

**NCCN Clinical Practice Guidelines In Oncology  
(NCCN Guidelines®) select recommendations**



National Comprehensive  
Cancer Network® (NCCN®)

**NCCN**  
RECOMMENDED

PRRT with lutetium Lu 177 dotatate (LUTATHERA®) is **NCCN Guidelines® recommended** as a systemic therapy option for SSTR+, well-differentiated GEP-NET patients<sup>1,\*</sup>

## GRADE 1/2

- An alternative first-line option for certain patients with locoregional advanced disease and/or distant metastases of gastrointestinal or pancreatic NETs (Ki-67  $\geq 10\%$  and clinically significant tumor burden)<sup>†</sup>—**NCCN Category 2A Preferred**
- Locoregional advanced disease and/or distant metastases—mid-gut NETs with progression on octreotide LAR/lanreotide—**Category 1 Preferred**
- Locoregional advanced disease and/or distant metastases of gastrointestinal or pancreatic NETs after progression on octreotide LAR/lanreotide—**Category 2A Preferred**

## GRADE 3

- Locally advanced and/or metastatic NETs with unresectable, clinically significant tumor burden or evidence of progression and favorable biology—**Category 2A**
- Locally advanced and/or metastatic NETs with unresectable, asymptomatic, low tumor burden and favorable biology—**Category 2B**

\*NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.  
<sup>†</sup>Consider for pancreatic NETs.

GEP-NET, gastroenteropancreatic neuroendocrine tumor; LAR, long-acting release; NCCN, National Comprehensive Cancer Network; NETs, neuroendocrine tumors; PRRT, peptide receptor radionuclide therapy; SSTR+, somatostatin receptor-positive.

## 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.

Please see additional Important Safety Information on reverse and full [Prescribing Information](#).

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

## 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. 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.
- **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.
- **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. 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.
- **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.
- **Hypersensitivity Reactions:** Hypersensitivity reactions, including angioedema, occurred in patients treated with LUTATHERA. 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.
- **Hypersensitivity Reactions (continued):** 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.
- **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.
- **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. 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.
- **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 ( $\geq 4\%$  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.

### SPECIFIC POPULATIONS

**Lactation:** Advise patients not to breastfeed during LUTATHERA treatment.

**Please see additional Important Safety Information on reverse and full [Prescribing Information](#).**

**Reference: 1.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for Neuroendocrine and Adrenal Tumors V.1.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed April 8, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org.

