

POLICY: Somatostatin Analogs – Lutathera® (lutetium Lu 177 dotatate – Advanced Accelerator Applications USA, Inc.)

APPROVAL DATE: 08/07/2019

OVERVIEW

Lutathera, a radiolabeled somatostatin analog, is indicated for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors (NETs) in adults.¹ Lutathera binds to somatostatin receptors with highest affinity for the subtype 2 receptors. The compound is internalized upon binding to somatostatin receptor expressing cells, including malignant somatostatin receptor-positive tumors. The beta emission from Lu 177 induces cellular damage by formation of free radicals in somatostatin receptor-positive cells and in neighboring cells.

The recommended dose of Lutathera is 7.4 gigabecquerel (GBq) [200 millicuries {mCi}] administered intravenously (IV) over 30 to 40 minutes, once every 8 weeks for a total of four doses. Lutathera is a radiopharmaceutical; therefore, it must be handled with appropriate safety measures to minimize radiation exposure. It should be used by or under the control of physicians who are qualified by specific training and experience.

While on Lutathera treatment, Sandostatin® LAR Depot (octreotide acetate for injectable suspension) 30 mg should be administered intramuscularly (IM) between 4 to 24 hours after each Lutathera dose. Sandostatin LAR Depot cannot be administered within 4 weeks of each subsequent Lutathera dose. Short-acting octreotide may be given for symptomatic management during Lutathera treatment, but it must be withheld for at least 24 hours before each Lutathera dose. An amino acid IV solution containing L-lysine and L-arginine should be initiated 30 minutes before administering Lutathera to reduce radiation dose to the kidneys. This infusion is continued during and for 3 hours after Lutathera infusion. Antiemetics should be administered 30 minutes prior to the amino acid solution. The prescribing information details dose modifications for Lutathera for adverse events.

Lutathera is available as a 370 MBq/mL (10 mCi/mL) injection of lutetium Lu 177 dotatate in a single-dose, sterile, preservative-free vial. It is supplied for administration in a 30 mL single-dose vial containing 7.4 GBq (200 mCi) \pm 10% of lutetium Lu 177 dotatate at the time of injection. The product container is in a lead shield container.

Dosing Information

Extended approval is not needed since only a total of 4 doses of Lutathera is administered for treatment, with each dose given once every 8 weeks (total of 32 weeks of treatment or 8 months). The initial approval is provided for 12 months in case of treatment interruptions due to adverse events. According to the prescribing information, if there is a treatment delay of 16 weeks or longer due to adverse events, Lutathera should be discontinued permanently. So even with treatment delays of up to 16 weeks (4 months), the 12 month initial approval should be sufficient.

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines for neuroendocrine and adrenal tumors (version 1.2019 – March 5, 2019) recommends Lutathera as a category 1 treatment option for midgut tumors.² The compendium notes Lutathera as a category 2A recommended option for other gastrointestinal tract

NETs.³ It is also recommended for NETs of the pancreas, bronchopulmonary, or thymus, and for pheochromocytoma and paraganglioma.^{2,3} In all of these conditions the recommendation is to use Lutathera for locoregional advanced disease and/or distant metastases if somatostatin-receptor positive on imaging. For NETs of gastrointestinal, bronchopulmonary, thymus, or pancreas, Lutathera is recommended if the patient is progressing on Sandostatin[®] LAR Depot (octreotide acetate for injectable suspension) or Somatuline[®] Depot (lanreotide injection). It is recommended as one of the primary treatment options in pheochromocytoma/paraganglioma.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Lutathera. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Lutathera as well as the monitoring required for adverse events and long-term efficacy, approval requires Lutathera to be prescribed by or in consultation with a physician who specializes in the condition being treated in some circumstances.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Lutathera is recommended in those who meet one of the following criteria.

FDA-Approved Indications

1. Neuroendocrine Tumors (NETs) of the Gastrointestinal Tract, Lung, Thymus (Carcinoid Tumors), and Pancreas. Approve for 1 year if the patient meets the following criteria (A, B, C, D, and E):

- A) The patient is an adult \geq 18 years of age; AND
- B) The patient has locally advanced or metastatic disease; AND
- C) The patient has somatostatin receptor-positive tumor as detected by somatostatin receptor-based imaging (e.g., Gallium-68 dotatate [⁶⁸Ga-dotatate] positron emission tomography [PET]/computed tomography [CT], somatostatin receptor scintigraphy); AND
- D) The patient has progressed on Sandostatin[®] LAR Depot (octreotide acetate for injectable suspension) or Somatuline[®] Depot (lanreotide injection); AND
- E) Lutathera is prescribed by or in consultation with an oncologist, radiologist, or endocrinologist.

Dosing. Approve if the dose meets the following (A, B, and C):

- A) Each dose is \leq 7.4 GBq [200 mCi] administered intravenously; AND
- B) Each dose is given no more frequently than once every 8 weeks; AND
- C) No more than 4 doses total.

Other Uses with Supportive Evidence

2. Pheochromocytoma/Paraganglioma. Approve for 1 year if the patient meets the following criteria (A, B, C, and D):

- A) The patient is an adult \geq 18 years of age; AND
- B) The patient has locally unresectable disease or distant metastases; AND

- C) The patient has somatostatin receptor-positive tumor as detected by somatostatin receptor-based imaging (e.g., Gallium-68 dotatate [⁶⁸Ga-dotatate] positron emission tomography [PET]/computed tomography [CT], somatostatin receptor scintigraphy); AND
- D) Lutathera is prescribed by or in consultation with an oncologist or radiologist.

Dosing. Approve if the dose meets the following (A, B, and C):

- A) Each dose is ≤ 7.4 GBq [200 mCi] administered intravenously; AND
- B) Each dose is given no more frequently than once every 8 weeks; AND
- C) No more than 4 doses total.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Lutathera has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

1. **Retreatment with Lutathera.** Lutathera is administered with a maximum of 4 total doses. Repeat usage in previously treated patients is not recommended.
2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Lutathera® for intravenous injection [prescribing information]. Millburn, NJ: Advanced Accelerator Applications USA, Inc.; January 2018.
2. The NCCN Neuroendocrine and Adrenal Tumors Clinical Practice Guidelines in Oncology (Version 2.2018 – May 4, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on August 1, 2018.
3. The NCCN Drugs & Biologics Compendium. © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on August 1, 2018. Search term: Lutetium Lu 177 dotatate.

HISTORY

Type of Revision	Summary of Changes	Approval Date
New Policy	--	08/22/2018
Annual revision	The following sections were removed throughout the policy; Initial Approval/Extended Approval, Duration of Therapy, Labs/Diagnostics, and Waste Management. In addition, the following was changed: <ol style="list-style-type: none"> 1. Neuroendocrine Tumors (NETs) of the Gastrointestinal Tract, Lung, Thymus (Carcinoid Tumors), and Pancreas. The Dosing was changed from a specific regimen to a range utilizing criteria verbiage of “each dose is ≤” and “each dose is given no more frequently than”. Extended Approval for “Not recommended use” was removed and added to the Conditions Not Recommended for Approval section of the policy. 2. Pheochromocytoma/Paraganglioma. The Dosing was changed from a specific regimen to a range utilizing criteria verbiage of “each dose is ≤” and “each dose is given no more frequently than”. Extended Approval for “Not recommended use” was removed and added to the Conditions Not Recommended for Approval section of the policy. 3. Retreatment with Lutathera was added as a condition not recommended for approval. Lutathera is administered with a maximum of 4 total doses. Repeat usage in previously treated patients is not recommended. 	08/07/2019