Clinical Policy: Lutetium Lu 177 Dotatate (Lutathera)

Reference Number: ERX.SPA.242
Effective Date: 09.01.18
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Lutetium Lu 177 dotatate (Lutathera®) is a radiolabeled somatostatin analog.

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

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

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Lutathera is **medically necessary** when the following criteria are met:

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 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: 32 weeks (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: 32 weeks (no more than 4 total doses)

C. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Lutathera for a covered indication;

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: 32 weeks (no more than 4 total doses)

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CT: computed tomography
FDA: Food and Drug Administration
GEP-NET: gastroenteropancreatic 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 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
Sandostatin® (octreotide)	150 – 250 mcg SC TID	450 mcg/day

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

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 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 somatostatin analogs:

- Before initiating Lutathera: Long-acting somatostatin analogs (e.g., long-acting octreotide) should be discontinued for at least 4-6 weeks prior to initiation of Lutathera. Short-acting octreotide can be administered as needed up to 24 hours prior to initiating Lutathera.
- After Lutathera: Administer long-acting octreotide 30 mg intramuscularly 4 to 24 hours after each Lutathera dose and short-acting octreotide for symptomatic management.
- Continue long-acting octreotide 30 mg intramuscularly every 4 weeks after completing Lutathera until disease progression or for up to 18 months following treatment initiation.
- During Lutathera treatment: IV infusion of amino acids is critical for nephron protection and should be infused 30 minutes and 3 hours after Lutathera treatment
- Following Lutathera treatment: Octreotide or lanreotide (short and long acting) can be administered 4 to 24 hours after completing Lutathera.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
GEP-NET	7.4 GBq (200 mCi) IV every 8 weeks for a total of 4 doses	7.4 BGq (200 mCi) IV (4 doses)
NET of lung or thymus origin, pheochromocytoma, paraganglioma*		

**Off-label – dosing recommendations are per the NCCN guidelines*

VI. Product Availability

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

VII. References

1. Lutathera Prescribing Information. Millburn, NJ: Advanced Accelerator Applications USA, Inc.; July 2018. Available at: https://www.lutathera.com. Accessed May 4, 2021.
2. National Comprehensive Cancer Network. Neuroendocrine and Adrenal Tumors. Version 1.2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed May 4, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed May 4, 2021.
4. Strosberg J, El-Haddad G, Wolin E, et al. Phase 3 trial of 177Lu-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 [177Lu-DOTA0,Tyr3]octreotate in patients with gastroenteropancreatic and bronchial neuroendocrine tumors. Clin Cancer Res. 2017; 1-8.
6. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	05.22.18	08.18
3Q 2019 annual review: no significant changes; removed “Member has not received ≥ 4 doses of Lutathera” from the Initial Approval Criteria section since it doesn’t apply when a request is for initial therapy; references reviewed and updated.	05.20.19	08.19
3Q 2020 annual review: revised criteria requiring disease progression while on a long-acting somatostatin analog to allow short and long acting somatostatin analogs; updated Appendix B and D; references reviewed and updated.	05.05.20	08.20
3Q 2021 annual review: no significant changes; references reviewed and updated.	05.04.21	08.21

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.