STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Lutathera (lutetium Lu 177 dotatate)
PAM-027

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	01/01/2021
Revision Number:	4	**Last Rev Date:**	01/19/2024
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	01/17/2025
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	12/23/2020

Overview

Medication:[1]	lutetium Lu 177 dotatate
Brand Name:	Lutathera®
Pharmacologic Category:	Radiolabeled somatostatin analog
FDA-Approved Indication(s):	Treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults
How Supplied:	30 mL single-dose vial containing 7.4 GBq (200 mCi) ± 10% of lutetium Lu 177 dotatate at the time of injection
Dosage and Administration:	• 7.4 GBq (200 mCi) every 8 weeks for a total of 4 doses • Discontinue long-acting somatostatin analogs (e.g., long-acting octreotide) for at least 4 weeks prior to initiating Lutathera® • Administer short-acting octreotide as needed (discontinue at least 24 hours prior to initiating Lutathera®)
Benefit Category:	Medical

Descriptive Narrative

Neuroendocrine tumors (NETs) are a heterogeneous group of malignancies arising in the diffuse neuroendocrine system. They are characterized by a relatively slow rate of growth and the production of a variety of peptide hormones and biogenic amines. Although NETs may develop in almost any organ, they arise predominately within the gastrointestinal (GI) tract and the pancreas. The term carcinoid is still widely used to describe NETs originating in the GI tract.

Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) have distinct clinical features based on their site of origin. Metastatic mid-gut carcinoids often secrete serotonin and other vasoactive substances, producing the typical carcinoid syndrome with symptoms of flushing, diarrhea, and right-sided valvular heart disease.

Lutathera® is a targeted form of systemic radiotherapy (radioactive drug) peptide receptor radionuclide therapy that binds to cell surface somatostatin receptors which may be present in certain tumors. After binding to the receptor, the drug enters the cell, allowing radiation to

cause damage to the tumor cells. Most GEP-NETs express high-affinity receptors for somatostatin. Somatostatin-based imaging can also provide information on tumor burden and location. Lutathera® is a treatment option in adult patients with GEP-NETs who progress despite first-line therapy.

Guidelines

As new and emerging therapies are rapidly coming to market, oncology treatment recommendations and guidelines are constantly changing. To keep up with these changes, the National Comprehensive Cancer Network (NCCN) publishes guidelines which are developed and updated by 60 individual panels, comprising over 1,660 clinicians and oncology researchers from the 31 NCCN Member Institutions.[2]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

The information referenced at the time of this policy writing/revision is from:

- NCCN Guidelines for Neuroendocrine and Adrenal Tumors (Version 1.2023 – August 2, 2023)[3]

NCCN Guidelines® Recommendation(s) for lutetium Lu 177 dotatate (Lutathera®)
(1) Neuroendocrine Tumors of the Gastrointestinal Tract (Well-Differentiated Grade 1/2) [a,b,c] A. Peptide receptor radionuclide therapy (PRRT) with lutetium Lu 177 dotatate [if somatostatin receptor (SSTR)-positive and progression on octreotide long-acting release (LAR)/lanreotide)]: i. Category 2A, preferred regimen (Category 1 preferred regimen for progressive mid-gut tumors) (2) Bronchopulmonary/Thymus Neuroendocrine Tumors [d] A. PRRT with lutetium Lu 177 dotatate (if SSTR-positive and progression on octreotide LAR or lanreotide): i. Category 2A, useful in certain circumstances: (3) Pancreatic Neuroendocrine Tumors (Well-Differentiated Grade 1/2) [d] A. Locoregional Advanced Disease and/or Distant Metastases i. PRRT with lutetium Lu 177 dotatate (if SSTR-positive and progression on octreotide LAR or lanreotide: Category 2A, preferred regimen (4) Well-Differentiated, Grade 3 Neuroendocrine Tumors A. Locally advanced/metastatic disease with favorable biology (unresectable with clinically significant tumor burden or evidence of disease progression) i. PRRT with lutetium Lu 177 dotatate (if SSTR-positive): Category 2A [e] (5) Pheochromocytoma/Paraganglioma A. Locally unresectable: Consider PRRT with lutetium Lu 177 dotatate (if SSTR-positive): Category 2A [f, g] B. Distant metastases: Consider PRRT with lutetium Lu 177 dotatate (if SSTR-positive): Category 2A [f, g]
[a] For symptom and/or tumor control, octreotide LAR 20–30 mg IM or lanreotide 120 mg SC every 4 weeks. Higher doses have been shown to be safe. For breakthrough symptoms, octreotide 100–250 mcg SC TID can be considered. [b] The PROMID trial showed an antitumor effect of octreotide LAR in advanced neuroendocrine tumors of the midgut. The CLARINET trial showed an antitumor effect of lanreotide in advanced, well-differentiated metastatic grade 1 and grade 2 GEP NETs. [c] If injection site-related complications occur, consider switching to another SSA. [d] If clinically significant disease progression, treatment with octreotide LAR or lanreotide should be discontinued for non-functional tumors and continued in patients with functional tumors; these regimens may be used in combination with any of the subsequent options. [e] Consider trial of somatostatin analog (SSA) before PRRT. Preliminary data suggest reduced efficacy if high Ki-67 and/or FDG-PET avid. [f] SSTR PET tracers include: 68Ga-DOTATATE, 64Cu-DOTATATE, and 68Ga-DOTATOC. [g] Data are limited on the use of PRRT with lutetium Lu 177 dotatate in this setting.

NCCN Guidelines®: Principles of therapy with lutetium Lu 177 dotatate (Lutathera®)

• Lutetium Lu 177 dotatate is a radiolabeled SSA used as peptide receptor radionuclide therapy (PRRT). It is approved for the treatment of SSTR-positive GEP NETs, including foregut, midgut, and hindgut NET in adults.
• Currently there are no randomized data, but there are reports of treatment efficacy and favorable outcomes when PRRT is used for PanNETs, pheochromocytomas, paragangliomas, and bronchopulmonary/thymic NETs.
• If feasible, participation in clinical trials of PRRT is strongly recommended for patients with rare groups of NET.
• PRRT may reduce symptoms for symptomatic insulinoma and other functional NETs.
• Key eligibility:
  ○ Well-differentiated NET
  ○ SSTR expression of NET as detected by SSTR-PET/CT or SSTR-PET/MR *
  ○ Adequate bone marrow, renal, and hepatic function
* Scan Types
PET/CT Procedure that combines a positron emission tomography (PET) scan and a computed tomography (CT) scan. The PET and CT scans are done at the same time with the same machine. The combined scans give more detailed pictures of areas inside the body than either scan gives by itself.[4]
PET/MR Procedure that combines a positron emission tomography (PET) scan and a magnetic resonance imaging (MRI) in one scanner, allowing for simultaneous acquisition of MR and PET images. The MR's capacity to produce high-resolution images, combined with the PET's ability to display cell metabolism and molecular events results in outstanding images that denote organ position, function, and metabolism all in one image. The simultaneous image acquisition technique greatly reduces radiation exposure for the subject and reduces image acquisition time and effort.[5]

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Eastern Cooperative Oncology Group (ECOG) Performance Status[6]

Developed by the Eastern Cooperative Oncology Group (ECOG), now part of the ECOG-ACRIN Cancer Research Group, and published in 1982, the ECOG Performance Status Scale describes a patient's level of functioning in terms of their ability to care for themself, daily activity, and physical ability (walking, working, etc.). It is used by doctors and researchers to assess how a patient's disease is progressing, how the disease affects the daily living abilities of the patient and determine appropriate treatment and prognosis.

GRADE	ECOG PERFORMANCE STATUS [Synonyms: WHO/Zubrod score]
0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours.
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours.
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair.
5	Dead.

Criteria

Prior authorization is required.

Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs)

Lutathera® is considered medically necessary for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut NETs, when **ALL** of the following are met:

1. Member is 18 years of age or older; **AND**
2. Member has experienced disease progression despite receiving somatostatin analog therapy (octreotide or lanreotide); **AND**
3. Member has locally advanced, inoperable, or metastatic well-differentiated disease; **AND**
4. Member has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2; **AND**
5. Prescribed by, or in consultation with, an oncologist; **AND**
6. Dose does not exceed 7.4 GBq (200 mCi) every 8 weeks, up to a total of 4 doses.

Pheochromocytoma[≠] or Paraganglioma[≠]

Lutathera® is considered medically necessary for the treatment of pheochromocytoma or paraganglioma when **ALL** of the following criteria are met:

1. Member is age 18 years of age or older; **AND**
2. Member has somatostatin receptor-positive, locally advanced, unresectable, or metastatic disease; **AND**
3. Member has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2; **AND**
4. Prescribed by, or in consultation with, an oncologist; **AND**
5. Dose does not exceed 7.4 GBq (200 mCi) every 8 weeks, up to a total of 4 doses.

Bronchopulmonary or Thymus Neuroendocrine Tumors (NETS)[≠]

Lutathera® is considered medically necessary for the treatment of bronchopulmonary or thymus neuroendocrine tumors (NETS) when **ALL** of the following criteria are met:

1. Member is 18 years of age or older; **AND**
2. Disease is locally unresectable or metastatic; **AND**
3. Member has experienced has experienced disease progression despite receiving somatostatin analog therapy (octreotide or lanreotide); **AND**
4. Member has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2; **AND**
5. Prescribed by, or in consultation with, an oncologist; **AND**
6. Dose does not exceed 7.4 GBq (200 mCi) every 8 weeks, up to a total of 4 doses.

[≠]Off-label indication supported by NCCN guidelines (level of evidence 2A).

Continuation Therapy (all above indications)

Lutathera® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
3. Prescribed by, or in consultation with, an oncologist; **AND**
4. Member has not received ≥ 4 doses of Lutathera®; **AND**
5. Dose does not exceed 7.4 GBq (200 mCi) every 8 weeks, up to a total of 4 doses.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	4 doses (32 weeks)	Only authorized for up to a total of 4 doses. If member did not receive all 4 doses on the initial authorization, may approve remaining doses if criteria are met.
Quantity Limits	7.4 GBq (200 mCi) per dose	7.4 GBq (200 mCi) per dose

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
A9513	Lutetium Lu 177, dotatate, therapeutic, 1 mCi

ICD-10	Description
C7A.00	Malignant carcinoid tumor of unspecified site
C7A.010	Malignant carcinoid tumor of the duodenum
C7A.011	Malignant carcinoid tumor of the jejunum
C7A.012	Malignant carcinoid tumor of the ileum
C7A.019	Malignant carcinoid tumor of the small intestine, unspecified portion
C7A.020	Malignant carcinoid tumor of the appendix
C7A.021	Malignant carcinoid tumor of the cecum
C7A.022	Malignant carcinoid tumor of the ascending colon
C7A.023	Malignant carcinoid tumor of the transverse colon
C7A.024	Malignant carcinoid tumor of the descending colon
C7A.025	Malignant carcinoid tumor of the sigmoid colon
C7A.026	Malignant carcinoid tumor of the rectum
C7A.029	Malignant carcinoid tumor of the large intestine, unspecified portion
C7A.092	Malignant carcinoid tumor of the stomach
C7A.094	Malignant carcinoid tumor of the foregut NOS
C7A.095	Malignant carcinoid tumor of the midgut NOS
C7A.096	Malignant carcinoid tumor of the hindgut NOS
C7A.098	Malignant carcinoid tumors of other sites

ICD-10	Description
C7A.1	Malignant poorly differentiated neuroendocrine tumors
C7B.00	Secondary carcinoid tumors, unspecified site
C7B.01	Secondary carcinoid tumors of distant lymph nodes
C7B.02	Secondary carcinoid tumors of liver
C7B.04	Secondary carcinoid tumors of peritoneum
C25.0	Malignant neoplasm of head of pancreas
C25.1	Malignant neoplasm of body of pancreas
C25.2	Malignant neoplasm of tail of pancreas
C25.4	Malignant neoplasm of endocrine pancreas
C25.7	Malignant neoplasm of other parts of pancreas
C25.8	Malignant neoplasm of overlapping sites of pancreas
C25.9	Malignant neoplasm of pancreas, unspecified

NDC	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
69488-0003-01	Advanced Accelerator Applications USA, Inc.	1 mCi	1	EA	200

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Lutathera prescribing information (03/2023). Advanced Accelerator Applications USA, Inc.: Millburn, NJ. Available online at www.hcp.novartis.com/products/lutathera/gep-nets. Accessed December 17, 2023.

[2] National Comprehensive Cancer Network (NCCN). Development and Update of Guidelines. Available online at www.nccn.org. Accessed October 11, 2023.

[3] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Neuroendocrine and Adrenal Tumors (v.1.2023 – August 2, 2023. Accessed December 17, 2023. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guideline, go online to NCCN.org.

[4] NCI Dictionary of Cancer Terms. National Cancer Institute, a division of the National Institutes of Health (NIH). Online at www.cancer.gov/publications/dictionaries/cancer-terms.

[5] Human Imaging Modalities. Biomedical Research Imaging Center: UNC School of Medicine. Online at www.med.unc.edu/bric/human-imaging/human-imaging-modalities/pet-mr/.

[6] Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5:649-655.

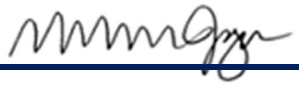
Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]			
Signature			

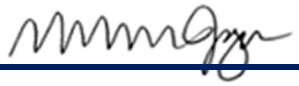
Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]			
Signature			

Change Date	Changed By	Description of Change	Version
01/19/2024	CAC	Annual review. Updated NCCN Guidelines.	4
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
01/20/2023	CAC	Added details of NCCN Guidelines recommendation. Added information on scans used in diagnosis (e.g., PET/CT). Added continuation criteria (only applicable if Member did not receive all 4 doses on initial authorization). Removed "Not Covered If" section as these were all accounted for in initial criteria.	3
Signature William (Bill) Jagiello, DO			

Criteria Change History *(continued)*

Change Date	Changed By	Description of Change	Version
01/21/2022	CAC	Annual review. Formatting changes.	2
Signature			
William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
01/15/2021	CAC	Criteria implementation.	1
Signature			
William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee