Treatment Day Checklist

Advanced Accelerator Applications

LUTATHERA® (lutetium Lu 177 dotatate) injection, for intravenous use

Date of Treatment _____

LUTATHERA® (lutetium Lu 177 dotatate) Lot Number _____ Labeled Quantity (mCi) _____

1 Considerations before LUTATHERA Administration[1]

- ☐ Discontinue long-acting somatostatin analogs (eg, long-acting octreotide) for at least 4 weeks prior to initiating LUTATHERA
- ☐ Short-acting octreotide may be given for acute or urgent symptomatic management during LUTATHERA treatment, but must be withheld for at least 24 hours prior to each LUTATHERA dose
- ☐ Verify pregnancy status of females of childbearing potential

2 Items Required for LUTATHERA Administration

- ☐ Patient prescription or directive for LUTATHERA
- ☐ Patient release instructions (to be determined by Radiation Safety Officer [RSO])
- ☐ Signed informed consent (today or previously)
- ☐ Geiger-Mueller (GM) survey meter
- ☐ Radioactive materials spill kit
- ☐ Neuroendocrine hormonal crisis intervention medications
- ☐ Contamination protection applied in the patient bathroom and on surface of medication administration cart

Have the following items available:

Pharmaceuticals

- ☐ 0.9% sterile sodium chloride, 500 mL
- ☐ Saline for priming the lines
- ☐ Amino acid solution bag
- ☐ Antiemetics

Radiopharmaceutical

- ☐ LUTATHERA in lead shielded container

Equipment

Use aseptic technique and radiation shielding when administering LUTATHERA solution.

- ☐ Tongs to handle the LUTATHERA vial
- ☐ 2 infusion poles
- ☐ Pump(s) to regulate flow rate
- ☐ 2.5 cm, 20 gauge needle (short needle)
- ☐ 9 cm, 18 gauge needle (long needle)
- ☐ 10 mL syringe
- ☐ 2 IV pump infusion sets with clamp and Y-connector to regulate flow
- ☐ Male-to-male (m/m) patient line with clamp
- ☐ 25-60 mL syringe (empty)
- ☐ 3-way stopcock
- ☐ Sterile gloves
- ☐ Towels/gauze/alcohol wipes
- ☐ Waste container for contaminated items
- ☐ Emesis bags

Please see Important Safety Information on pages 3 and 4 and accompanying full Prescribing Information.

3 *Preparation Prior to LUTATHERA® (lutetium Lu 177 dotatate) Administration (Nursing)*

- ☐ Have patient change into hospital gown
- ☐ Premedication and concomitant medications
  - Administer antiemetics 30 minutes before the recommended amino acid solution
  - Open one (1) of the sterile tubing sets and spike the bag containing the amino acid solution; prime tubing set
  - Initiate an intravenous (IV) amino acid solution containing L-lysine and L-arginine 30 minutes before administering LUTATHERA
  - The amino acid solution is administered using the same venous access as LUTATHERA or through a separate venous access in the patient's other arm
  - Set amino acid infusion at a constant rate to ensure the infusion of the total volume within 4 hours
- ☐ Contact nuclear medicine department to let them know administration has started
- ☐ Open 500 mL, 0.9% sterile sodium chloride and prime IV pump infusion set, set up IV infusion pump, and program to 50 mL/hour to 100 mL/hour
- ☐ **IMPORTANT:** Immediately prior to LUTATHERA administration, have the patient use the bathroom to empty bladder

4 *Administration Set Up (Nuclear Medicine)*

- ☐ Ensure 1/8th of the amino acid solution is infused before beginning the LUTATHERA infusion
- ☐ Confirm saline line has been primed and that saline line is closed
- ☐ Place wedge under the dose vial in the lead shielded container to enhance air pocket visibility; can also mark the vial to act as visual aid
- ☐ Prime the m/m tubing with 0.9% sterile sodium chloride
- ☐ Connect the end of the m/m tubing to the saline tubing
- ☐ Flush the patient's access catheter with 0.9% sterile sodium chloride
- ☐ Connect patient line to patient catheter and ensure patient line is closed
- ☐ Connect the white end of the m/m tubing to the long, 18 gauge needle
- ☐ Insert the short needle into the LUTATHERA vial and connect via a catheter to 500 mL, 0.9% sterile sodium chloride solution
- ☐ **WARNING:** Do not allow the short needle to touch the LUTATHERA solution in the vial and do not connect this short needle directly to the patient
- ☐ Insert the long needle into the LUTATHERA vial, ensuring that this long needle touches and is secured to the bottom of the LUTATHERA vial during the entire infusion
- ☐ Connect the long needle to the patient by an IV catheter that is prefilled with 0.9% sterile sodium chloride and that is used exclusively for the LUTATHERA infusion into the patient

5 *Administration (Nuclear Medicine)*

- ☐ Using a survey meter, survey the top of the LUTATHERA vial to have a baseline for comparison at end of administration
- ☐ Open the patient line
- ☐ Open the saline line
- ☐ Set IV flow rate of LUTATHERA to 50 mL/hour to 100 mL/hour for 5 to 10 minutes
- ☐ Use a survey meter to confirm flow into the patient catheter
- ☐ Continue administration of LUTATHERA at 200 mL/hour to 300 mL/hour for an additional 25 to 30 minutes
- ☐ Do not administer LUTATHERA as an IV bolus
- ☐ During the infusion, ensure that the level of solution in the LUTATHERA vial remains constant
- ☐ After 25 to 30 minutes, survey the top of the vial; alternatively, survey meter can be placed underneath the m/m line. Survey every 5 minutes until the reading is stable
- ☐ Once the reading is stable for at least 5 minutes, stop the flow from the saline bag and close the saline line
- ☐ Follow the infusion with an IV flush of 25 mL of 0.9% sterile sodium chloride

Please see Important Safety Information on pages 3 and 4 and accompanying full Prescribing Information.

6 *Disassembly*

- ☐ Clamp patient line
- ☐ Disconnect tubing from the patient catheter; cap the line and the patient catheter to prevent radiation contamination
- ☐ Disconnect saline tubing from the short needle
- ☐ Carefully remove the long needle with tubing attached and place it in a sharps container for radioactive waste
- ☐ Remove short needle and place it in a sharps/radioactive waste container
- ☐ Leave the vial inside the lead shielded container, for transportation to the nuclear medicine department
- ☐ Assay the LUTATHERA vial for residual activity in the dose calibrator

7 *DC Measurements*

- ☐ Measure LUTATHERA activity in dose calibrator and record activity

8 *Cleanup and Waste Disposal*

- ☐ Use GM survey meter to check for contamination on equipment and affected locations
- ☐ Decontaminate and/or dispose of items as described by RSO

Indication and Important Safety Information

INDICATION

LUTATHERA® (lutetium Lu 177 dotatate) is indicated for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut and hindgut neuroendocrine tumors in adults.

IMPORTANT SAFETY INFORMATION[1]

WARNINGS AND PRECAUTIONS

- **Radiation Exposure:** Treatment with LUTATHERA contributes to a patient's overall long-term cumulative radiation exposure and is associated with an increased risk for cancer. Radiation can be detected in the urine for up to 30 days following LUTATHERA administration. Minimize radiation exposure to patients, medical personnel, and household contacts during and after treatment with LUTATHERA consistent with institutional good radiation safety practices and patient management procedures.
- **Myelosuppression:** In NETTER-1 clinical trial, myelosuppression occurred more frequently in patients receiving LUTATHERA with long acting octreotide at the following rates (all grades/grade 3 or 4): anemia (81%/0), thrombocytopenia (53%/1%), and neutropenia (26%/3%). Blood cell counts must be monitored prior to, during, and after treatment. Withhold, reduce dose, or permanently discontinue based on severity of adverse reaction.
- **Secondary Myelodysplastic Syndrome and Leukemia:** In NETTER-1, with a median follow-up time of 24 months, myelodysplastic syndrome (MDS) was reported in 2.7% of patients receiving LUTATHERA with long-acting octreotide. In ERASMUS, a Phase I/II clinical study, 15 patients (1.8%) developed MDS and 4 (0.5%) developed acute leukemia. The median time to the development of MDS was 28 months (9 to 41 months) and 55 months (32 to 155 months) for acute leukemia.

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- **Renal Toxicity:** Treatment with LUTATHERA will expose kidneys to radiation, which may impair renal function. In ERASMUS <1% of patients developed renal failure 3 to 36 months following LUTATHERA. Monitor serum creatinine and creatinine clearance to assess changes in renal function. Advise patients to urinate frequently during and after administration of LUTATHERA. A concomitant intravenous infusion of amino acids before, during and after LUTATHERA administration is mandatory for renal protection. Patients with baseline renal impairment may be at greater risk of toxicity. Perform more frequent assessments of renal function in patients with mild or moderate impairment. Withhold, reduce dose, or permanently discontinue based on severity of reaction. Do not decrease the dose of amino acid solution if the dose of LUTATHERA is reduced. LUTATHERA has not been studied in patients with severe renal impairment (CrCL < 30 mL/min).
- **Hepatotoxicity:** In ERASMUS, <1% of patients were reported to have hepatic tumor hemorrhage, edema, or necrosis, with one patient experiencing intrahepatic congestion and cholestasis. Patients with hepatic metastasis may be at increased risk of hepatotoxicity due to radiation exposure. Monitor transaminases, bilirubin, and serum albumin during treatment. Withhold, reduce dose, or permanently discontinue based on severity of reaction.
- **Neuroendocrine hormonal crisis:** Manifesting with flushing, diarrhea, bronchospasm and hypotension, neuroendocrine hormonal crisis occurred in 1% of patients in ERASMUS and typically occurred during or within 24 hours following the initial LUTATHERA dose. Monitor patients for flushing, diarrhea, hypotension, bronchoconstriction or other signs and symptoms of tumor-related hormonal release. Administer intravenous somatostatin analogs, fluids, corticosteroids, and electrolytes as indicated.
- **Embryo-Fetal Toxicity:** LUTATHERA can cause fetal harm. Advise females and males of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for 7 months after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 4 months after the final dose. Verify pregnancy status of females of reproductive potential prior to initiating LUTATHERA.
- **Risk of Infertility:** LUTATHERA may cause infertility in males and females. Radiation absorbed by testis and ovaries from the recommended cumulative LUTATHERA dose falls within the range in which temporary or permanent infertility can be expected following external beam radiotherapy.

ADVERSE REACTIONS

The most common Grade 3-4 adverse reactions (≥ 4% with a higher incidence in LUTATHERA arm) observed in NETTER-1 were lymphopenia (44%), increased GGT (20%), vomiting (7%), nausea (5%), elevated AST (5%), increased ALT (4%), hyperglycemia (4%), and hypokalemia (4%).

In ERASMUS, the following serious adverse reactions have been observed with a median follow-up time of more than 4 years after treatment with LUTATHERA: myelodysplastic syndrome (2%), acute leukemia (1%), renal failure (2%), hypotension (1%), cardiac failure (2%), myocardial infarction (1%), and neuroendocrine hormonal crisis (1%). Patients should be counseled and monitored in accordance with the LUTATHERA Prescribing Information.

DRUG INTERACTIONS

Somatostatin and its analogs competitively bind to somatostatin receptors and may interfere with the efficacy of LUTATHERA. Discontinue long-acting somatostatin analogs at least 4 weeks and short-acting octreotide at least 24 hours prior to each LUTATHERA dose. Administer short- and long-acting octreotide during LUTATHERA treatment as recommended.

SPECIFIC POPULATIONS

- **Lactation:** Because of the potential risk for serious adverse reactions in breastfed infants, advise women not to breastfeed during treatment with LUTATHERA and for 2.5 months after the final dose.

To report SUSPECTED ADVERSE REACTIONS, contact Advanced Accelerator Applications USA, Inc. at 1-844-863-1930, or us-pharmacovigilance@adacap.com, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see accompanying full Prescribing Information.

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