RXADVANCE
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Clinical Policy Title:	lutetium 177 dotatate
Policy Number:	RxA.399
Drug(s) Applied:	Lutathera®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

Lutetium Lu 177 dotatate (Lutathera®) is a radiolabeled somatostatin analog.
It is indicated for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut NETs in adults.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Lutetium Lu 177 Dotatate (Lutathera®)	GEP-NET	7.4 GBq (200 mCi) IV every 8 weeks for a total of 4 doses	See regimen
Lutetium Lu 177 Dotatate (Lutathera®)	NET of lung or thymus origin, pheochromocytoma, paraganglioma*	7.4 GBq (200 mCi) IV every 8 weeks for a total of 4 doses	See regimen

Dosage Forms

- Single-dose vial for injection: 370 MBq/mL (10 mCi/mL).

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Neuroendocrine Tumors (must meet all):

1. Diagnosis of a somatostatin receptor-positive NET of one of the following origins (a or b):
   a. Gastrointestinal tract or pancreas;
   b. Lung or thymus (off-label);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is metastatic or locally advanced, and unresectable;
5. Member experienced disease progression while on a long-acting somatostatin analog (e.g., octreotide, lanreotide);
6. Dose does not exceed 7.4 GBq (200 mCi) every 8 weeks, up to a total of 4 doses.

Approval Duration
Commercial: 224 days (no more than 4 total doses)
Medicaid: 224 days (no more than 4 total doses)

B. Pheochromocytoma/Paraganglioma (off-label) (must meet all):
1. Diagnosis of a somatostatin receptor-positive pheochromocytoma/paraganglioma;
2. Prescribed by or in consultation with an oncologist;
3. Disease is metastatic or locally advanced, and unresectable;
4. Dose does not exceed 7.4 GBq (200 mCi) every 8 weeks, up to a total of 4 doses.

Approval Duration
Commercial: 224 days (no more than 4 total doses)
Medicaid: 224 days (no more than 4 total doses)

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Member has not received ≥ 4 doses of Lutathera;
4. If request is for a dose increase, new dose does not exceed 7.4 GBq (200 mCi) every 8 weeks, up to a total of 4 doses.

Approval Duration
Commercial: 224 days (no more than 4 total doses**)**
Medicaid: 224 days (no more than 4 total doses)

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
CT: computed tomography
FDA: Food and Drug Administration
GEP-NET: gastroentero pancreatic neuroendocrine tumor
mCi: millicurie
NCCN: National Comprehensive Cancer Network

APPENDIX B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Somatuline® Depot (lanreotide)	120 mg SC every 4 weeks	120 mg/month
Sandostatin® LAR Depot (octreotide LAR)*	30 mg IM once monthly (20 mg may be used for pancreatic NETs)	30 mg/month

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

*Off-label for the treatment of NETs (octreotide is only FDA-approved for the treatment of symptoms associated with carcinoid tumors) – NET dosing recommendations are per the NCCN guidelines.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None
- Boxed Warning(s):
  - None

APPENDIX D: General Information

- Somatostatin receptor expression can be detected by somatostatin receptor-based imaging, which includes ^{68}Ga-dotatate PET/CT (preferred per the NCCN) and somatostatin receptor scintigraphy.
- The NCCN Neuroendrocrine and Adrenal Tumors guidelines recommend the use of Lutathera:
  - For somatostatin receptor-positive bronchopulmonary/thymus, gastrointestinal, and pancreatic NETs that have progressed following therapy with octreotide or lanreotide and are locoregionally advanced or have distant metastases (category 2A, except for mid-gut tumors [category 1]); and
  - For the primary treatment of somatostatin receptor-positive pheochromocytoma/ paraganglioma that is locally unresectable or has distant metastases (category 2A).
- Use of Lutathera with long-acting somatostatin analogs:
  - Before initiating Lutathera: Long-acting somatostatin analogs (e.g., long-acting octreotide) should be discontinued for at least 4 weeks prior to initiation of Lutathera. Short-acting octreotide can be administered as needed up to 24 hours prior to initiating Lutathera.
  - During Lutathera treatment: Long-acting octreotide 30 mg should be administered intramuscularly between 4 to 24 hours after each Lutathera dose. Long-acting octreotide should not be administered within 4 weeks of each subsequent Lutathera dose. Short-acting octreotide may be given for symptomatic management during Lutathera treatment, but must be withheld for at least 24 hours before each Lutathera dose.
  - Following Lutathera treatment: Long-acting octreotide 30 mg intramuscularly should be continued every 4 weeks after completing Lutathera until disease progression or for up to 18 months following treatment initiation.

References

1. Lutathera Prescribing Information. Millburn, NJ: Advanced Accelerator Applications USA, Inc.; May 2020. Available at: https://www.lutathera.com. Accessed July 21, 2020.
2. National Comprehensive Cancer Network. Neuroendocrine and Adrenal Tumors. Version 1.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed July 21, 2020.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 21, 2020.
4. Strosberg J, El-Haddad G, Wolin E, et al. Phase 3 trial of ^{177}Lu-dotatate for midgut neuroendocrine tumors. N Engl J Med. 2017; 376(2): 125-135.
5. Brabander T, van der Zwan WA, Teunissen JJM, et al. Long-term efficacy, survival, and safety of [^{177}Lu-DOTA^{0},Tyr^{3}]octreotate in patients with gastroenteropancreatic and bronchial neuroendocrine tumors. Clin Cancer Res. 2017; 1-8.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Line of Business Policy Applies to was updated to all lines of business. 3. Initial and Continued approval duration was updated to include Medicaid & Commercial approval duration. 4. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 5. References were reviewed and updated.	7/21/2020	9/14/2020