

Radiopharmaceutical Therapy: Agent/Protocol-Specific Procedure

Lu-177 Dotatate (Lutathera) Therapy

Somatostatin positive tumors

Radiopharmaceutical Agent:	<p>Lu-177 DOTA⁰-Tyr³-Octreotate (<i>Lutathera</i>), is a radiolabeled somatostatin analog indicated for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GET-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults</p> <p>¹⁷⁷Lu-DOTA⁰-Tyr³-Octreotate, (<i>Lutathera</i>), is a lutetium-177 (¹⁷⁷Lu) labelled somatostatin analog peptide conjugated with the metal chelating moiety 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA). The compound has a high affinity for somatostatin subtype 2 (sst₂) receptors. Many cancers, including neuroendocrine tumors, overexpress sst₂ receptors.</p> <p>¹⁷⁷Lu is a β⁻ emitting radionuclide that decays to hafnium (¹⁷⁷Hf) with a half-life of 6.7 days. It decays with a maximum energy 0.498 MeV with a mean path length of 2.2 mm, which is sufficient to effectively kill targeted tumor cells, with a limited effect on neighboring normal cells. It also decays with γ photons of 0.208 MeV and 0.113 MeV</p>
Drug Information Source:	FDA approved for sst2 receptor tumor positive therapy. For additional information regarding this agent, consult package insert or other standard references
Applicability of Worksheet:	Clinical use of commercial product; standard of care
Target Patient Process:	<i>Lutathera</i> will be administered to patients with metastasized or locally advanced, inoperable, somatostatin receptor positive neuroendocrine tumors (NETs) with progressive disease during or after Somatostatin Antagonist (SSA) therapy. Supportive care with SSA can be administered during <i>Lutathera</i> treatment at physician discretion.
Written Directive and Validation:	<p>The Nuclear Pharmacist will initiate the ¹⁷⁷Lu <i>Lutathera</i> written directive, obtaining patient's labs and dates obtained, last Octreotide therapy dose, and date for the next set of labs to be obtained. Previous written directives will also be obtained (if applicable). The Nuclear Pharmacist will determine the Authorized User that will be administering the dose and pass the material on for signature. The Authorized User will determine the appropriateness of the therapy and sign the written directive.</p> <p>Section D on the Written Directive "Patient Preparation Verification" will be completed by the Authorized User before administration of the therapy. Actual patient consent and training may be done up to 4 weeks before actual therapy by Radiation Safety.</p>
Drug Procurement/Preparation:	<p>¹⁷⁷Lu <i>Lutathera</i> may only be administered on Wednesday, Thursday, or Friday.</p> <p>¹⁷⁷Lu <i>Lutathera</i> is provided by Advance Accelerator Applications (dba Novartis) as a sterile, preservative-free and clear, colorless to yellowish solution for infusion (pH 4.5-8.5) in a single-dose vial.</p> <p>The dose arrives on the day of calibration in a 30mL Type I glass vial containing 370 MBq/mL (10 mCi/mL) of ready to use injection.</p> <p>The solution volume in the vial is adjusted from 20.5 mL to 25 mL to provide to a total of 7.4 GBq (200 mCi) ± 10% of lutetium Lu 177 for a standard patient*. (Solution volume may vary based on calibration date). *Dose may be reduced by 50% for a patient with renal insufficiency.</p>

Store Lutathera below 25 °C (77 °F) (room temperature)

Lutathera has a shelf-life of 72 hours post manufacturing.

Patient Pre-treatment Prep:

Patient Prep:

Patient has completed a confirmed SSR2 receptor positive imaging procedure. Imaging should be completed within one (1) year of Lutathera administration, preferably with Ga-68 DOTATATE, but In-111 Octreoscan is acceptable. Authorized User will verify the positive findings with reviewing the scans in PACS or HealthLink.

Patient has no untreated or non-stable brain metastases.

Radiation Safety will contact patient to conduct Radiation Safety training and identify areas of radiation safety concern.

Due to the logistics of the patient's visit to the Oncology Clinic, written consent will not be obtained until the morning of the therapy.

Prior to treatment regime:

- Treatment with long-acting analogs of somatostatin must be discontinued for at least **4 weeks** prior to Lutathera administration.
- Treatment with short-acting octreotide may be administered during treatment but must be withheld **24 hours** prior to Lutathera administration.

During the treatment regime:

- Treatment with long-acting octreotide (30 mg) intramuscularly may be given **4 to 24 hours after** each administration of Lutathera.

Following LUTATHERA treatment:

- Continue long-acting octreotide (30 mg) intramuscularly every 4 weeks until disease progression or up to 18 months following treatment initiation.

Minimum lab tests performed within 8-weeks pre- infusion and every 4 weeks after infusion for at least 3 months after the last infusion and every 6 months thereafter:

Deviation from these results may require consultation between AU and Oncologist.

- Liver function (AST,ALT, bilirubin)
 - AST, ALT < 3x ULN, bilirubin <1.5x ULN
- Kidney function (creatinine and creatinine clearance)
 - SCr ≤ 1.5 mg/dl or CrCl ≥ 40
- Hematology (Hgb, platelet count, ANC)
 - Hgb ≥ 8 g/dl, PLT > 100,000/mm³ ANC ≥ 1000
- Pregnancy test (urine or blood) within 24 hours of infusion for females of childbearing potential (12-55 years of age).

Patient is encouraged to drink a sufficient amount of water (approximately 8 ounces every hour) to urinate every hour or two on the day of infusion and the following day.

Patient is encouraged to have at least 1 bowel movement per day after treatment.

Administration/Treatment Schedule:

Treatment Regimen:

~200 mCi of Lutathera is administered on four (4) separate occasions with 8(+/-1) week intervals between administrations. Note that the vial that is procured from AAA is considered a unit dose vial, and due to travel logistics, activity actually received from the vendor can vary within 20% of the labelled 200 mCi. To ensure in-house quality standards, the written directive has an entry for the actual activity received from the manufacturer. This activity will be used to calculate the actual dose administered to the patient.

¹⁷⁷Lu *Lutathera* dose may be adjusted by 50% for patients with renal insufficiency. Dose of Amino Acids will not be adjusted to ensure adequate renal protection. In addition to the AU filling out the dose on the written directive, there is the additional options to be chosen by the AU of "Full Dose" or "Half Dose."

Angiocatheter:

- A peripheral intravenous catheter is to be placed in each arm of the patient.
- A single peripheral intravenous catheter may be used due difficulty of peripheral intravenous catheter placement.

NOTE: Infusa-port catheter, Hickman catheter or PICC lines are not to be used for administration of Lutathera.

Antiemetics:

Antiemetic therapy, as defined by procedure order in HealthLink, will be initiated by Oncology Nursing as standard of care 30-60 minutes prior to the start of the amino acid infusion to avoid treatment related nausea and vomiting.

THERAPY WORKFLOW

PRETREATMENT:

Upon identification of a potential patient, the referring Oncologist will place the Lutathera Treatment plan into HealthLink. This entry will initiate the prior approval process with the Pharmacy Prior Authorization team. Oncology will send an in basket message to the Nuclear Medicine Technologist and Nuclear Pharmacy general in baskets. Upon receiving these messages, Nuclear Medicine Technologist will confirm the dates with Oncology, schedule the patient and in basket the Nuclear Pharmacy, who will initiate the written directive process as described above. The Nuclear Pharmacist will verify that the treatment has received prior authorization and will order the Lu-177 Lutathera and the amino acid solution using established order processes. The above information flow applies to all four cycles, however, for cycles 2 through 4 Nuclear Medicine will verify with Oncology the patient is to continue and make this notification to the Nuclear Pharmacy approximately 4 weeks before the specific cycle date to initiate the written directive process for that cycle.

TREATMENT DAY:

Prior to receiving the patient, Radiation Safety will prepare the room for radiopharmaceutical infusion.

Patient will report to Oncology and be received by Oncology Nursing into the therapy room.

The Nuclear Medicine Technologist (NMT) will be notified by Oncology Nursing that the patient is ready to begin the Amino Acid infusion. NMT will retrieve the Amino Acid prescription from the Nuclear Pharmacy and proceed to the therapy room for the Oncology Nurse to infuse the Amino Acid solution. Upon approaching 30 minutes of infusion, the NMT will contact the Nuclear Pharmacist to deliver the *Lutathera* dose to the therapy room.

A co-infusion of an amino acid solution will be started 30 minutes prior to *Lutathera* infusion and continue for 4 hours total. This solution will contain L-lysine and L-arginine.

Due to *Lutathera* primarily being eliminated renally the amino acid solution is for renal protection.

NOTES:

- When infusing the amino acids and the *Lutathera* via a single venous access line a four-way high flow stopcock may be used.
- The amino acids may be administered through a separate venous access line in the patient's opposite arm.
- Do **NOT** decrease the dose of amino acid solution if the *Lutathera* dose is reduced.
- *Lutathera* is a unit dose that is administered via slow intravenous infusion over a 20-30 minute time span.
- Lutathera* cannot be administered as a bolus. 0.9 % Sodium Chloride is used to carry the *Lutathera* to the patient via the instructions below.

ADMINISTRATION OF THERAPY DOSE:

Therapy dose may be administered by different methods, depending on preference:

- 1) **Gravimetric method as described in the package insert. Vial is taken to the administration area by the Nuclear Medicine Technologist for administration.**
- 2) **Vial contents will be drawn from the vendor vial into a 60 mL syringe, including a vial rinse which may provide a final volume of 30-60 mL. This syringe will be placed in a shielded syringe pump and transported via cart to the administration area. Nuclear Medicine technologist will administer dose. Due the presence of a Nuclear Pharmacy on site, the aseptic manipulation of radioactive material is acceptable.**

Release criteria for the patient is less than or equal to 7 mR/hr at one meter from the patient, as read with a pressurized ion chamber survey meter. The Office of Radiation Safety shall meter the patient after infusion and confirm with the Authorized User that the patient is able to be released.

Pharmacy Product Validation:

As instructed on the **Radiopharmaceutical Therapy Dose Documentation Form**. The verification of the product will include placement of the dose into the dose calibrator, and comparison of the assay to the product label generated at the completion of dose assay, as well as the written directive. The administering clinician will verify that the dose is dispensed within 10% of the received dose and that the correct isotope is selected on the dose calibrator.

Patient Instructions/Education Validation:

¹⁷⁷Lu-DOTA⁰-Tyr³-Octreotate (*Lutathera*) training will be done by Radiation Safety, with follow up conducted by the Authorized User; no additional procedures required.

Administration Validation:

Dosing of the Lutathera and the Amino Acid Solution charge codes are completed in HealthLink by the administering Nuclear Medicine Technologist. The original Written Directive will be maintained in the Lu-177 Lutathera Dose Binder in the Nuclear Pharmacy.

Other information/instructions:

If for any reason the patient must be admitted to University Hospital within 96 hours of treatment, the **Radiopharmaceutical Therapy: Agent/Protocol-Specific Procedure for I-131 Sodium Iodide for Inpatient Use** should be followed by hospital admitting personnel.

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