Gravity Method Treatment Day Checklist

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

The following guidelines and considerations are provided for informational purposes only.

Radiopharmaceuticals, including LUTATHERA® (lutetium Lu 177 dotatate), should be used by or under the control of health care professionals who are qualified by specific training and experience in the safe use and handling of radiopharmaceuticals, and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radiopharmaceuticals.

Please refer to the Prescribing Information for additional information, including the instructions for the infusion pump method. Use the infusion pump method when administering a reduced dose of LUTATHERA following a dosage modification for an adverse reaction; using the gravity method to administer a reduced dose of LUTATHERA may result in delivery of the incorrect volume of LUTATHERA, if the dose is not adjusted prior to administration.

Date of Treatment _____

LUTATHERA Batch Number _____

This information can be found on the Batch Release Certificate, which must be received prior to injection.

1 *Before Administering LUTATHERA*

Required

- ☐ Discontinue long-acting somatostatin analogs (eg, long-acting octreotide) for at least 4 weeks prior to initiating dose of LUTATHERA *(see Drug Interactions [7.1])*[1]
- ☐ Verify pregnancy status of females of childbearing potential *(see Use in Specific Populations [8.1, 8.3])*[1]
- ☐ Short-acting octreotide may be given for management during treatment with LUTATHERA, but must be withheld for at least 24 hours prior to each dose of LUTATHERA[1]

2 *Items Checklist for Administering LUTATHERA (Please refer to the Administration Guide for further information)*

- ☐ Patient prescription or directive for LUTATHERA[2]
- ☐ Patient release instructions (to be determined by Radiation Safety Officer)[3]
- ☐ Signed informed consent (prior to initiation of LUTATHERA)[3]
- ☐ Geiger-Mueller (GM) survey meter[4]
- ☐ Radioactive materials spill kit[4]
- ☐ Neuroendocrine hormonal crisis intervention medications[1]
- ☐ Contamination protection such as in the patient bathroom and on surface of the medication administration cart[3]

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

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, patient management procedures, Nuclear Regulatory Commission patient-release guidance, and instructions to the patient for follow-up radiation protection at home.

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

Have the following items available for the gravity method:

Pharmaceuticals

- ☐ 500 mL of 0.9% sterile sodium chloride[1]
- ☐ Saline for priming the lines[5]
- ☐ Amino acid solution bag[1]
- ☐ Antiemetics[1]

Radiopharmaceuticals

- ☐ LUTATHERA® (lutetium Lu 177 dotatate) is in a lead-shielded container placed in a plastic sealed container[1]

Equipment

Use aseptic technique and radiation shielding when administering LUTATHERA.[1]

- ☐ Tongs to handle the vial of LUTATHERA[1]
- ☐ Infusion pole[6]

Equipment (continued)

- ☐ 2.5-cm, 20-gauge needle (short needle)[1]
- ☐ 9-cm, 18-gauge needle (long needle)[1]
- ☐ Syringe for saline flush[1]
- ☐ 2 intravenous (IV) pump infusion sets with clamp and Y-connector to regulate flow[5]
- ☐ Male-to-male (m/m) patient line with clamp[5]
- ☐ 3-way stopcock[5]
- ☐ Waterproof gloves[1]
- ☐ Gowns and shoe covers[4]
- ☐ Waste container for contaminated items[1]
- ☐ Radioactive waste disposable bag or container (eg, emesis bag)[5,7]

3 Preparation Prior to Administering LUTATHERA (Nursing)

- ☐ Have patient change into hospital gown[7]
- ☐ Premedication and concomitant medications[1]
- ☐ Administer antiemetics before the recommended amino acid solution[1]
  - Initiate an IV amino acid solution containing L-lysine and L-arginine 30 minutes before administering LUTATHERA[1]
  - Do not inject LUTATHERA directly into any other IV solution[1]
  - Use a 3-way valve to administer amino acids using the same venous access as LUTATHERA or administer amino acids through a separate venous access in the patient's other arm[1]
  - Confirm the amount of radioactivity of LUTATHERA in the radiopharmaceutical vial with an appropriate dose calibrator prior to and after administration of LUTATHERA[1]
  - Continue the infusion during and for at least 3 hours after the infusion of LUTATHERA[1]
- ☐ Advise patients to hydrate and urinate frequently during and after administration of LUTATHERA[1]
- ☐ Inspect the product visually for particulate matter and discoloration prior to administration under a shielded screen. Discard vial if particulates or discoloration are present[1]

4 Administration Setup (Nuclear Medicine)

- ☐ Confirm saline line has been primed and that saline line is closed[5]
- ☐ Prime the m/m tubing with 0.9% sterile sodium chloride[5]
- ☐ Connect the end of the m/m tubing to the saline tubing[5]
- ☐ Connect patient line to the patient catheter and ensure patient line is closed[5]
- ☐ Connect the white end of the m/m tubing to the long, 18-gauge needle[1]
- ☐ Insert the short needle into the vial of LUTATHERA and connect via a catheter to 500 mL, 0.9% sterile sodium chloride solution[1]
- ☐ **WARNING:** Do not allow the short needle to touch the solution of LUTATHERA in the vial and do not connect this short needle directly to the patient. Do not allow sodium chloride solution to flow into the vial of LUTATHERA prior to the initiation of the infusion of LUTATHERA and do not inject LUTATHERA directly into the sodium chloride solution[1]
- ☐ Insert a second needle that is 9 cm, 18 gauge (long needle) into the vial of LUTATHERA ensuring that this long needle touches and is secured to the bottom of the vial of LUTATHERA during the entire infusion[1]
- ☐ 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 infusion of LUTATHERA into the patient[1]

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

5 Administration (Nuclear Medicine)

- ☐ Using a survey meter, survey the top of the vial of LUTATHERA® (lutetium Lu 177 dotatate) to have a baseline for comparison at the end of administration of LUTATHERA[5]
- ☐ Do not decrease the dose of the amino acid solution if the dose of LUTATHERA is reduced[1]
- ☐ Confirm the amount of radioactivity of LUTATHERA in the radiopharmaceutical vial with an appropriate dose calibrator prior to and after administration of LUTATHERA[1]
- ☐ Open the patient line[5]
- ☐ Open the saline line[5]
- ☐ Use a clamp or pump to regulate the flow of the sodium chloride solution via the short needle into the vial of LUTATHERA at a rate of 50 mL/h to 100 mL/h for 5 to 10 minutes[1]
- ☐ Use a survey meter to confirm flow into the patient catheter[1]
- ☐ Continue administration at 200 mL/h to 300 mL/h for an additional 25 to 30 minutes (the sodium chloride solution entering the vial through the short needle will carry the LUTATHERA from the vial to the patient via the catheter connected to the long needle over a total duration of 30 to 40 minutes)[1]
- ☐ Do not administer LUTATHERA as an IV bolus[7]
- ☐ During the infusion, ensure that the level of solution in the vial of LUTATHERA remains constant[1]
- ☐ After 25 to 30 minutes, survey the top of the vial; alternatively, the survey meter can be placed underneath the m/m line. Survey every 5 minutes until the reading is stable[1,5]
- ☐ Disconnect the vial from the long needle line and clamp the saline line once the level of radioactivity is stable for at least 5 minutes
- ☐ Follow the infusion with an IV flush of 25 mL of 0.9% sterile sodium chloride[1]
- ☐ Assay the vial of LUTATHERA for residual activity in the dose calibrator[1,5,7]

6 Dose Calibrator Measurements

- ☐ Confirm the amount of radioactivity of LUTATHERA in the radiopharmaceutical vial with an appropriate dose calibrator prior to and after administration of LUTATHERA[1]

7 Cleanup and Waste Disposal

- ☐ Use the GM survey meter to check for contamination on equipment and affected locations[1,5]
- ☐ Dispose of any unused medicinal product or waste material in accordance with local and federal laws[1]

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

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, patient management procedures, Nuclear Regulatory Commission patient-release guidance, and instructions to the patient for follow-up radiation protection at home.
- **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 myelosuppression.
- **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 II clinical study, 16 patients (2%) 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.
- **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

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

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (CONTINUED)

- **Renal Toxicity (Continued):** 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 renal toxicity. Do not decrease the dose of amino acid solution if the dose of LUTATHERA is reduced. LUTATHERA® (lutetium Lu 177 dotatate) 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 hepatic impairment.
- **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 pregnant women 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 testes 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.

Corticosteroids can induce down-regulation of subtype 2 somatostatin receptors (SSTR2). Avoid repeated administration of high doses of glucocorticosteroids during treatment with LUTATHERA.

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 at 1-888-669-6682 or http://www.report.novartis.com, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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

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References: 1. Lutathera [prescribing information]. Millburn, NJ: Advanced Accelerator Applications; 2021. **2.** United States Nuclear Regulatory Commission. Subpart E—unsealed byproduct material—written directive required. Updated January 16, 2019. Accessed July 13, 2021. https://www.nrc.gov/reading-rm/doc-collections/cfr/part035/part035-0300.html. **3.** Abbott A, Sakellis CG, Anderson E, et al. Guidance on ^{177}Lu-DOTATATE peptide receptor radionuclide therapy from the experience of a single nuclear medicine division. *J Nucl Med Technol.* 2018;46(3):237-244. **4.** United States Nuclear Regulatory Commission. Item 19 emergency procedures. Revision 103/08. Accessed July 12, 2021. https://www.nrc.gov/docs/ML0827/ML082750235.pdf. **5.** Data on file. Advanced Accelerator Applications. Accessed July 12, 2021. **6.** Davis AB, Pietryka MH, Passalaqua S. Technical aspects and administration methods of ^{177}Lu-DOTATATE for nuclear medicine technologists. *J Nucl Med Technol.* 2019;47(4):288-291. **7.** Hope TA, Abbott A, Colucci K, et al. NANETS/SNMMI procedure standard for somatostatin receptor–based peptide receptor radionuclide therapy with ^{177}Lu-DOTATATE. *J Nucl Med.* 2019;60(7):937-943. **8.** Doyle GR, McCutcheon JA. *Clinical procedures for safer patient care.* Published 2015. Accessed July 12, 2021. https://opentextbc.ca/clinicalskills/.

Advanced Accelerator Applications
A Novartis Company

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

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