# Lutathera (lutetium Lu 177 dotatate)
## PAM – 027

| | | | |
|---|---|---|---|
| **Iowa Medicaid Program** | Prior Authorization | **Effective Date** | 01/01/2021 |
| **Revision Number** | 5 | **Last Reviewed** | 01/17/2025 |
| **Reviewed By** | Medicaid Medical Director | **Next Review** | 01/16/2026 |
| **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 adult and pediatric patients 12 years and older with somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors |
| 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<br>• Discontinue long-acting somatostatin analogs (e.g., long-acting octreotide) for at least 4 weeks prior to initiating Lutathera®<br>• 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 and pediatric patients 12 years and older with GEP-NETs who progress despite first-line therapy.

## Guidelines

The National Comprehensive Cancer Network (NCCN) publishes guidelines for the prevention, diagnosis, and management of malignancies across the continuum of care. The NCCN Guidelines® are a comprehensive set of guidelines detailing the sequential management decisions and interventions that currently apply to 97 percent of cancers affecting patients in the United States. The guidelines are developed and updated by 61 individual panels, comprising over 1,700 clinicians and oncology researchers from the 33 NCCN Member Institutions.

Guidelines are reviewed and updated on a continual basis to ensure that the recommendations take into account the most current evidence. To view the most recent and complete version of the guidelines, 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.[2,3]

The information referenced at the time of this policy writing/revision is from the NCCN Guidelines® for (note version number and effective date):[4]

- Neuroendocrine and Adrenal Tumors (v.2.2024 – August 1, 2024)

| NCCN Guidelines® Recommendation(s) in Neuroendocrine and Adrenal Tumors |
|---|
| (1) Neuroendocrine Tumors of the Gastrointestinal Tract (Well-Differentiated Grade 1/2) [a]<br>a. Locoregional Advanced Disease and/or Distant Metastases<br>i. PRRT with lutetium Lu 177 dotatate (if SSTR-positive and progression on octreotide LAR/lanreotide): Category 1, Preferred Regimen for progressive mid-gut tumors<br>(2) Distant Metastatic Neuroendocrine Tumors of Lung and Thymus [a]<br>a. Distant Metastases (clinically significant tumor burden and low grade [typical carcinoid] or evidence of disease progression or intermediate grade [atypical carcinoid] or symptomatic)<br>i. PRRT with lutetium Lu 177 dotatate (if SSTR-positive and progression on octreotide LAR or lanreotide): Category 2A, Useful in Certain Circumstances<br>(3) Pancreatic Neuroendocrine Tumors (Well-Differentiated Grade 1/2) [a]<br>a. Locoregional Advanced Disease and/or Distant Metastases<br>i. PRRT with lutetium Lu 177 dotatate (if SSTR-positive and progression on octreotide LAR or lanreotide): Category 2A, Preferred Regimen |

**NCCN Guidelines® Recommendation(s) in Neuroendocrine and Adrenal Tumors**

(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. Clinical trial preferred
    ii. PRRT with lutetium Lu 177 dotatate [b] (if SSTR-positive): Category 2A
(5) Pheochromocytoma/Paraganglioma
  a. Locally Unresectable
    i. Clinical trial
    ii. PRRT with lutetium Lu 177 dotatate (if SSTR-positive) [c, d]: Category 2A
  b. Distant Metastases
    i. Clinical trial
    ii. PRRT with lutetium Lu 177 dotatate (if SSTR-positive) [c, d]: Category 2A

**PRRT** peptide receptor radionuclide therapy **SSTR** somatostatin receptor

[a] 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.
[b] Consider trial of SSA before PRRT. Preliminary data suggest reduced efficacy if high Ki-67 and/or FDG-PET avid.
[c] SSTR PET tracers include: 68Ga-DOTATATE, 64Cu-DOTATATE, and 68Ga-DOTATOC.
[d] Data are limited on the use of PRRT with lutetium Lu 177 dotatate in this setting.

**Principles of PRRT with Lutetium Lu 177 Dotatate**

- Lutetium Lu 177 dotatate is a radiolabeled SSA used as PRRT.
- It is approved by the FDA for the treatment of adult and pediatric patients ≥ 12 years of age with SSTR-positive GEP NETs, including foregut, midgut, and hindgut NETs.
- Currently there are no randomized data, but there are reports of treatment efficacy and favorable outcomes when PRRT is used for PanNETs, PCCs, PGLs, and lung/thymic NETs. If feasible, participation in clinical trials of PRRT is strongly recommended for patients with such 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

| | | | |
|---|---|---|---|
| **GEP** | gastroenteropancreatic | **PGL** | paraganglioma |
| **NET** | neuroendocrine tumor | **PRRT** | peptide receptor radionuclide therapy |
| **PanNET** | pancreatic neuroendocrine tumor | **SSA** | somatostatin analog |
| **PCC** | pheochromocytoma | **SSTR** | somatostatin receptor |

**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.[5]

**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.[6]

**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 Scale [7]

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 themselves, 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 to 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 housework, 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 when **ALL** of the following are met:

1. Diagnosis of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut NETs which is locally advanced, inoperable, or metastatic well-differentiated; **AND**
2. Member has experienced disease progression despite receiving somatostatin analog therapy (octreotide or lanreotide); **AND**
3. Member is 12 years of age or older; **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 (± 1 week), up to a total of 4 doses.

## Pheochromocytoma≠ or Paraganglioma≠

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

1. Diagnosis of pheochromocytoma or paraganglioma and disease is somatostatin receptor-positive, locally advanced, unresectable, or metastatic; **AND**
2. Member is 12 years of age or older; **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 (± 1 week), up to a total of 4 doses.

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

## Lung or Thymus Neuroendocrine Tumors≠

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

1. Diagnosis of lung or thymus neuroendocrine tumor and disease is locally unresectable or metastatic; **AND**
2. Member has experienced has experienced disease progression despite receiving somatostatin analog therapy (octreotide or lanreotide); **AND**
3. Member is 12 years of age or older; **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 (± 1 week), 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 (± 1 week), 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 |
| 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 (Strength) | Labeler | Dosage | Pkg Size | Pkg Qty | Units /Pkg |
|---|---|---|---|---|---|
| 69488-0003-01 (30 mL single-dose vial containing 7.4 GBq (200 mCi) ± 10%) | Advanced Accelerator Applications USA, Inc. (69488) | 1 mCi | 1 | EA | 200 |

## Compliance

1. Should conflict exist between the 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 (10/2024). Advanced Accelerator Applications USA, Inc.: Millburn, NJ. Available online: www.lutathera-hcp.com. Accessed November 4, 2024.

[2] National Comprehensive Cancer Network (NCCN). Guidelines Process: About Clinical Practice Guidelines. Available online at www.nccn.org. Accessed July 29, 2024.

[3] National Comprehensive Cancer Network (NCCN). Guidelines Process: Development and Update of Guidelines. Available online at www.nccn.org. Accessed July 29, 2024.

[4] NCCN Clinical Practice Guidelines in Oncology. 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, go online to NCCN.org. NCCN Guidelines® referenced (note version number and effective date):

- Neuroendocrine and Adrenal Tumors (v.2.2024 – August 1, 2024)

[5] 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.

[6] 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/.

[7] 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. PMID 7165009.

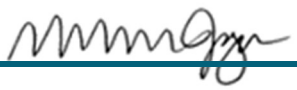
Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published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

## Criteria Change History

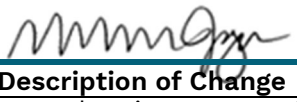
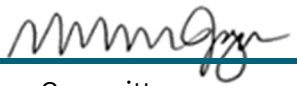
| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| [mm/dd/yyyy] | CAC | | |
| **Signature** | | | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| [mm/dd/yyyy] | CAC | | |
| **Signature** | | | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| 01/17/2025 | CAC | Annual review. Changed criteria requirement to 12 years and older to align with FDA approval on 4/23/2024 which expanded the eligible population (previously only approved for ages 18 years and older). Updated age range change in Overview table and Descriptive Narrative as well. Updated NCCN references. | 5 |
| **Signature**<br>William (Bill) Jagiello, DO | |  | |

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

## Criteria Change History *(continued)*

| 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**<br>William (Bill) Jagiello, DO | |  | |
| **Change Date** | **Changed By** | **Description of Change** | **Version** |
| 01/21/2022 | CAC | Annual review. Formatting changes. | 2 |
| **Signature**<br>William (Bill) Jagiello, DO | |  | |
| **Change Date** | **Changed By** | **Description of Change** | **Version** |
| 01/15/2021 | CAC | Criteria implementation. | 1 |
| **Signature**<br>William (Bill) Jagiello, DO | |  | |

CAC = Medicaid Clinical Advisory Committee