Reference number(s)
4236-A

STANDARD MEDICARE PART B MANAGEMENT

LUTATHERA (lutetium Lu 177 dotatate)

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 Indication
Lutathera is indicated for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults.

B. Compendial Uses
1. Carcinoid syndrome
2. Neuroendocrine tumors (NETs) of the lung and thymus (carcinoid tumors)
3. Pheochromocytoma/paraganglioma
4. Well-differentiated grade 3 NETs with favorable biology

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following documentation must be available, upon request, for all submissions:
Somatostatin receptor status as detected by somatostatin receptor-based imaging

III. CRITERIA FOR INITIAL APPROVAL

A. **Neuroendocrine tumors (NETs)**
1. Tumors of the gastrointestinal (GI) tract (carcinoid tumors)
Authorization of 12 months and 4 doses total may be granted for treatment of somatostatin receptor-positive NETs of the gastrointestinal tract when the member has recurrent, locoregional advanced disease and/or distant metastases and one of the following criteria are met:
   i. Member has clinically significant tumor burden, or
   ii. Member experienced disease progression on octreotide or lanreotide.

2. Tumors of the pancreas

Authorization of 12 months and 4 doses total may be granted for treatment of somatostatin receptor-positive NETs of the pancreas when both of the following criteria are met:
i. Member has symptomatic disease, clinically significant tumor burden, or progressive recurrent, locoregional advanced disease and/or distant metastases.
ii. Member experienced disease progression on octreotide or lanreotide.

3. Neuroendocrine tumors (NETs) of the lung and thymus (carcinoid tumors)
Authorization of 12 months and 4 doses total may be granted for treatment of somatostatin receptor-positive NETs of the lung and thymus when one of the following criteria are met:
i. Member has recurrent or locoregional unresectable disease and has progressed on octreotide or lanreotide
ii. Member has distant metastatic disease, has experienced disease progression on octreotide or lanreotide, and meets one of the following criteria:
a. Clinically significant tumor burden and low grade (typical carcinoid) histology
b. Evidence of disease progression
c. Intermediate grade (atypical carcinoid) histology
d. Symptomatic disease

4. Well-differentiated grade 3 NETs with favorable biology
Authorization of 12 months and 4 doses total may be granted for treatment of well-differentiated grade 3 unresectable locally advanced or metastatic NETs with favorable biology (e.g., relatively low Ki-67 [less than 55%], positive somatostatin receptor [SSTR]-based PET imaging) when member meets one of the following criteria:
i. Clinically significant tumor burden, or
ii. Evidence of disease progression

B. Carcinoid Syndrome
Authorization of 12 months and 4 doses total may be granted for treatment of poorly controlled carcinoid syndrome when all of the following criteria are met:
1. Member has somatostatin receptor-positive neuroendocrine tumors of the gastrointestinal tract, lung or thymus.
2. Member experienced progression on octreotide or lanreotide.
3. The requested medication will be used in combination with either a) octreotide LAR or lanreotide for persistent symptoms (i.e., flushing, diarrhea) or b) telotristat for persistent diarrhea in combination with octreotide LAR or lanreotide.

C. Pheochromocytoma/paraganglioma
Authorization of 12 months and 4 doses total may be granted for treatment of somatostatin receptor-positive pheochromocytoma/paraganglioma when the member meets one of the following criteria:
1. Member has locally unresectable disease, or
2. Member has distant metastases

IV. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:
1. The prescribing information for Lutathera.
2. The available compendium
a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
b. Micromedex DrugDex

   c. American Hospital Formulary Service- Drug Information (AHFS-DI)
   d. Lexi-Drugs
   e. Clinical Pharmacology
3. NCCN Guideline: Neuroendocrine and adrenal tumors

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Lutathera are covered in addition to the following:

1. Carcinoid syndrome
2. Neuroendocrine tumors (NETs) of the lung and thymus (carcinoid tumors)
3. Pheochromocytoma/paraganglioma
4. Well-differentiated grade 3 NETs with favorable biology

V. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Lutathera for all compendial indications listed in section IV can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

VI. REFERENCES

1. Lutathera [package insert]. Millburn, NJ: Advanced Accelerator Applications USA, Inc.; June 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed January 3, 2023.