Reference number
1734-A

SPECIALTY GUIDELINE MANAGEMENT

SANDOSTATIN (octreotide acetate injection)
BYNFEZIA PEN (octreotide acetate injection)
MYCAPSSA (octreotide delayed-release capsule)
SANDOSTATIN LAR DEPOT (octreotide acetate for injectable suspension)
octreotide acetate injection

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. octreotide acetate/Sandostatin/Bynfezia Pen:
      a. Indicated to reduce blood levels of growth hormone (GH) and insulin growth factor-1 (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.
      b. 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.
      c. Indicated for the treatment of the profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors.

   2. Sandostatin LAR: Sandostatin LAR Depot is indicated in patients who have responded to and tolerated Sandostatin subcutaneous injection for:
      a. Long-term maintenance therapy in acromegalic patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option.
      b. Long-term treatment of the severe diarrhea and flushing episodes associated with metastatic carcinoid tumors.
      c. Long-term treatment of the profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors.

   3. Mycapssa is indicated for long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide.

B. Compendial Uses *(applies to injectable products)*
   1. Neuroendocrine tumors (NETs):
      a. Tumors of the gastrointestinal (GI) tract, lung, and thymus (carcinoid tumors)
      b. Tumors of the pancreas (islet cell tumors)
      c. Gastroenteropancreatic neuroendocrine tumors (GEP-NETs)
   2. Pheochromocytoma and paraganglioma
   3. Thymomas and thymic carcinomas
   4. Congenital hyperinsulinism (CHI)/persistent hyperinsulinemic hypoglycemia of infancy (PHHI)(octreotide and Sandostatin only)
   5. Acquired immune deficiency syndrome (AIDS)-associated diarrhea

6. Inoperable bowel obstruction
7. Cancer-related diarrhea
8. Enterocutaneous fistula
9. Gastroesophageal varices
10. Pancreatic fistulas
11. Pituitary adenoma
12. Short bowel syndrome
13. Zollinger-Ellison syndrome

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. For acromegaly:
   1. For initial approval: Laboratory report indicating high pretreatment insulin-like growth factor-1 (IGF-1) level and chart notes indicating an inadequate or partial response to surgery or radiotherapy or a clinical reason for not having surgery or radiotherapy.
   2. For continuation: Laboratory report indicating normal current IGF-1 levels or chart notes indicating that the member's IGF-1 level has decreased or normalized since initiation of therapy.

B. Cancer-related diarrhea: Chart notes indicating grade 3 or 4 diarrhea.

III. CRITERIA FOR INITIAL APPROVAL

A. Acromegaly

Authorization of 12 months may be granted for the treatment of acromegaly when all of the following criteria are met:

1. Member has a high pretreatment IGF-1 level for age and/or gender based on the laboratory reference range.
2. Member had an inadequate or partial response to surgery or radiotherapy OR there is a clinical reason why the member has not had surgery or radiotherapy.
3. For Mycapssa requests, member has previously responded to and tolerated treatment with octreotide or lanreotide.

B. Neuroendocrine tumors (NETs) (injectable products only)

1. Authorization of 12 months may be granted for treatment of NETs of the gastrointestinal (GI) tract, lung, and thymus (carcinoid tumors).
2. Authorization of 12 months may be granted for treatment of NETs of the pancreas (islet cell tumors), including gastrinomas, glucagonomas, and insulinomas.
3. Authorization of 12 months may be granted for treatment of gastroenteropancreatic neuroendocrine tumors (GEP-NETs).

C. Carcinoid syndrome (injectable products only)

Authorization of 12 months may be granted for treatment of carcinoid syndrome.

D. Vasoactive intestinal peptide tumors (VIPomas) (injectable products only)

Authorization of 12 months may be granted for management of symptoms related to hormone hypersecretion of VIPomas.

E. Pheochromocytoma and paraganglioma (injectable products only)

Authorization of 12 months may be granted for treatment of pheochromocytoma and paraganglioma.

F. Thymomas and thymic carcinomas (injectable products only)
Authorization of 12 months may be granted for treatment of thymomas and thymic carcinomas.

G. Congenital hyperinsulinism (CHI)/persistent hyperinsulinemic hypoglycemia of infancy (octreotide and Sandostatin only)
Authorization of 6 months may be granted for treatment of CHI and persistent hyperinsulinemic hypoglycemia in an infant.

H. AIDS-associated diarrhea (injectable products only)
Authorization of 12 months may be granted for treatment of AIDS-associated severe secretory diarrhea when anti-microbial (e.g., ciprofloxacin or metronidazole) or anti-motility agents (e.g., loperamide or diphenoxylate and atropine) have become ineffective.

I. Inoperable bowel obstruction in cancer (injectable products only)
Authorization of 12 months may be granted for management of GI symptoms (e.g., nausea, pain, vomiting) of inoperable bowel obstruction in members with cancer.

J. Cancer-related diarrhea (injectable products only)
Authorization of 12 months may be granted for treatment of cancer-related diarrhea when the member has grade 3 or greater diarrhea according to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE).

K. Enterocutaneous fistula (injectable products only)
Authorization of 12 months may be granted for management of volume depletion from enterocutaneous fistula.

L. Gastroesophageal varices (injectable products only)
Authorization of 6 months may be granted for treatment of acute bleeding of gastroesophageal varices associated with cirrhosis.

M. Pancreatic fistulas (injectable products only)
Authorization of 6 months may be granted for prevention and treatment of pancreatic fistulas following pancreatic surgery.

N. Pituitary adenoma (injectable products only)
Authorization of 12 months may be granted for treatment of pituitary adenoma.

O. Short bowel syndrome (injectable products only)
Authorization of 12 months may be grated for treatment of short bowel syndrome when the daily intravenous fluid requirement is greater than 3 liters.

P. Zollinger-Ellison syndrome (injectable products only)
Authorization of 12 months may be grated for treatment of Zollinger-Ellison syndrome.

IV. CONTINUATION OF THERAPY

A. Acromegaly
Authorization of 12 months may be granted for continuation of therapy for acromegaly when the member's IGF-1 level has decreased or normalized since initiation of therapy.

B. NETs, Carcinoid syndrome, VIPomas, pheochromocytoma/paraganglioma, thymomas/thymic carcinomas, AIDS-associated diarrhea, bowel obstruction, cancer-related diarrhea, and Zollinger-Ellison syndrome (injectable products only)
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when the member is experiencing clinical benefit as evidenced by improvement or stabilization in clinical signs and symptoms since initiation of therapy.

C. All other indications
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. REFERENCES

1. Octreotide acetate [package insert]. Morgantown, WV: Mylan Institutional LLC; November 2022.
2. Sandostatin [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; November 2023.
3. Sandostatin LAR Depot [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2023.
4. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed November 14, 2023.
5. Katznelson L, Laws ER, Melmed S, et al. Acromegaly: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99:3933-3951.
6. American Association of Clinical Endocrinologists Acromegaly Guidelines Task Force. Medical guidelines for clinical practice for the diagnosis and treatment of acromegaly – 2011 update. *Endocr Pract*. 2011;17(suppl 4):1-44.
7. The NCCN Clinical Practice Guidelines in Oncology® Neuroendocrine and Adrenal Tumors (Version 1.2023). © 2023 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed November 14, 2023.
8. Rinke A, Muller H, Schade-Brittinger C, et al. Placebo-controlled, double-blind, prospective, randomized study on the effect of octreotide LAR in the control of tumor growth in patients with metastatic neuroendocrine midgut tumors: a report from the PROMID study group. *J Clin Oncol*. 2009;27:4656-4663.
9. Thapar K, Kovacs K, Stefaneanu L, et al: Antiproliferative effect of the somatostatin analogue octreotide on growth hormone-producing pituitary tumors: Results of a multicenter randomized trial. Mayo Clin Proc 1997; 72:893-900.
10. The NCCN Clinical Practice Guidelines in Oncology® Thymomas and Thymic Carcinomas. (Version 1.2023). © 2023 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed November 14, 2023.
11. The NCCN Clinical Practice Guidelines in Oncology® Palliative Care (Version 2.2023). © 2023 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed November 14, 2023.
12. Harris AG, O'Dorisio TM, Woltering EA, et al. Consensus statement: Octreotide dose titration in secretory diarrhea. Diarrhea Management Consensus Development Panel. Dig Dis Sci. 1995;40(7):1464-1473.
13. Fried M. Octreotide in the treatment of refractory diarrhea. Digestion. 1999,60:42-46.
14. Edmunds MC, Chen JD, Soykan I, et al. Effect of octreotide on gastric and small bowel motility in patients with gastroparesis. Aliment Pharmacol Ther. 1998;12(2):167-174.
15. Ripamonti C, Mercadante S, Groff L, et al. Role of octreotide, scopolamine butylbromide, and hydration in symptom control of patients with inoperable bowel obstruction and nasogastric tubes: A prospective randomized trial. J Pain Symptom Manage. 2000;19(1):23-34.
16. Mercadante S, Ripamonti C, Casuccio A, et al. Comparison of octreotide and hyoscine butylbromide in controlling gastrointestinal symptoms due to malignant inoperable bowel obstruction. Support Care Cancer. 2000;8(3):188-191.
17. Dorta G. Role of octreotide and somatostatin in the treatment of intestinal fistulae. Digestion. 1999;60 Suppl 2:53-56.

18. Jamil M, Ahmed U, Sobia H. Role of somatostatin analogues in the management of enterocutaneous fistulae. J Coll Physicians Surg Pak. 2004;14(4):237-240.
19. Rahbour G, Siddiqui MR, Ullah MR, et al. A meta-analysis of outcomes following use of somatostatin and its analogues for the management of enterocutaneous fistulas. Ann Surg. 2012;256(6):946-954.
20. Freitas DS, Sofia C, Pontes JM, et al. Octreotide in acute bleeding esophageal varices: A prospective randomized study. Hepatogastroenterology. 2000;47(35):1310-1314.
21. Imperiale TF, Teran JC, McCullough AJ. A meta-analysis of somatostatin versus vasopressin in the management of acute esophageal variceal hemorrhage. Gastroenterology. 1995;109(4):1289-1294.
22. Gøtzsche PC, Hróbjartsson A. Somatostatin analogues for acute bleeding oesophageal varices. Cochrane Database Syst Rev. 2008;(3):CD000193.
23. Erstad BL. Octreotide for acute variceal bleeding. Ann Pharmacother. 2001;35(5):618-626.
24. Corley DA, Cello JP, Adkisson W, et al. Octreotide for acute esophageal variceal bleeding: A meta-analysis. Gastroenterology. 2001;120(4):946-954.
25. Gross M, Schiemann U, Muhlhofer A, Zoller WG. Meta-analysis: Efficacy of therapeutic regimens in ongoing variceal bleeding. Endoscopy. 2001;33(9):737-746.
26. Li-Ling J, Irving M. Somatostatin and octreotide in the prevention of postoperative pancreatic complications and the treatment of enterocutaneous pancreatic fistulas: A systematic review of randomized controlled trials. Br J Surg. 2001;88(2):190-199.
27. Machado NO. Pancreatic fistula after pancreatectomy: Definitions, risk factors, preventive measures, and management – Review. Int J Surg Oncol. 2012;2012:602478.
28. Adachi T, Kuroki T, Kitasato A, et al. Safety and efficacy of early drain removal and triple-drug therapy to prevent pancreatic fistula after distal pancreatectomy. Pancreatology 2015;15:411-416.
29. Gurusamy KS, Koti R, Fusai G, Davidson BR. Somatostatin analogues for pancreatic surgery. Cochrane Database Syst Rev. 2013;4:CD008370.
30. Alberta Provincial CNS Tumour Team. Pituitary adenomas. Clinical Practice Guideline No. CNS-006 Edmonton, AB: Alberta Health Services, Cancer Care; August 2012.
31. Peeters M, Van den Brande J, Francque S. Diarrhea and the rationale to use Sandostatin. Acta Gastroenterol Belg. 2010;73(1):25-36.
32. Mystakidou K, Tsilika E, Kalaidopoulou O, et al. Comparison of octreotide administration vs conservative treatment in the management of inoperable bowel obstruction in patients with far advanced cancer: A randomized, double- blind, controlled clinical trial. Anticancer Res. 2002;22(2B):1187-1192.
33. American Gastroenterological Association. American Gastroenterological Association medical position statement: Short bowel syndrome and intestinal transplantation. Gastroenterology. 2003;124(4):1105-1110.
34. Loehrer PJ Sr, Wang W, Johnson DH, et al. Octreotide alone or with prednisone in patients with advanced thymoma and thymic carcinoma: An Eastern Cooperative Oncology Group Phase II Trial. J Clin Oncol. 2004;22(2):293-299.
35. Leandros E, Antonakis PT, Albanopoulos K, et al. Somatostatin versus octreotide in the treatment of patients with gastrointestinal and pancreatic fistulas. Can J Gastroenterol. 2004;18(5):303-306.
36. Allen PJ, Gonen M, Brennan MF, et al. Pasireotide for postoperative pancreatic fistula. N Engl J Med. 2014;370(21):2014-2022.
37. Bynfezia Pen [package insert]. Cranbury, NJ: Sun Pharmaceutical Industries Inc.; April 2020.
38. Mycapssa [package insert]. Dublin, Ireland: Amryt Pharmaceuticals, Inc.; March 2022.
39. Lexicomp Online®, Lexi-Drugs. Waltham, MA: UpToDate, Inc.; Updated November 1 , 2023. http://online.lexi.com [available with subscription]. Accessed November 10, 2023.