Clinical Policy Title:	lutetium lu 177 dotatate
Policy Number:	RxA.399
Drug(s) Applied:	Lutathera®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
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) intravenously every 8 weeks for a total of 4 doses.	7.4 GBq (200 mCi) Intravenously (Maximum cumulative dose of 29.6 GBq)

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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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. Pregnancy status in females of reproductive potential prior to initiating Lutathera® has been verified;
4. Age ≥ 18 years;
5. Disease is metastatic or locally advanced, and unresectable;
6. Member experienced disease progression while on a long-acting somatostatin analog (e.g., octreotide,

lanreotide);
7. 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. Age ≥ 18 years;
4. Disease is metastatic or locally advanced, and unresectable;
5. Member experienced disease progression while on a 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)

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Member is 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: Gastroenteropancreatic neuroendocrine tumor
mCi: Millicurie
GBq: Gigabecquerel
NCCN: National Comprehensive Cancer Network

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

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

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

- Boxed Warning(s):
  - None reported.

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 Neuroendocrine 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.
- Renal Toxicity: Advise patients to urinate frequently during and after administration of LUTATHERA. Monitor serum creatinine and calculated creatinine clearance. Withhold, reduce dose, or permanently discontinue based on severity.
- Hepatotoxicity: Monitor transaminases, bilirubin and albumin.

References

1. Lutathera® Prescribing Information. Millburn, NJ: Advanced Accelerator Applications USA, Inc.; May 2020. Available at: https://www.lutathera.com. Accessed June 01, 2021.
2. National Comprehensive Cancer Network. Neuroendocrine and Adrenal Tumors. Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed June 01, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed June 01, 2021.
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/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
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
Policy was reviewed: 1. .Dosing Information maximum dose was updated to include "7.4 GBq (200 mCi) Intravenously (Maximum cumulative dose of 29.6 GBq)…" 2. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 3. Initial Approval Criteria I.A.3 was updated to include "Pregnancy status in females of reproductive potential…" 4. Initial Approval Criteria I.B.5 was updated to include "Member experienced disease progression while on…" 5. Appendix A was updated to include "GBq: Gigabecquerel." 6. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by	06/01/2021	09/14/2021

both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 7. Appendix D: General Information was updated to include “For somatostatin receptor-positive bronchopulmonary/thymus…”, “Renal toxicity…”, and “Hepatotoxicity…” 8. References were reviewed and updated. 9.		