Medical Coverage Policy | Lutathera (lutetium Lu 177 dotatate)

EFFECTIVE DATE: 07|01|2018
POLICY LAST UPDATED: 06|5|2018

OVERVIEW

Lutathera (lutetium Lu 177 dotatate) is used for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendrocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults.

This policy is applicable to BlueCHiP for Medicare products only. For Commercial Products, see related policy section

PRIOR AUTHORIZATION

Prior authorization is required for BlueCHiP for Medicare

POLICY STATEMENT

Blue CHiP for Medicare

Lutathera is medically necessary when the criteria is met.

MEDICAL CRITERIA

Initial Evaluation

Lutathera will be approved when ALL of the following are met:

1. ONE of the following:
   - A. There is documentation that the patient is currently being treated with the requested agent
     OR
   - B. The prescriber states the patient is currently being treated with the requested agent AND is at risk if therapy is changed
     OR
   - C. The patient has a diagnosis of somatostatin-positive, gastroenteropancreatic neuroendocrine tumor (GEP-NETS) AND BOTH of the following:
     - i. The patient has locally advanced, inoperable, or metastatic carcinoid tumor **AND**
     - ii. The patient will discontinue long-acting somatostatin analog (e.g. octreotide LAR) for at least 4 weeks prior to initiating the requested agent

     OR
   - D. The patient has another FDA approved indication for the requested agent

   AND
2. The prescriber is a specialist (e.g., oncologist) or the prescriber has consulted with a specialist
   AND
3. The patient does NOT have any FDA labeled contraindications to the requested agent
   AND
4. The requested dose is within FDA labeled dosing for the requested indication
   AND
5. The patient has NOT exceeded 4 treatment doses in lifetime

Length of Approval: GEP-NETs – 12 months for maximum 4 doses per lifetime; All other FDA approved diagnosis – 12 months.

Renewal Evaluation
Lutathera will be approved when ALL of the following are met:

1. The patient has been previously approved for the requested agent through the Medical Drug Review process
   AND
2. Treatment-related toxicities (e.g., anemia, hepatotoxicity, neutropenia, renal toxicity, thrombocytopenia) are resolved prior to re-starting the requested agent
3. The patient has NOT exceeded 4 treatment doses in lifetime

Length of Approval: GEP-NETs – 12 months for maximum 4 doses per lifetime; All other FDA approved diagnosis – 12 months.

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

1. The patient has been previously approved
   AND
2. Treatment-related toxicities (e.g., anemia, hepatotoxicity, neutropenia, renal toxicity, thrombocytopenia) are resolved prior to re-starting the requested agent

Length of Approval: 12 months

BACKGROUND

Carcinoid Syndrome
Carcinoid syndrome is a constellation of symptoms resulting from hormones secreted by carcinoid tumors. These tumors can either be active or inactive. Active tumors secrete various hormones and vasoactive peptide substances such as adrenocorticotropic hormone (ACTH), serotonin, histamine, and tachykinins. The most common symptoms of carcinoid syndrome are flushing and diarrhea.

Somatostatin analogs (octreotide or lanreotide) are recommended as initial therapy in patients with carcinoid syndrome. Addition of telotristat to somatostatin analog therapy is recommended for patients who are refractory to somatostatin analog therapy.

Neuroendocrine Tumors
Neuroendocrine tumors are thought to arise from cells throughout the diffuse endocrine system. The comprise of a broad family of tumors, the most common of which are carcinoid tumors (most commonly arising in the lungs and bronchi, small intestine, appendix, rectum, and thymus) and pancreatic neuroendocrine tumors. Other less common neuroendocrine tumors include those arising in the parathyroid, thyroid, adrenal, and pituitary glands.

Patients with neuroendocrine tumors may or may not have symptoms attributable to hormonal hypersecretion. These symptoms include intermittent flushing and diarrhea in patients with carcinoid syndrome, hypertension in patients with pheochromocytoma, and symptoms attributable to secretion of insulin, glucagon, gastrin, and other peptides in patients with pancreatic neuroendocrine tumors. Patients with hormonal symptoms are considered to have functional tumors and those without symptoms are considered to have nonfunctional tumors.

Two-thirds of carcinoid tumors arise in the GI tract, including the stomach, small intestine, appendix, and rectum. Neuroendocrine tumors of the GI tract, lung, or thymus may secrete various hormones and vasoactive peptides. Tumors arising in the small intestine or appendix are more commonly associated with

carcinoid syndrome. Approximately 50 to 66% of patients with carcinoid syndrome develop valvular cardiac complications consisting of tricuspid regurgitation and/or pulmonary stenosis.

Somatostatin receptor-based imaging is recommended to assess the somatostatin receptor status of locoregional unresectable and/or metastatic neuroendocrine tumors of the GI tract, lung, or thymus, if treatment with octreotide or lanreotide is being considered. Somatostatin analogs (octreotide or lanreotide) are recommended for control of symptoms and tumor growth in patients who have metastatic neuroendocrine tumors and carcinoid syndrome. The long-acting release (LAR) formulation of octreotide is commonly used for the chronic management of symptoms in patients with carcinoid syndrome. Telotristat in combination with octreotide or lanreotide should be considered for persistent diarrhea.

Approximately 1% of pancreatic cancers are malignant pancreatic neuroendocrine tumors. Majority of pancreatic neuroendocrine tumors are nonfunction (40 to 91%). The remaining manifest with clinically evident hormonal symptoms. VIPoma is the rarest form of pancreatic neuroendocrine tumors, also described as cholecystokininoma (CCKoma). Primary treatment approach for localized pancreatic neuroendocrine tumors is resection, when possible. For patients with unresectable disease, those who initially present with clinically significant tumor burden, or those with clinically significant disease progression, octreotide or lanreotide should be considered. Patients with pancreatic neuroendocrine tumors and symptoms of hormone secretion should, in most cases, receive treatment with either lanreotide or octreotide and/or other medication to manage their symptoms.

Efficacy

The efficacy of Lutathera in patients with progressive, well-differentiated, locally advanced/inoperable or metastatic somatostatin receptor positive midgut carcinoid tumors was established in NETTER-1 (NCT01578239), a randomized, multicenter, open-label, active-controlled trial. Key eligibility criteria included Ki67 index ≤ 20%, Karnofsky performance status ≥ 60, confirmed presence of somatostatin receptors on all lesions (OctreoScan uptake ≥ normal liver), creatinine clearance ≥ 50 mL/min, no prior treatment with peptide receptor radionuclide therapy (PRRT), and no prior external radiation therapy to more than 25% of the bone marrow.

Two hundred twenty-nine (229) patients were randomized (1:1) to receive either Lutathera 7.4 GBq (200 mCi) every 8 weeks for up to 4 administrations (maximum cumulative dose of 29.6 GBq) or high-dose long-acting octreotide (defined as 60 mg by intramuscular injection every 4 weeks). Patients in the Lutathera arm also received long-acting octreotide 30 mg as an intramuscular injection 4 to 24 hours after each Lutathera dose and every 4 weeks after completion of Lutathera treatment until disease progression or until week 76 of the study. Patients in both arms could receive short-acting octreotide for symptom management; however, short-acting octreotide was withheld for at least 24 hours before each Lutathera dose.

Randomization was stratified by OctreoScan tumor uptake score (Grade 2, 3 or 4) and the length of time that patients had been on the most recent constant dose of octreotide prior to randomization (≤ 6 or > 6 months). The major efficacy outcome measure was progression free survival (PFS) as determined by a blinded independent radiology committee (IRC) per RECIST v1.1. Additional efficacy outcome measures were overall response rate (ORR) by IRC, duration of response, and overall survival (OS).

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Evidence of Coverage for applicable physician administered drug services benefits/coverage.

CODING

Blue CHiP for Medicare and Commercial

For claims with a date of service before 7/12/2018

There is no specific HCPCS code, claims must be filed with an unlisted code such as J3490 and the NDC number

For claims filed after 7/1/2018

C9031 Lutetium Lu 177, dotatate, therapeutic, 1 mCi

RELATED POLICIES

Unlisted Drugs Policy

PUBLISHED

Provider Update July 2018

REFERENCES

1. Lutathera prescribing information. Advanced Accelerator Applications S.A. January 2018.
2. Jonathan R Strosberg. Treatment of carcinoid syndrome. UpToDate. Accessed September 2017.
3. NCCN Clinical Practice Guidelines. Neuroendocrine Tumors. Version 3.2017 – June 13,2017. Available at: https://www.nccn.org/professionals/physician_gls/PDF/neuroendocrine.pdf. Accessed February 2018.