0.5 MG/ML)	500 MCG/ML	90	Ampules	30	DAYS			

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Sandostatin lar depot	Octreotide Acetate For IM Inj Kit 10 MG	10 MG	1	Kit	28	DAYS			
Sandostatin lar depot	Octreotide Acetate For IM Inj Kit 20 MG	20 MG	1	Kit	28	DAYS			
Sandostatin lar depot	Octreotide Acetate For IM Inj Kit 30 MG	30 MG	1	Kit	28	DAYS			
Somatuline depot	Lanreotide Acetate Extended Release Inj 120 MG/0.5ML	120 MG/0.5 ML	1	Syringe	28	DAYS			
Somatuline depot	Lanreotide Acetate Extended Release Inj 60 MG/0.2ML	60 MG/0.2 ML	1	Syringe	28	DAYS			
Somatuline depot	Lanreotide Acetate Extended Release Inj 90 MG/0.3ML	90 MG/0.3 ML	1	Syringe	28	DAYS			
Somavert	Pegvisomant For Inj 10 MG (As Protein)	10 MG	30	Vials	30	DAYS			
Somavert	Pegvisomant For Inj 15 MG (As Protein)	15 MG	30	Vials	30	DAYS			
Somavert	Pegvisomant For Inj 20 MG (As Protein)	20 MG	30	Vials	30	DAYS			
Somavert	Pegvisomant For Inj 25 MG (As Protein)	25 MG	30	Vials	30	DAYS			
Somavert	Pegvisomant For Inj 30 MG (As Protein)	30 MG	30	Vials	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
	octreotide acetate subcutaneous soln pref syr	100 MCG/ML ; 50 MCG/ML ; 500 MCG/ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Mycapssa	octreotide acetate cap delayed release	20 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Sandostatin	octreotide acetate inj	100 MCG/ML ; 1000 MCG/5ML ; 1000 MCG/ML ; 200 MCG/ML ; 50 MCG/ML ; 500 MCG/ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Sandostatin lar depot	octreotide acetate for im inj kit	10 MG ; 20 MG ; 30 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Somatuline depot	lanreotide acetate extended release inj	120 MG/0.5ML ; 60 MG/0.2ML ; 90 MG/0.3ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Somavert	pegvisomant for inj	10 MG ; 15 MG ; 20 MG ; 25 MG ; 30 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
	Octreotide Acetate Inj 1000 MCG/ML (1 MG/ML)	1000 MCG/ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
	Octreotide Acetate Inj 200 MCG/ML (0.2 MG/ML)	1000 MCG/5ML ; 200 MCG/ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
	Octreotide Acetate Subcutaneous Soln Pref Syr	100 MCG/ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
	Octreotide Acetate Subcutaneous Soln Pref Syr	50 MCG/ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
	Octreotide Acetate Subcutaneous Soln Pref Syr	500 MCG/ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Mycapssa	Octreotide Acetate Cap Delayed Release 20 MG	20 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Sandostatin	Octreotide Acetate Inj 100 MCG/ML (0.1 MG/ML)	100 MCG/ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Sandostatin	Octreotide Acetate Inj 50 MCG/ML (0.05 MG/ML)	50 MCG/ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Sandostatin	Octreotide Acetate Inj 500 MCG/ML (0.5 MG/ML)	500 MCG/ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Sandostatin lar depot	Octreotide Acetate For IM Inj Kit 10 MG	10 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Sandostatin lar depot	Octreotide Acetate For IM Inj Kit 20 MG	20 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Sandostatin lar depot	Octreotide Acetate For IM Inj Kit 30 MG	30 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
			Marketplace/BasicRx ; KeyRx
Somatuline depot	Lanreotide Acetate Extended Release Inj 120 MG/0.5ML	120 MG/0.5ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Somatuline depot	Lanreotide Acetate Extended Release Inj 60 MG/0.2ML	60 MG/0.2ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Somatuline depot	Lanreotide Acetate Extended Release Inj 90 MG/0.3ML	90 MG/0.3ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Somavert	Pegvisomant For Inj 10 MG (As Protein)	10 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Somavert	Pegvisomant For Inj 15 MG (As Protein)	15 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Somavert	Pegvisomant For Inj 20 MG (As Protein)	20 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Somavert	Pegvisomant For Inj 25 MG (As Protein)	25 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Somavert	Pegvisomant For Inj 30 MG (As Protein)	30 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

<table>
<tr><th>Module</th><th>Clinical Criteria for Approval</th></tr>
<tr><td>Mycapssa (octreotide)</td><td>
Initial Evaluation

Target agents will be approved when ALL of the following are met:

1. ONE of the following:
A. The requested agent is eligible for continuation of therapy AND ONE of the following:

<table>
<tr><th>Agents Eligible for Continuation of Therapy</th></tr>
<tr><td>All target agents are eligible for continuation of therapy</td></tr>
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Module	Clinical Criteria for Approval
	1. Information has been provided that indicates the patient has been treated with the requested agent within the past 180 days **OR** 2. The prescriber states the patient has been treated with the requested agent within the past 180 days AND is at risk if therapy is changed **OR** B. The patient has a diagnosis of acromegaly AND BOTH of the following: 1. ONE of the following: A. The patient has responded to and tolerated treatment with octreotide or lanreotide **OR** B. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** C. The prescriber has provided documentation that BOTH octreotide AND lanreotide 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 **AND** 2. The patient will NOT be using the requested agent in combination with Signifor LAR (pasireotide) **OR** C. The patient has another FDA approved indication for the requested agent **OR** D. The patient has another indication that is supported in compendia for the requested agent **AND** 2. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist, oncologist) or the prescriber 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 **Length of Approval:** 6 months **Compendia Allowed:** AHFS, NCCN 1 or 2a recommended use, or DrugDex 1 or 2a level of evidence NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target agent** will be approved 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 had clinical benefit with the requested agent (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 the prescriber 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 **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

Module	Clinical Criteria for Approval
Sandostatin (octreotide)/Octreotide prefilled syringes, vials and ampules	**Initial Evaluation** **Target agents** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** All target agents are eligible for continuation of therapy 1. Information has been provided that indicates the patient has been treated with the requested agent within the past 180 days **OR** 2. The prescriber states the patient has been treated with the requested agent within the past 180 days AND is at risk if therapy is changed **OR** B. The patient has a diagnosis of acromegaly AND BOTH of the following: 1. ONE of the following: A. 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** B. The patient is not a candidate for surgical resection **OR** C. The requested agent will be used in combination with or following pituitary radiation therapy **AND** 2. The patient will NOT be using the requested agent in combination with Signifor LAR (pasireotide) **OR** C. The patient has flushing and/or diarrhea associated with metastatic carcinoid tumors **OR** D. The patient has profuse watery diarrhea associated with Vasoactive Intestinal Peptide (VIP) secreting tumors **OR** E. The patient has another FDA approved indication for the requested agent and route of administration **OR** F. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** 2. If the request is for one of the following brand agents with an available generic equivalent (listed below), then ONE of the following: **Brand** / **Generic Equivalent** Sandostatin / octreotide A. The patient's medication history includes the required generic equivalent as indicated by: 1. Evidence of a paid claim(s) within the past 999 days **OR** 2. The prescriber has stated that the patient has tried the generic equivalent AND the generic equivalent was discontinued due to lack of effectiveness or an adverse event **OR** B. The patient has an intolerance or hypersensitivity to the generic equivalent that is NOT expected to occur with the brand agent **OR** C. The patient has an FDA labeled contraindication to the generic equivalent that is NOT expected to occur with the brand agent **OR** D. The prescriber has provided information to support the use of the requested brand agent over the generic equivalent **OR** E. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND**

Module	Clinical Criteria for Approval
	3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** F. The prescriber has provided documentation that the generic equivalent 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 **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist, oncologist) or the prescriber 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 **Length of Approval:** 6 months **Compendia Allowed:** AHFS, NCCN 1 or 2a recommended use, or DrugDex 1 or 2a level of evidence NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target agent** will be approved 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 had clinical benefit with the requested agent (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 the prescriber 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 **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.
Sandostatin LAR (octreotide)	**Initial Evaluation** **Target agents** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** All target agents are eligible for continuation of therapy 1. Information has been provided that indicates the patient has been treated with the requested agent within the past 180 days **OR**

Module	Clinical Criteria for Approval
	2. The prescriber states the patient has been treated with the requested agent within the past 180 days AND is at risk if therapy is changed **OR** B. The patient has a diagnosis of acromegaly AND BOTH of the following: 1. ONE of the following: A. 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** B. The patient is not a candidate for surgical resection **OR** C. The requested agent will be used in combination with or following pituitary radiation therapy **AND** 2. The patient will NOT be using the requested agent in combination with Signifor LAR (pasireotide) **OR** C. The patient has flushing and/or diarrhea associated with metastatic carcinoid tumors **OR** D. The patient has profuse watery diarrhea associated with Vasoactive Intestinal Peptide (VIP) secreting tumors **OR** E. The patient has another FDA approved indication for the requested agent and route of administration **OR** F. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** 2. ONE of the following: A. The patient has responded to and tolerated Sandostatin (octreotide) **OR** B. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** C. The prescriber has provided documentation that Sandostatin (octreotide) 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 **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist, oncologist) or the prescriber 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 **Length of Approval:** 6 months **Compendia Allowed:** AHFS, NCCN 1 or 2a recommended use, or DrugDex 1 or 2a level of evidence NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target agent** will be approved 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 had clinical benefit (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 the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**

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<tr><th>Module</th><th>Clinical Criteria for Approval</th></tr>
<tr><td></td><td>4. The patient does NOT have any FDA labeled contraindications to the requested agent

Length of Approval: 12 months

NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.</td></tr>
<tr><td>Somatuline Depot (lanreotide)/Lanreotide</td><td>Initial Evaluation

Target agents will be approved when ALL the following are met:

1. ONE of the following:
A. The requested agent is eligible for continuation of therapy AND ONE of the following:

<table><tr><th>Agents Eligible for Continuation of Therapy</th></tr><tr><td>All target agents are eligible for continuation of therapy</td></tr></table>
1. Information has been provided that indicates the patient has been treated with the requested agent within the past 180 days OR
2. The prescriber states the patient has been treated with the requested agent within the past 180 days AND is at risk if therapy is changed OR
B. The patient has a diagnosis of acromegaly AND BOTH of the following:
1. ONE of the following:
A. 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
B. The patient is not a candidate for surgical resection OR
C. The requested agent will be used in combination with or following pituitary radiation therapy AND
2. The patient will NOT be using the requested agent in combination with Signifor LAR (pasireotide) OR
C. The patient has a diagnosis of gastroenteropancreatic neuroendocrine tumors (GEP-NETs) AND BOTH of the following:
1. The tumors are well differentiated or moderately differentiated AND
2. ONE of the following:
A. The tumors are unresectable locally advanced OR
B. The patient has metastatic disease OR
D. The patient has a diagnosis of carcinoid syndrome (i.e., flushing and/or diarrhea) OR
E. The patient has another FDA approved indication for the requested agent and route of administration OR
F. The patient has another indication that is supported in compendia for the requested agent and route of administration AND
2. If the patient has an FDA approved indication, then ONE of the following:
A. The patient’s age is within FDA labeling for the requested indication for the requested agent OR
B. The prescriber has provided information in support of using the requested agent for the patient’s age for the requested indication AND
3. The prescriber is a specialist in the area of the patient’s diagnosis (e.g., endocrinologist, oncologist) or the prescriber 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

Length of Approval: 6 months

Compendia Allowed: AHFS, NCCN 1 or 2a recommended use, or DrugDex 1 or 2a level of evidence</td></tr>
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<tr><th>Module</th><th>Clinical Criteria for Approval</th></tr>
<tr><td></td><td>NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

Renewal Evaluation

Target agent will be approved 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 had clinical benefit (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 the prescriber 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

Length of Approval: 12 months

NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.</td></tr>
<tr><td>somavert (pegvisomant)</td><td>Initial Evaluation

Target agents will be approved when ALL the following are met:

1. ONE of the following:
A. The requested agent is eligible for continuation of therapy AND ONE of the following:

<table><tr><th>Agents Eligible for Continuation of Therapy</th></tr><tr><td>All target agents are eligible for continuation of therapy</td></tr></table>
1. Information has been provided that indicates the patient has been treated with the requested agent within the past 180 days OR
2. The prescriber states the patient has been treated with the requested agent within the past 180 days AND is at risk if therapy is changed OR
B. The patient has a diagnosis of acromegaly AND ALL of the following:
1. ONE of the following:
A. 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
B. The patient is not a candidate for surgical resection OR
C. The requested agent will be used in combination with or following pituitary radiation therapy AND
2. ONE of the following:
A. The patient has tried and had an inadequate response to Sandostatin LAR (octreotide suspension) or Somatuline Depot (lanreotide) OR
B. The patient has an intolerance or hypersensitivity to Sandostatin LAR (octreotide suspension) OR Somatuline Depot (lanreotide) OR
C. The patient has an FDA labeled contraindication to BOTH Sandostatin LAR (octreotide suspension) AND Somatuline Depot (lanreotide) OR
D. The patient is currently using Sandostatin LAR (octreotide suspension) or Somatuline Depot (lanreotide) and the requested agent will be used as add on (adjunctive) therapy OR</td></tr>
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Module	Clinical Criteria for Approval
	E. The prescriber has provided information in support of use of the requested agent over BOTH Sandostatin LAR (octreotide suspension) AND Somatuline Depot (lanreotide) **OR** F. The patient has tried Signifor LAR (pasireotide) AND had severe hyperglycemia **OR** G. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** H. prescriber has provided documentation that BOTH Sandostatin LAR (octreotide suspension) AND Somatuline Depot (lanreotide) 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 **AND** 3. The patient will NOT be using the requested agent in combination with Signifor LAR (pasireotide) **OR** C. The patient has another FDA approved indication for the requested agent and route of administration **OR** D. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** 2. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist, oncologist) or the prescriber 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 **Length of Approval:** 6 months **Compendia Allowed:** AHFS, NCCN 1 or 2a recommended use, or DrugDex 1 or 2a level of evidence NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target agent** will be approved 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 had clinical benefit (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 the prescriber 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 **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA	**Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** C. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Length of Approval**: Initial: 6 months; Renewal: 12 months