A Guide to NURSING CARE FOR ADMINISTERING STAFF AT TREATMENT CENTERS

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

Caring for patients during and after LUTATHERA administration

Not actual patients.

INDICATION

LUTATHERA® (lutetium Lu 177 dotatate) is indicated for the treatment of adult and pediatric patients aged 12 years and older with somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors.

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.

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Please see additional Important Safety Information throughout and full Prescribing Information.

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A Guide to NURSING CARE

FOR ADMINISTERING STAFF AT TREATMENT CENTERS

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Coordinating care: Multidisciplinary roles and responsibilities

As an administering nurse, you help put patients at ease. Your communication with their referring staff can be crucial in helping ensure their continuity of care.

Below are some of the multidisciplinary roles and responsibilities of those involved in a patient's journey with LUTATHERA. It's important to keep in mind that guidelines for such roles may vary by institution.

1: IDENTIFY

Referring Medical Oncology Practice

Identify and test appropriate patients for LUTATHERA

The referring oncologist examines the patient holistically, including testing for SSTR presence and tumor localization via imaging—part of each patient's staging and eligibility process for LUTATHERA.[1,2]

- Your medical oncology practice identifies a patient with an SSTR+ GEP-NET in the foregut, midgut, or hindgut[1]

Referring nurses may help identify appropriate patients for LUTATHERA early by[1,3,4]:

- Monitoring patients with newly diagnosed SSTR+ metastatic or advanced GEP-NETs
- Closely monitoring patients for disease progression on an SSA, regardless of the presence of symptoms

2: REFER

Referring Medical Oncology Practice

Refer patient to treatment site

Nurse coordinates patient care with the care team at the treatment site and makes sure to follow the recommendations from the treating physician, such as:

- Discontinue long-acting SSA ≥4 weeks prior to the administration of LUTATHERA[1]
- Administer short-acting SSA as needed; discontinue at least 24 hours prior to initiating LUTATHERA[1]
- Confirm schedule of periodic laboratory testing[1]
- Verify pregnancy status for patients of childbearing potential[1]

3: ADMINISTER

Administering Nuclear Medicine or Radiation Oncology Practice

Initiate LUTATHERA at treatment site

- Patient may undergo additional testing at the treatment site to confirm eligibility or readiness to initiate treatment[1,2]
- Assist in administration of treatment: the recommended dosing is 4 cycles of treatment at 8-week intervals[1]

GEP-NET, gastroenteropancreatic neuroendocrine tumor; SSA, somatostatin analogue; SSTR, somatostatin receptor; SSTR+, somatostatin receptor-positive.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Myelosuppression:** In the NETTER-1 clinical trial, myelosuppression occurred more frequently in patients receiving LUTATHERA with long-acting octreotide compared with patients receiving high-dose long-acting octreotide (all grades/grade 3/4): anemia (81%/0 vs 54%/1%), thrombocytopenia (53%/1% vs 17%/0), and neutropenia (26%/3% vs 11%/0). In NETTER-1, platelet nadir occurred at a median of 5.1 months following the first dose.

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Coordinating care for LUTATHERA administration and follow-up

Administering nurses have responsibilities and challenges that can go beyond treatment, including communicating and aligning with the referring staff, understanding timing and the medications that must be coadministered, and managing any infusion safety concerns.

Treatment Site: Administering Nuclear Medicine or Radiation Oncology Practice

Before initiating LUTATHERA

- Patient is checked in for treatment and provided assessment, expectations for the day, and orientation of the room
- Antiemetics are administered 30 minutes before the recommended amino acid solution to prevent nausea and vomiting[1,2]
- An IV sterile amino acid solution containing L-lysine and L-arginine is initiated 30 minutes before administering LUTATHERA[1]
- Patients who have had prior grade 1/2 hypersensitivity reactions to LUTATHERA are premedicated[1]

During LUTATHERA administration[1]

- Infusion is continued during and for at least 3 hours after the completion of the infusion of LUTATHERA
- The dose of the amino acid solution is not decreased if a reduced dose of LUTATHERA is administered
- Patients who experience grade 3/4 hypersensitivity reactions to LUTATHERA are not rechallenged

Treatment Site: Administering Nuclear Medicine or Radiation Oncology Practice

AFTER each dose of LUTATHERA[1]

- Long-acting octreotide 30 mg IM is administered between 4 and 24 hours after each dose of LUTATHERA
- Patient is monitored for adverse reactions and laboratory abnormalities
- Patient is reminded when and where they will receive their next SSA treatment

IM, intramuscular; IV, intravenous.

Referring Medical Oncology Practice

AFTER all doses of LUTATHERA are completed

- Long-acting octreotide 30 mg IM should continue every 4 weeks until disease progression or for 18 months following treatment initiation at the discretion of the physician[1]
- Patients are closely monitored for disease progression on an SSA, regardless of the presence of symptoms[1,3]

Have you confirmed the details of your patient's treatment with the referring staff?

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Myelosuppression (continued):** Of the 59 patients who developed thrombocytopenia, 68% had platelet recovery to baseline or normal levels. The median time to platelet recovery was 2 months. Fifteen of the 19 patients in whom platelet recovery was not documented had post-nadir platelet counts. Among these 15 patients, 5 improved to grade 1, 9 to grade 2, and 1 to grade 3. Monitor blood cell counts. Withhold dose, reduce dose, or permanently discontinue LUTATHERA based on the severity of myelosuppression.

Gathering essential patient information before treatment

Before treatment with LUTATHERA, it's important to gather the following information from patients and their referring team.

Eligibility[1]

- ✓ Confirmed SSTR+ GEP-NET in the foregut, midgut, or hindgut

Patient management

- ✓ Any medical conditions patients may have
- ✓ Urinary or fecal incontinence
- ✓ Changes in symptoms
  - Anticipate patient accommodations and potential treatment reactions

Compatibility with treatment

- ✓ Pregnancy status and breastfeeding intentions
  - Advise patients who are able to get pregnant to use effective contraception during treatment with LUTATHERA and **for 7 months after the last dose**[1]
  - Advise patients with partners who are able to get pregnant to use effective contraception during treatment with LUTATHERA and **for 4 months after the last dose**[1]
  - Patients should not breastfeed during treatment with LUTATHERA and **for 2.5 months after the last dose**[1]
  - See the full Prescribing Information for risks associated with pregnancy and breastfeeding
- ✓ Any medications (including over-the-counter medications)
  - SSAs: See the dosing section on page 6 and the full Prescribing Information for discontinuation timing and other details[1]
  - Repeated administration of high doses of glucocorticoids can affect LUTATHERA efficacy and are to be avoided during treatment[1]
  - Timing and administration of other concomitant medications may need to be taken under consideration[1]

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

- **Secondary Myelodysplastic Syndrome and Leukemia:** In NETTER-1, with a median follow-up time of 76 months in the main study, myelodysplastic syndrome (MDS) was reported in 2.3% of patients receiving LUTATHERA with long-acting octreotide compared with no patients receiving high-dose long-acting octreotide. In ERASMUS, a phase 2 clinical study, 16 patients (2.0%) developed MDS and 4 (0.5%) developed acute leukemia. The median time to onset was 29 months (range, 9-45 months) for MDS and 55 months (range, 32-125 months) for acute leukemia.

Patient tips for treatment day and follow-up

When discussing treatment day and onward, these reminders can help prepare your patients for LUTATHERA. Patients will receive additional specific details or directions from their treatment facility.

Infusion day medications

- Any required **antinausea therapy will be given on the same day**, before both the amino acid solution and LUTATHERA[1,2]
- **Amino acid infusion will be started on the same day** 30 minutes before—and last for at least 3 hours after—the LUTATHERA infusion[1]

Staying hydrated

- **Patients should drink liquids and urinate frequently** before, on the day of, and on the day after administration of LUTATHERA[1]

Breastfeeding

- **Patients should not breastfeed during treatment** with LUTATHERA and for 2.5 months after the last infusion of LUTATHERA[1]

Using birth control

- **Patients should use effective birth control** during treatment with LUTATHERA and for[1]:
  - 7 months after the last dose if the patient is able to get pregnant
  - 4 months after the last dose if the patient has a partner who is able to get pregnant

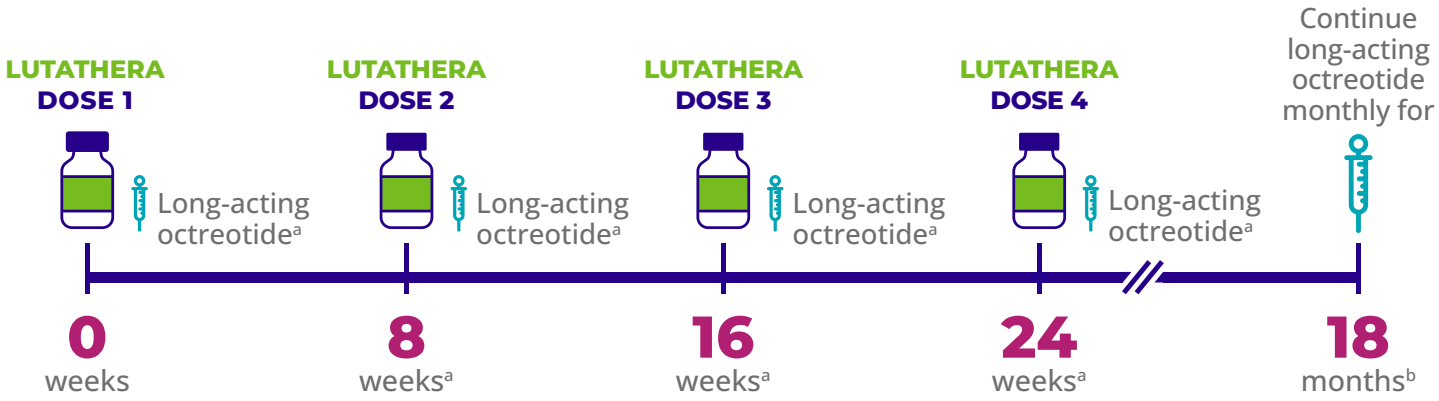
IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Renal Toxicity:** In ERASMUS, 8 patients (<1%) developed renal failure 3 to 36 months following LUTATHERA. Two of these patients had underlying renal impairment or risk factors for renal failure (eg, diabetes or hypertension) and required dialysis. Administer the recommended amino acid solution before, during, and after LUTATHERA to decrease the reabsorption of lutetium Lu 177 dotatate through the proximal tubules and decrease the radiation dose to the kidneys. Advise patients to hydrate and to urinate frequently before, on the day of, and on the day after administration of LUTATHERA. Monitor serum creatinine and calculated creatinine clearance. Withhold dose, reduce dose, or permanently discontinue LUTATHERA based on the severity of renal toxicity.

The dosing regimen for LUTATHERA remains the same, regardless of patient type[1]

The defined 4-dose LUTATHERA regimen is available at treatment centers nationwide[1]



[a]Administer long-acting octreotide 30 mg IM between 4 to 24 hours after each dose of LUTATHERA. Do not administer long-acting octreotide within 4 weeks prior to each subsequent dose of LUTATHERA. The interval between infusions may be extended up to 16 weeks in the case of a dose modification due to an adverse reaction. Permanently discontinue LUTATHERA in patients who experience grade 3/4 hypersensitivity reactions. Please see the Prescribing Information for additional information on dose modifications.[1]

[b]Continue long-acting octreotide 30 mg IM every 4 weeks after completing LUTATHERA until disease progression or for 18 months following treatment initiation at the discretion of the physician.[1]

During treatment, long-acting octreotide 30 mg IM will be administered between 4 to 24 hours after each dose of LUTATHERA[1]

- LUTATHERA dosage should be modified based on hematologic, renal, hepatic, hypersensitivity, or other adverse reactions (see full Prescribing Information)[1]
- For reduced dose administration instructions, refer to section 2.5 (Preparation and Administration) of the full Prescribing Information

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Renal Toxicity (continued):** Patients with baseline renal impairment may be at increased risk of toxicity due to increased radiation exposure; perform more frequent assessments of renal function in patients with baseline mild or moderate impairment. LUTATHERA has not been studied in patients with baseline severe renal impairment (creatinine clearance <30 mL/min) or those with end-stage renal disease.

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

Dosing regimen

Before each dose of LUTATHERA[1]

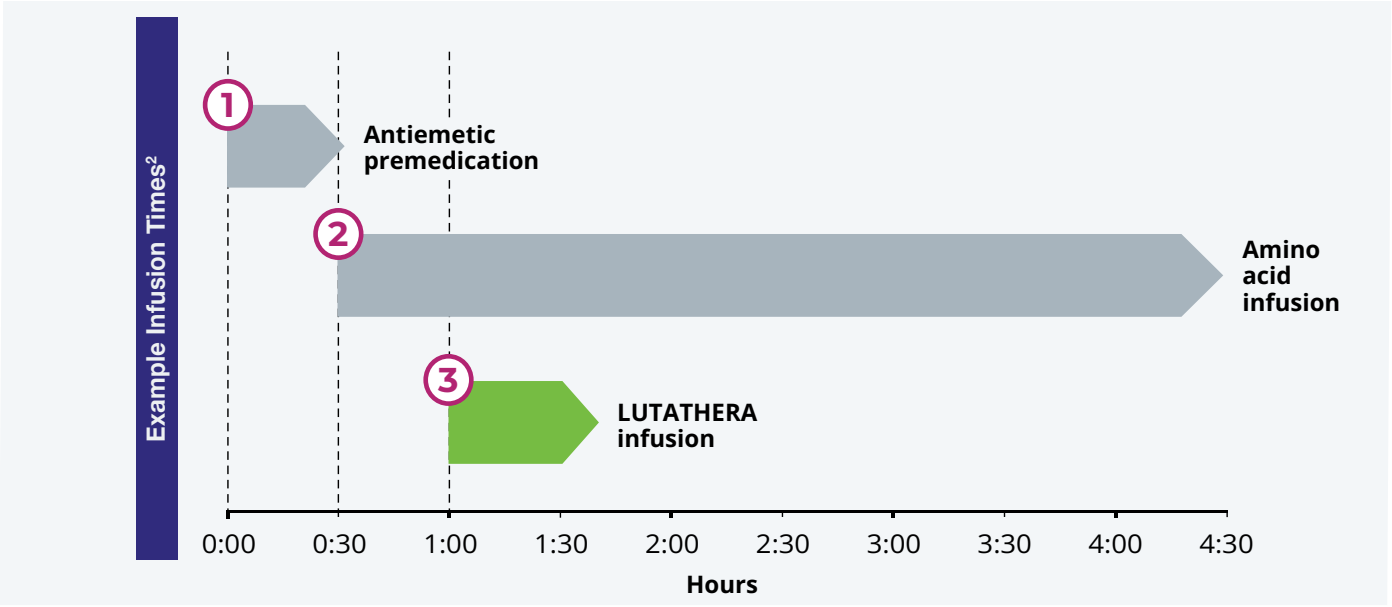
LONG-ACTING SSAs	Must be withheld **at least 4 weeks**
SHORT-ACTING SSAs	Must be withheld **at least 24 hours**
ANTIEMETICS	Premedication with antiemetics should be administered **prior to the start** of the amino acid solution infusion
AMINO ACID INFUSION	START 30 minutes before and CONTINUE during LUTATHERA infusion and for **at least 3 hours after**
TIMING	Time for the actual LUTATHERA infusion ranges from **30 to 40 minutes** depending on the method of administration See the LUTATHERA Prescribing Information for additional infusion protocol

88% of patients completed all 4 doses of LUTATHERA in NETTER-2 and 77% of patients completed all 4 doses of LUTATHERA in NETTER-1[5,6]

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

- **Hepatotoxicity:** In ERASMUS, 2 patients (<1%) were reported to have hepatic tumor hemorrhage, edema, or necrosis, with 1 patient experiencing intrahepatic congestion and cholestasis. Patients with hepatic metastasis may be at increased risk of hepatotoxicity due to radiation exposure. Monitor transaminases, bilirubin, serum albumin, and the international normalized ratio during treatment. Withhold dose, reduce dose, or permanently discontinue LUTATHERA based on the severity of hepatotoxicity.

Preparing for the infusion process



1. • **Antiemetic** premedication must be given 30 minutes before both the amino acid solution and LUTATHERA[1,2]
2. • Sterile **amino acid IV solution** (containing L-lysine and L-arginine) must begin 30 minutes before the start of LUTATHERA[1,2]
   • Continue the amino acid infusion during and for at least 3 hours after the completion of the infusion of LUTATHERA[1,2]
   • Do not decrease the dose of the amino acid solution if a reduced dose of LUTATHERA is administered[1,2]
   • Use a 3-way valve to administer the amino acid solution using the same venous access as LUTATHERA, or administer in the patient's other arm (separate venous access)[1,2]
3. **LUTATHERA** infusion:
   • Premedicate patients who have had prior grade 1/2 hypersensitivity reactions[1,2]
   • Do not rechallenge patients who experience grade 3/4 hypersensitivity reactions[1,2]
   • Monitor patients closely for signs and symptoms of hypersensitivity reactions, including anaphylaxis, during and following LUTATHERA administration for a minimum of 2 hours in a setting where cardiopulmonary resuscitation medication and equipment are available[1,2]
   • Discontinue the infusion upon the first observation of any signs or symptoms consistent with a severe hypersensitivity reaction and initiate appropriate therapy[1,2]

Confirm the administration method, as well as roles and responsibilities of infusion timing, with the nuclear medicine professional in your treatment center

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Hypersensitivity Reactions:** Hypersensitivity reactions, including angioedema, occurred in patients treated with LUTATHERA.

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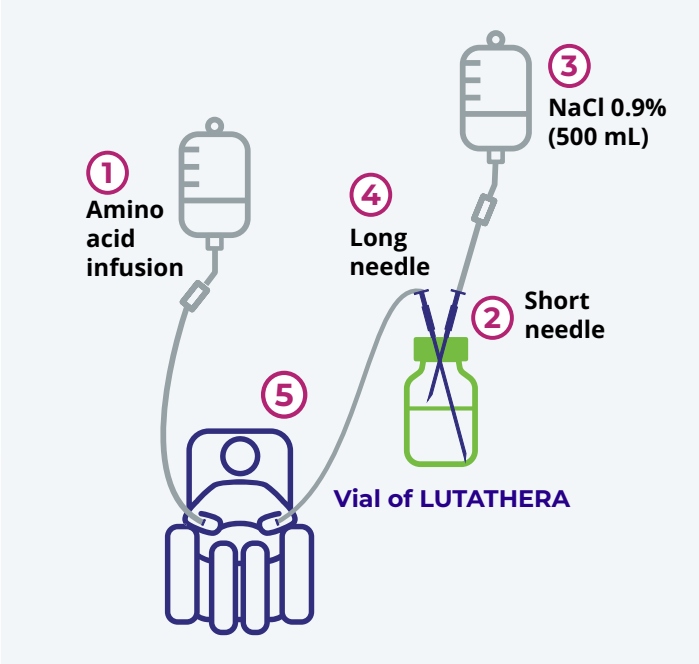
It is likely that the nuclear medicine professional will administer LUTATHERA using the gravity method*



The gravity method of administration[1,2]

1. Administer amino acid solution 30 minutes before the start of LUTATHERA.
2. Insert the 2.5-cm, 20-gauge needle (short needle) into the vial of LUTATHERA.
3. Connect the short needle to the 500 mL of 0.9% sterile sodium chloride solution via catheter.
4. Insert the 9-cm, 18-gauge needle (long needle) into the vial of LUTATHERA.
5. Connect the long needle to the patient by an IV catheter. Catheter should be prefilled with 0.9% sterile sodium chloride and used exclusively for LUTATHERA.

- The short needle must not touch the solution of LUTATHERA inside the vial
- Do not allow sterile sodium chloride to flow into the vial prior to the start of the infusion
- Do not connect the short needle directly to the patient
- Do not inject LUTATHERA directly into the sodium chloride solution
- The long needle must touch and be secured to the bottom of the vial during the entire infusion of LUTATHERA
- Amino acid solution can be administered via a 3-way valve using the same venous access as LUTATHERA, or in the patient's other arm (separate venous access)[1,2]

These are not inclusive of every administrative step. Please refer to the full Prescribing Information (section 2.5) for detailed instructions.

*The gravity method, peristaltic pump method, or the syringe pump method may be used for LUTATHERA administration. The peristaltic pump or syringe pump methods are used when administering a reduced dose of LUTATHERA following a dosage modification for an adverse reaction. When using the gravity method for a reduced dose, adjust the LUTATHERA dose before the administration to avoid the delivery of an incorrect volume of LUTATHERA.

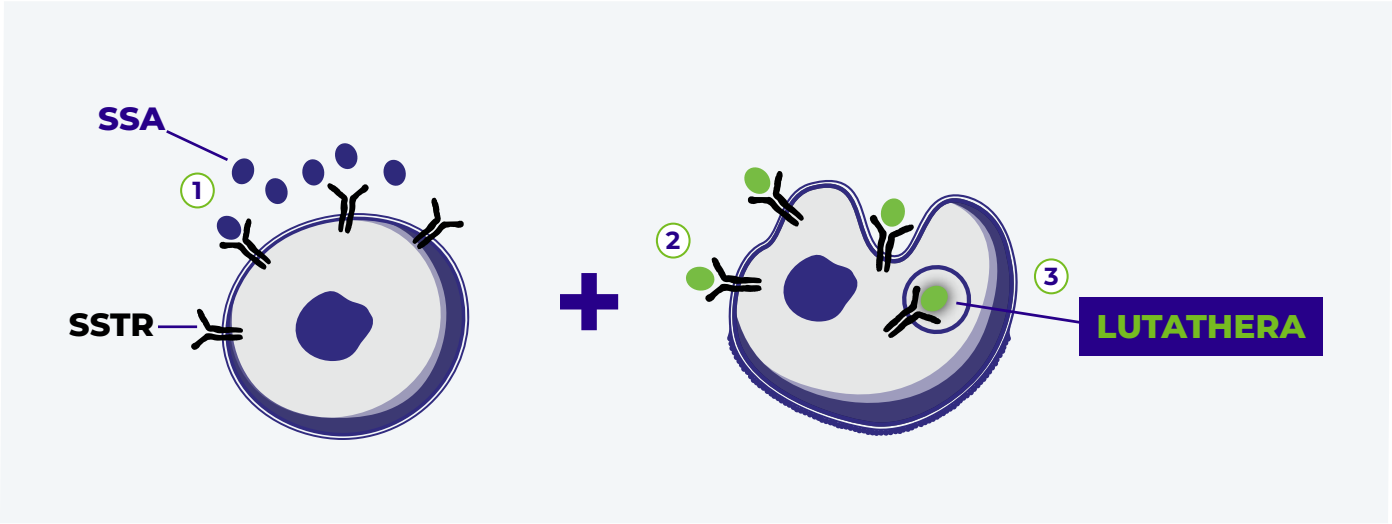
IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Hypersensitivity Reactions (continued):** Monitor patients closely for signs and symptoms of hypersensitivity reactions, including anaphylaxis, during and following LUTATHERA administration for a minimum of 2 hours in a setting in which cardiopulmonary resuscitation medication and equipment are available. Discontinue the infusion upon the first observation of any signs or symptoms consistent with a severe hypersensitivity reaction and initiate appropriate therapy. Premedicate patients with a history of grade 1/2 hypersensitivity reactions to LUTATHERA before subsequent doses. Permanently discontinue LUTATHERA in patients who experience grade 3/4 hypersensitivity reactions.

How LUTATHERA works

Almost 90% of GEP-NETs overexpress SSTR[7]



1. SSA targets and binds to SSTR+ GEP-NET cells[1,8-11]

2. Alongside SSAs, LUTATHERA also destroys SSTR+ cells and ultimately results in tumor cell death[1,8-11]

3. LUTATHERA is infused into the bloodstream, where it targets the malignant cells overexpressing SSTR and releases radioactive lutetium 177, causing DNA damage[1,8-11]

Based on preclinical models. LUTATHERA delivers radiation that causes damage to the SSTR+ cells, as well as neighboring, healthy cells.[1,8-11]

LUTATHERA specifically targets and destroys SSTR+ cells[1]

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Neuroendocrine Hormonal Crisis:** Neuroendocrine hormonal crises, manifesting with flushing, diarrhea, bronchospasm, and hypotension, occurred in <1% of patients in ERASMUS and typically occurred during or within 24 hours following the initial LUTATHERA dose. Two (<1%) patients were reported to have hypercalcemia. Monitor patients for flushing, diarrhea, hypotension, bronchoconstriction, or other signs and symptoms of tumor-related hormonal release. Administer intravenous somatostatin analogues, fluids, corticosteroids, and electrolytes as indicated.

Radiation guidelines for patients

Treatment safety guidelines for HCPs: ALARA (As Low As Reasonably Achievable)

Following the principles of ALARA can help minimize radiation exposure. These principles include avoiding unnecessary exposure to radiation by using 3 protective measures[12]:

Minimize the time spent near radioligand therapy[12]

Maximize the distance from radioligand therapy[12]

Use appropriate shielding from radioligand therapy[12]

Posttreatment patient safety guidelines[12] (NANETS/SNMMI consensus and Mayo Clinic recommendations)

Your patients will receive more details from the treatment center, but here are some frequently discussed topics regarding posttreatment LUTATHERA radiation precautions.

Using the toilet
For at least 3 days, patients should use the toilet in a seated position (even for men) and flush the toilet twice after use.[2]

Sleeping
For at least 3 days, patients should sleep in a separate bed and avoid intimate contact.[2]

Showering and personal hygiene
For at least 7 days, patients should shower daily. For at least 3 days, patients should use separate towels and washcloths and wash laundry separately from the rest of their household.[2,13]

Interacting with others
For at least 3 days, patients should use a general distance guideline of no closer than 3 feet for no more than 1 hour per day. They should try to maintain a distance of 6 feet from others and minimize use of public transportation and public facilities.[2]

For more specific guidance, consult your patient's treatment center

HCPs, health care professionals; NANETS, North American Neuroendocrine Tumor Society; SNMMI, Society of Nuclear Medicine and Molecular Imaging.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Embryo-Fetal Toxicity:** LUTATHERA can cause fetal harm when administered to a pregnant woman. Verify the pregnancy status of females of reproductive potential prior to initiating LUTATHERA. Advise pregnant women of the potential risk to a fetus.

Radiation guidelines for HCPs and caregivers

Radiation exposures to the care team and caregivers were within ICRP limits of 20 mSv per year[14,15,*]

When discussing treatment day and onward, these reminders can help prepare your patients for LUTATHERA. Patients will receive additional specific details from the treatment facility.

Exposure to nurses was similar to that of a flight crew on regular round-trip flights from Los Angeles to Honolulu[14,16]

Mean whole-body radiation exposures per treatment day: 6.8 µSv (nuclear medicine technologist); 33.2 µSv (nurse)[14]

Exposure to caregivers was similar to that of a chest x-ray[14,17]

Mean total exposure during the day of therapy and at home for up to 5 days: 90 µSv (median, 40 µSv [range, 10 µSv-470 µSv])[14]

Exposure is 14.5 µSv on a 5.2-hour flight from Los Angeles, California to Honolulu, Hawaii[16]

X-ray exposure is 100 µSv[17]

*Averaged over a defined period of 5 years, with no single year exceeding 50 mSv[15]

Patients are discharged from the treatment center only when radiation exposure to others does not exceed regulatory thresholds[18]

Seventy-six patients with progressive, metastatic NETs received 4 cycles of 7.8 GBq of Lutetium 177 at 8-week intervals in an outpatient setting at 1 treatment center. Four patients were treated sequentially on each therapy day in a 4-bed room in the hospital's day procedure unit, with each patient remaining until radiation exposure was below the release limit. Radiation exposures to HCPs and caregivers were monitored by personal dosimeter. Twenty-five carers were provided with electronic dosimeters. In the nearby staff office with a 50% staff occupancy factor, the mean (range) exposure rate measured on 10 different therapy administration days was 1.6 µSv/h (1.3–2.0 µSv/h), and at the nursing station with 100% staff occupancy it was 3.5 µSv/h (2.9–4.0 µSv/h).[14]

µSv, microsievert; GBq, gigabecquerel; ICRP, International Commission on Radiological Protection; mSv, millisievert; NETs, neuroendocrine tumors.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Embryo-Fetal Toxicity (continued):** Advise females of reproductive potential to use effective contraception during treatment with LUTATHERA and for 7 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with LUTATHERA and for 4 months after the last dose.

1L safety and long-term safety data in 2L

Safety in NETTER-2 was consistent with the established safety demonstrated in NETTER-1

- The most common adverse events (≥20% in either arm) were nausea (27% vs 18%), diarrhea (26% vs 34%), and abdominal pain (18% vs 27%) for LUTATHERA + SSA vs SSA alone, respectively[6]
- The most common grade 3/4 adverse events (>3% in either arm) were lymphocyte count decreased (5% vs 0%), GGT increased (5% vs 3%), small intestinal obstruction (3% vs 0%), and abdominal pain (3% vs 4%) for LUTATHERA + SSA vs SSA alone, respectively[6]
- 2% of patients needed a reduced dose and 5% discontinued treatment with LUTATHERA due to AEs[6]

No new safety signals were reported in the 5-year, long-term follow-up for NETTER-1[19,*]

Adverse Events	During the long-term follow-up, only serious adverse events (SAEs) deemed related to treatment with LUTATHERA and AEs of special interest (hematotoxicity, cardiovascular events, and nephrotoxicity, regardless of causality) in the LUTATHERA arm were reported[19]
Grade ≥3 Treatment-Related SAEs During the Entire Study	7 (6%) of 111 patients treated in the LUTATHERA arm[19]
Incidence of Treatment-Related SAEs During the Long-Term Follow-Up Period	**3 (3%) of 111 patients treated with LUTATHERA**[19] — 2 (1.8%) patients experienced at least 1 grade ≥3 SAE (1 grade 5 MDS event)[19] — 1 (0.9%) patient experienced an SAE leading to study discontinuation[19]
MDS or Acute Leukemia	**No new cases were reported during long-term follow-up**[19] — MDS incidence from the Prescribing Information for LUTATHERA: In NETTER-1, with a median follow-up time of 76 months in the main study, MDS was reported in 2.3% of patients receiving LUTATHERA with long-acting octreotide compared with no patients receiving high-dose, long-acting octreotide[1,19] — In ERASMUS, 16 patients (2.0%) developed MDS and 4 (0.5%) developed acute leukemia. The median time to onset was 29 months (range, 9-45 months) for MDS and 55 months (range, 32-125 months) for acute leukemia[1,a]
Diffuse Large B-Cell Lymphoma	One patient developed diffuse large B-cell lymphoma during long-term follow-up that was deemed unrelated to treatment with LUTATHERA[19]
Nephrotoxicity of Grade ≥3, Regardless of Causality	Reported in 6 (5%) of 111 patients in the LUTATHERA arm and 4 (4%) of 112 patients in the control arm during the study[19]

*Cutoff date for final analysis was January 18, 2021.[19]

[a]ERASMUS study design: Retrospective safety data are available from 1214 patients in ERASMUS, an international, single-institution, single-arm, open-label trial of patients with SSTR+ tumors (neuroendocrine and other primaries). The median duration of follow-up was >4 years.[1]

1L, first line; 2L, second line; AEs, adverse events; GGT, gamma-glutamyl transferase; MDS, myelodysplastic syndrome.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Risk of Infertility:** LUTATHERA may cause infertility in males and females.

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

Dosing modifications

LUTATHERA dosing may require modification for patients who experience adverse reactions

See more details regarding adverse reactions in the LUTATHERA full Prescribing Information.

Adverse Reaction[1]	Severity of Adverse Reaction[1,a]	Dose Modification[1]
Thrombocytopenia	Grade 2, 3, or 4	Withhold dose until complete or partial resolution (grade 0 to 1). Resume LUTATHERA at 3.7 GBq (100 mCi) in patients with complete or partial resolution. If reduced dose does not result in grade 2, 3, or 4 thrombocytopenia, administer LUTATHERA at 7.4 GBq (200 mCi) for next dose. Permanently discontinue LUTATHERA for grade 2 or higher thrombocytopenia requiring a treatment delay of 16 weeks or longer.
	Recurrent grade 2, 3, or 4	Permanently discontinue LUTATHERA.
Anemia and Neutropenia	First occurrence of grade 3 or 4	Withhold dose until complete or partial resolution (grade 0, 1, or 2). Resume LUTATHERA at 3.7 GBq (100 mCi) in patients with complete or partial resolution. If reduced dose does not result in grade 3 or 4 anemia or neutropenia, administer LUTATHERA at 7.4 GBq (200 mCi) as next dose. Permanently discontinue LUTATHERA for grade 3 or higher anemia or neutropenia requiring a dosing interval beyond 16 weeks.
	Recurrent grade 3 or 4	Permanently discontinue LUTATHERA.
Renal Toxicity	First occurrence of: • Creatinine clearance less than 40 mL/min; calculated using Cockcroft-Gault formula with actual body weight, or • 40% increase from baseline serum creatinine, or • 40% decrease from baseline creatinine clearance; calculated using Cockcroft-Gault formula with actual body weight	Withhold dose until resolution or return to baseline. Resume LUTATHERA at 3.7 GBq (100 mCi) in patients with resolution or return to baseline. If reduced dose does not result in renal toxicity, administer LUTATHERA at 7.4 GBq (200 mCi) as next dose. Permanently discontinue LUTATHERA for renal toxicity requiring a dosing interval beyond 16 weeks.
	Recurrent renal toxicity	Permanently discontinue LUTATHERA.

[a]Grading of severity is defined in the most current National Cancer Institute CTCAE Version 4.03.
CTCAE, Common Terminology Criteria for Adverse Events; mCi, millicurie.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

- **Risk of Infertility (continued):** 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.

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Please see additional Important Safety Information throughout and full Prescribing Information.

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

Dosing modifications (continued)

Adverse Reaction[1]	Severity of Adverse Reaction[1,a]	Dose Modification[1]
Hepatotoxicity	First occurrence of: • Bilirubinemia greater than 3 times the upper limit of normal (grade 3 or 4), or • Serum albumin less than 30 g/L with international normalized ratio (INR) >1.5	Withhold dose until resolution or return to baseline. Resume LUTATHERA at 3.7 GBq (100 mCi) in patients with resolution or return to baseline. If reduced LUTATHERA dose does not result in hepatotoxicity, administer LUTATHERA at 7.4 GBq (200 mCi) as next dose. Permanently discontinue LUTATHERA for hepatotoxicity requiring a dosing interval beyond 16 weeks.
	Recurrent hepatotoxicity	Permanently discontinue LUTATHERA.
Hypersensitivity Reactions[b]	First occurrence of grade 3 or 4	Permanently discontinue LUTATHERA.
Any Other Adverse Reactions[c]	First occurrence of grade 3 or 4	Withhold dose until complete or partial resolution (grade 0 to 2). Resume LUTATHERA at 3.7 GBq (100 mCi) in patients with complete or partial resolution. If reduced dose does not result in grade 3 or 4 toxicity, administer LUTATHERA at 7.4 GBq (200 mCi) as next dose. Permanently discontinue LUTATHERA for grade 3 or higher adverse reactions requiring a dosing interval beyond 16 weeks.
	Recurrent grade 3 or 4	Permanently discontinue LUTATHERA.

[a]Grading of severity is defined in the most current National Cancer Institute CTCAE Version 4.03.
[b]Including allergic reaction and anaphylaxis.
[c]No dose modification required for hematological toxicities of grade 3 or grade 4 solely due to lymphopenia.

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS

The most common grade 3/4 adverse reactions (≥4% with a higher incidence in the LUTATHERA arm) observed in NETTER-1 were lymphopenia (44%), increased gamma-glutamyl transferase (20%), vomiting (7%), nausea (5%), increased aspartate aminotransferase (5%), increased alanine aminotransferase (4%), hyperglycemia (4%), and hypokalemia (4%).

In ERASMUS, the following serious adverse reactions have been observed with a median follow-up time of >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.

Adverse reactions observed in pediatric patients were similar to those observed in adults treated with LUTATHERA.

DRUG INTERACTIONS

Discontinue long-acting somatostatin analogues at least 4 weeks and short-acting octreotide at least 24 hours prior to each LUTATHERA dose.

Novartis Patient Support™: A dedicated team for you and your patients

Novartis Patient Support is a comprehensive program designed to help your patients start, stay, and save on LUTATHERA

We provide support throughout your patient's journey with:

Insurance & Reimbursement

Support includes:

- Benefits verification
- Prior authorization requirements
- Appeals support
- Billing, coding, and reimbursement education

Financial Support

Eligible patients may **pay as little as $0*** per dose. Enrollment is required to determine eligibility and participation.

Acquisition

Support includes:

- New treating site onboarding and access to ordering platform
- Real-time delivery tracking

Patient Education

Live 1-on-1 support is available for patients starting treatment. Our Patient Navigators can help answer the most common treatment questions.

Ask your Novartis Oncology Specialist to connect you with your local Access & Reimbursement Representative to help answer detailed questions on payer coverage, patient affordability, purchasing, pricing, and reimbursement.

Visit www.lutathera-hcp.com/novartis-patient-support for more information

*Limitations apply. Valid only for those patients with commercial insurance. Not valid under Medicare or any other federal or state program. Offer subject to a maximum benefit per course of treatment. See complete Terms and Conditions in the Start Form for details.

Community support for your patients

Are your patients looking to learn more about GEP-NETs on their own?

The following support networks may help patients with general information and social support.

The Carcinoid Cancer Foundation (CCF)
www.carcinoid.org

The Neuroendocrine Cancer Awareness Network (NCAN)
3074 Brookchase Boulevard
Fort Mill, SC 29707
1-866-850-9555
info@netcancerawareness.org
www.netcancerawareness.org

The Healing NET Foundation
415 Spence Lane
Nashville, TN 37210
1-615-369-6463
info@thehealingnet.org
www.thehealingnet.org

Neuroendocrine Tumor Research Foundation (NETRF)
100 Hancock Street, Third Floor
Quincy, MA 02171
1-617-946-1780
info@netrf.org
www.netrf.org

Neuroendocrine Cancer Foundation (NCF)
PO Box 370466
Denver, CO 80237
info@ncf.net
www.ncf.net

Northern California CarciNET Community (NorCal CarciNET)
info@norcalcarcinet.org
www.norcalcarcinet.org

These are provided for informational purposes only. This is not intended to be a recommendation or endorsement of any organization.

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For patients coming to you for LUTATHERA treatment, enable them to

START STRONG WITH LUTATHERA

You play an essential role in providing clarity concerning the LUTATHERA treatment process—and helping educate patients on what to expect from treatment

LUTATHERA has a defined 4-dose treatment regimen, given every 8 weeks, regardless of patient type and available nationwide[1]

Even if it's your first time caring for a patient receiving RLT, know that the radiation associated with LUTATHERA is established as safe within occupational limits (ICRP limits of 20 mSv per year*)[14,15]

Before each dose of LUTATHERA: DO NOT administer long-acting SSAs for at least 4 weeks, and DO NOT administer short-acting SSAs for at least 24 hours[1]

To learn more about LUTATHERA and administering treatment, **visit www.LUTATHERA-hcp.com**

*Averaged over a defined period of 5 years, with no single year exceeding 50 mSv.
RLT, radioligand therapy.

IMPORTANT SAFETY INFORMATION (continued)

SPECIFIC POPULATIONS

Lactation: Advise patients not to breastfeed during LUTATHERA treatment.

Visit www.LUTATHERA-hcp.com

Please see additional Important Safety Information throughout and full Prescribing Information.

NOVARTIS

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

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

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