



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

Subject **Octreotide (Sandostatin[®],
Sandostatin LAR[®] Depot)**

Effective Date 7/15/2011
Next Review Date.....6/15/2012
Coverage Policy Number 5015

Table of Contents

Coverage Policy	1
General Background	3
Coding/Billing Information	5
References	6
Policy History.....	6

Hyperlink to Related Coverage Policies

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations. Proprietary information of CIGNA. Copyright ©2011 CIGNA

Coverage Policy

CIGNA covers octreotide (Sandostatin[®], Sandostatin LAR[®] Depot) as medically necessary for any of the following indications:

- acromegaly
- acute bleeding from gastroesophageal varices associated with cirrhosis
- carcinoid tumor management
- chemotherapy/radiation-induced diarrhea when there is failure of conservative medical management such as anti-motility agents
- enterocutaneous fistulae
- glucagonoma pre-operative management
- high-grade or anaplastic/small cell/atypical lung carcinoid
- insulinoma pre-operative management to stabilize glucose levels when an octreoscan is positive
- management of life-threatening hypotension due to carcinoid crisis during induction of anesthesia
- meningioma that is surgically inaccessible and recurrent when further radiation is not possible
- pituitary adenoma producing growth hormone (GH) or thyroid stimulating hormone (TSH)
- pancreatic resection for malignancy
- pancreaticocutaneous fistulae
- primary non-metastatic gastrinoma

- secretory diarrhea in acquired immune deficiency syndrome (AIDS) when there is failure of antimicrobial or anti-motility agents
- thymoma or thymic carcinoma second-line therapy following radiation for locally advanced unresectable disease
- vasoactive intestinal polypeptidoma (VIPomas)
 - profuse watery diarrhea associated with VIPoma-secreting tumor
 - preoperative management

When coverage is available and medically necessary, the dosage, frequency, site of administration, and duration of therapy should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to octreotide (Sandostatin[®], Sandostatin LAR[®] Depot) therapy.

FDA Labeled Indications

Sandostatin

Acromegaly

Sandostatin (octreotide acetate) is indicated to reduce blood levels of growth hormone and IGF-I (somatomedin C) in acromegaly patients who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses.

Carcinoid Tumors

Sandostatin is indicated for the symptomatic treatment of patients with metastatic carcinoid tumors where it suppresses or inhibits the severe diarrhea and flushing episodes associated with the disease. Sandostatin studies were not designed to show an effect on the size, rate of growth or development of metastases.

Vasoactive Intestinal Peptide Tumors (VIPomas)

Sandostatin is indicated for the treatment of the profuse watery diarrhea associated with VIP-secreting tumors. Sandostatin studies were not designed to show an effect on the size, rate of growth or development of metastases.

Sandostatin LAR Depot

Sandostatin LAR is a somatostatin analogue indicated for treatment in patients who have responded to and tolerated Sandostatin Injection subcutaneous injection for acromegaly; severe diarrhea/flushing episodes associated with metastatic carcinoid tumors; and profuse watery diarrhea associated with VIP-secreting tumors.

FDA Recommended Dosing

Sandostatin

Sandostatin (octreotide acetate) may be administered subcutaneously or intravenously. Subcutaneous injection is the usual route of administration of Sandostatin for control of symptoms. The initial dosage is usually 50 mcg administered twice or three times daily. Dosage information for patients with specific tumors is as follows:

Acromegaly

Dosage may be initiated at 50 mcg t.i.d. Beginning with this low dose may permit adaptation to adverse gastrointestinal effects for patients who will require higher doses. IGF-I (somatomedin C) levels every 2 weeks can be used to guide titration. Alternatively, multiple growth hormone levels at 0-8 hours after Sandostatin (octreotide acetate) administration permit more rapid titration of dose. The goal is to achieve growth hormone levels less than 5 ng/mL or IGF-I (somatomedin C) levels less than 1.9 U/mL in males and less than 2.2 U/mL in females. The dose most commonly found to be effective is 100 mcg t.i.d., but some patients require up to 500 mcg t.i.d. for maximum effectiveness. Sandostatin should be withdrawn yearly for approximately 4 weeks from patients who have received irradiation to assess disease activity. If growth hormone or IGF-I (somatomedin C) levels increase and signs and symptoms recur, Sandostatin therapy may be resumed.

Carcinoid Tumors

The suggested daily dosage of Sandostatin during the first 2 weeks of therapy ranges from 100-600 mcg/day in 2-4 divided doses (mean daily dosage is 300 mcg). In the clinical studies, the median daily maintenance dosage was approximately 450 mcg, but clinical and biochemical benefits were obtained in some patients with as little

as 50 mcg, while others required doses up to 1500 mcg/day. However, experience with doses above 750mcg/day is limited.

VIPomas

Daily dosages of 200-300 mcg in 2-4 divided doses are recommended during the initial 2 weeks of therapy (range 150-750 mcg) to control symptoms of the disease. On an individual basis, dosage may be adjusted to achieve a therapeutic response, but usually doses above 450 mcg/day are not required.

Sandostatin LAR Depot

Patients not currently receiving Sandostatin Injection subcutaneously - Acromegaly: 50 mcg three times daily Sandostatin Injection subcutaneously for 2 weeks followed by Sandostatin LAR 20 mg intragluteally every 4 weeks for 3 months; Carcinoid Tumors and VIPomas: Sandostatin Injection subcutaneously 100-600 mcg/day in 2-4 divided doses for 2 weeks followed by Sandostatin LAR 20 mg every 4 weeks for 2 months. Patients currently receiving Sandostatin Injection subcutaneously - Acromegaly: 20 mg every 4 weeks for 3 months; • Carcinoid Tumors and VIPomas: 20 mg every 4 weeks for 2 months.

Drug Availability

Sandostatin

Sandostatin (octreotide acetate) Injection is available in 1-mL ampuls and 5-mL multi-dose vials.

Sandostatin LAR Depot

Sandostatin LAR Depot is available in single-use kits containing a 5-mL vial of 10 mg, 20 mg or 30 mg strength, a syringe containing 2.5 mL of diluent, two sterile 1½" 19 gauge needles, and two alcohol wipes. An instruction booklet for the preparation of drug suspension for injection is also included with each kit.

General Background

Pharmacology

Octreotide acetate for injectable suspension (Sandostatin LAR[®] Depot) is a long-acting dosage form consisting of microspheres of the biodegradable glucose polymer, D, L-lactic and glycolic acids copolymer, containing octreotide. It maintains all of the clinical and pharmacological characteristics of the immediate-release dosage form octreotide acetate (Sandostatin[®]) injection with the added feature of slow release of octreotide from the site of injection, reducing the need for frequent administration.

Guidelines

National Comprehensive Cancer Network (NCCN)

The NCCN recommendations include the following:

Sandostatin

Meningiomas

Grade 2A

Treatment for surgically inaccessible recurrent meningiomas when further radiation is not possible.

Carcinoid Tumors

Grade 2A

Management of unresectable locoregional disease and/or distant metastases for asymptomatic unresectable metastases with low tumor burden; as initial treatment in patients with carcinoid syndrome or clinically significant tumor burden; as treatment for clinically significant progressive disease; as supplemental treatment for breakthrough symptoms in patients taking long-acting octreotide.

Multiple Endocrine Neoplasia Type 1

Grade 2A

Preoperative management to stabilize glucose levels in patients with insulinoma only if octreoscan positive; glucose levels in patients with glucagonoma; patients with vasoactive intestinal polypeptidoma.

Treatment of pituitary adenoma producing growth hormone or thyroid stimulating hormone in symptomatic patients, those with visual changes, or tumor greater than 1 cm as primary treatment; preoperative treatment; post-operative treatment with or without radiation therapy after incomplete resection.

Islet Cell Tumors

Grade 2A

Consider for management of primary nonmetastatic gastrinoma. Preoperative management to stabilize patients with glucagonoma or to stabilize patients with vasoactive intestinal polypeptidoma.

Poorly differentiated (high-grade or anaplastic)/small cell/atypical lung carcinoids

Grade 2A

Primary treatment for hormone-secreting tumors in combination with chemotherapy (using small cell lung cancer regimen) with or without radiation therapy.

Thymomas or Thymic Carcinomas

Grade 2A

Second-line therapy with or without prednisone following radiation therapy for locally advanced unresectable disease

Sandostatin LAR Depot

Carcinoid Tumors

Grade 2A

Management of unresectable locoregional disease and/or distant metastases for asymptomatic unresectable metastases with low tumor burden; as initial treatment in patients with carcinoid syndrome or clinically significant tumor burden; as treatment for clinically significant progressive disease.

Multiple Endocrine Neoplasia Type 1

Grade 2A

Preoperative management to stabilize glucose levels in patients with insulinoma only if octreoscan positive; glucose levels in patients with glucagonoma; patients with vasoactive intestinal polypeptidoma.

Treatment of pituitary adenoma producing growth hormone or thyroid stimulating hormone in symptomatic patients, those with visual changes, or tumor greater than 1 cm as primary treatment; preoperative treatment; postoperative treatment with or without radiation therapy after incomplete resection.

Islet Cell Tumors

Grade 2A

Consider for management of primary nonmetastatic gastrinoma

Preoperative management to stabilize patients with glucagonoma or to stabilize patients with vasoactive intestinal polypeptidoma.

Poorly differentiated (high-grade or anaplastic)/small cell/atypical lung carcinoids

Grade 2A

Primary treatment for hormone-secreting tumors in combination with chemotherapy (using small cell lung cancer regimen) with or without radiation therapy

American Association of Clinical Endocrinologists (AACE)

The effect of somatostatin analogues on long term acromegaly-related complications and mortality remains to be demonstrated. Nevertheless, these agents are currently the drugs of first choice in the medical treatment of acromegaly. Determining their optimal use in the scheme of management of various patients, however, necessitates individual considerations.

Clinical Efficacy

Off Label Covered Indications

Fistulae / Pancreatic Surgery

In a Cochrane review, Gurusamy et al (2010) examined if prophylactic somatostatin analogs should be used routinely in pancreatic surgery. These investigators searched the Cochrane Upper Gastrointestinal and

Pancreatic Diseases Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2009, issue 4), MEDLINE, EMBASE and Science Citation Index Expanded to November 2009. They included randomized controlled trials comparing prophylactic somatostatin or one of its analogs versus no drug or placebo during pancreatic surgery. Two authors independently assessed trials for inclusion and independently extracted data. They analyzed data with both the fixed-effect and the random-effects models using Review Manager (RevMan). They calculated the risk ratio (RR), MD or standardized mean difference (SMD) with 95 % CI based on an intention-to-treat or available case analysis. A total of 17 trials (of high risk of bias) involving 2143 patients were identified. The overall number of patients with post-operative complications was lower in the somatostatin analog group (RR 0.71; 95 % CI 0.62 to 0.82) but there was no difference in the peri-operative mortality, re-operation rate or hospital stay between the groups. The incidence of pancreatic fistula was lower in the somatostatin analog group (RR 0.64; 95 % CI 0.53 to 0.78). The proportion of these fistulas that were clinically significant was not mentioned in most trials. On inclusion of trials that clearly distinguished clinically significant fistulas, there was no difference between the two groups (RR 0.69; 95 % CI 0.34 to 1.41). Subgroup analysis revealed a shorter hospital stay in the somatostatin analog group than the controls for patients with malignant etiology (MD -7.57; 95 % CI -11.29 to -3.84). The authors concluded that somatostatin analogs reduce peri-operative complications but do not reduce peri-operative mortality. Further adequately powered trials with low risk of bias are necessary. Based on the current available evidence, the authors recommended somatostatin and its analogs for routine use in patients undergoing pancreatic resection for malignancy. There is currently no evidence to support their routine use in pancreatic surgeries performed for other indications.

Adverse Reactions

The most common side effects reported with octreotide and long-acting octreotide therapy include: gallbladder stones, biliary sludge, sinus bradycardia (<50 bpm), conduction abnormalities, arrhythmias, diarrhea, loose stools, nausea, abdominal discomfort, vomiting, flatulence, abnormal stools, abdominal distention, constipation, hypoglycemia, hyperglycemia, hypothyroidism, and goiter.

Concomitant administration of octreotide injection with cyclosporine may cause decreased levels of cyclosporine and result in transplant rejection. Patients taking insulin, oral hypoglycemic agents, beta-blockers, calcium channel blockers, or agents used to control fluid and electrolyte imbalance, may require dose adjustments of these therapeutic agents. Concomitant use of octreotide and bromocriptine increase the availability of bromocriptine.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

HCPSC Codes	Description
J2353	Injection, Octreotide, depot form for intramuscular injection, 1 mg
J2354	Injection, Octreotide, nondepot form for subcutaneous or intravenous injection, 25 mcg

ICD-9-CM Diagnosis Codes	Description
157.4	Malignant neoplasm of islet of langerhans
164.0	Malignant neoplasm of thymus
209.20-209.29	Malignant carcinoid tumors of other and unspecified sites
209.30	Malignant poorly differentiated neuroendocrine carcinoma, any site
225.2	Benign neoplasm of cerebral meninges
227.3	Benign neoplasm of pituitary gland and craniopharyngeal duct (pouch)
253.0	Acromegaly and gigantism

456.0	Esophageal varices with bleeding
458.29	Other iatrogenic hypotension
458.8	Other specified hypotension
787.94	Diarrhea

References

1. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice. Endocrine Practice Vol 10 No. 3 May/June 2004. Accessed 5/20/10. Available at <http://www.aace.com/pub/pdf/guidelines/AcromegalyGuidelines2004.pdf>
2. Gurusamy KS, Koti R, Fusai G, Davidson BR. Somatostatin analogues for pancreatic surgery. Cochrane Database Syst Rev. 2010;2:CD008370.
3. McEvoy GK, ed. AHFS 2011 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc; 2011.
4. NCCN Drugs & Biologics Compendium™. Sandostatin® (octreotide). Copyright 2011, National Comprehensive Cancer Network (NCCN).
5. NCCN Drugs & Biologics Compendium™. Sandostatin LAR® Depot (octreotide). Copyright 2011, National Comprehensive Cancer Network (NCCN).
6. Novartis Pharmaceuticals Corporation. Octreotide (Sandostatin LAR®) injection suspension package insert. East Hanover, NJ: Novartis Pharmaceuticals Corporation, Jan 2010.
7. Novartis Pharmaceuticals Corporation. Octreotide (Sandostatin®) injection package insert. East Hanover, NJ: Novartis Pharmaceuticals Corporation, Jan 2010.

Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	6/15/2008	5015	Octreotide (Sandostatin®), Sandostatin LAR® Depot)

“CIGNA”, “CIGNA HealthCare” and the “Tree of Life” logo are registered service marks of CIGNA Intellectual Property, Inc., licensed for use by CIGNA Corporation and its operating subsidiaries. All products and services are provided by such operating subsidiaries and not by CIGNA Corporation. Such operating subsidiaries include Connecticut General Life Insurance Company, CIGNA Health and Life Insurance Company, CIGNA Behavioral Health, Inc., CIGNA Health Management, Inc., and HMO or service company subsidiaries of CIGNA Health Corporation and CIGNA Dental Health, Inc. In Arizona, HMO plans are offered by CIGNA HealthCare of Arizona, Inc. In California, HMO plans are offered by CIGNA HealthCare of California, Inc. In Connecticut, HMO plans are offered by CIGNA HealthCare of Connecticut, Inc. In North Carolina, HMO plans are offered by CIGNA HealthCare of North Carolina, Inc. In Virginia, HMO plans are offered by CIGNA HealthCare Mid-Atlantic, Inc. All other medical plans in these states are insured or administered by Connecticut General Life Insurance Company or CIGNA Health and Life Insurance Company.