

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

For your patients
with SSTR+ GEP-NETs,¹⁻³

Not an actual patient.

START STRONG WITH LUTATHERA

Early **LUTATHERA + SSA**: Enhancing the standard of care for
patients who are newly diagnosed or after SSA progression^{3,4}

GEP-NETs, gastroenteropancreatic neuroendocrine tumors; SSA, somatostatin analogue; 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 throughout and full [Prescribing Information](#).



NEWLY DIAGNOSED

AFTER SSA PROGRESSION

SAFETY

DOSING + PATIENT SUPPORT

ISI

SUMMARY

LUTATHERA can be used to treat SSTR+ GEP-NETs in the foregut, midgut, and hindgut²



LUTATHERA + SSA was studied as 1L* therapy in **NEWLY DIAGNOSED** patients¹

NETTER-2 is a phase 3, randomized, open-label, active comparator, multicenter study of the efficacy of LUTATHERA with 30 mg octreotide LAR (n=151) vs 60 mg octreotide LAR (n=75) in patients with newly diagnosed, well-differentiated, grade 2/3 advanced SSTR+ GEP-NETs. SSA-naïve patients were eligible, as well as patients previously treated with SSAs in the absence of progression. The primary end point of the study was centrally assessed PFS.^{1,4,†}

LUTATHERA is for patients with newly diagnosed GEP-NETs^{2,4}

Consider these characteristics



Diagnosis^{2,4}

Well-differentiated, SSTR+,
metastatic or locally advanced,
inoperable GEP-NETs

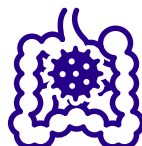


Treatment stage^{2,4}

Newly diagnosed
(within the last 6 months)



Ki-67
≥10% and ≤55%
Grade 2/3⁴



Any GEP-NET
primary site²



Karnofsky
Performance Score
≥60⁴

*In NETTER-2, 44 patients (19.5%) received prior treatment in the absence of progression, including CAPTEM (1 patient), everolimus (1 patient), and SSAs (42 patients, with the majority receiving 1 or 2 doses).^{4,5}

†Defined as the time from randomization to first documented disease progression (centrally assessed according to RECIST v1.1) or death due to any cause.¹

1L, first line; CAPTEM, capecitabine and temozolomide; LAR, long-acting release; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors.

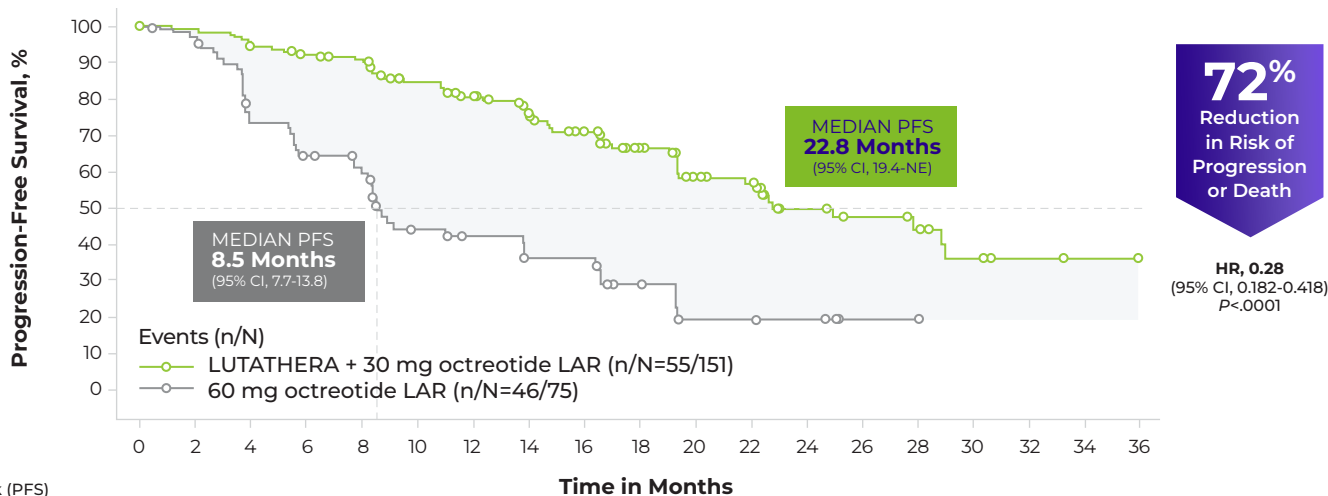
IMPORTANT SAFETY INFORMATION (continued) WARNINGS AND PRECAUTIONS (continued)

• **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.

Start with superior PFS results, start with LUTATHERA^{1,4}

LUTATHERA + SSA prolonged PFS for patients with **NEWLY DIAGNOSED, GRADE 2/3 GEP-NETs**^{1,4}

Statistically Significant Improvement in PFS (Primary End Point)^{1,4}



- PFS was defined as the time from randomization to first documented disease progression or death due to any cause. Centrally assessed according to RECIST v1.1 criteria¹
- The primary PFS analysis data cutoff was July 20, 2023. Median duration of follow-up was 23.2 months (from randomization to cutoff date)⁴

Objective Response Rate

- LUTATHERA + 30 mg octreotide LAR delivered a statistically significant increase (>4x) in objective response rate (ORR) compared with 60 mg octreotide LAR (ORR was a secondary end point)⁵
- 43% of patients (65 of 151) saw partial or complete tumor shrinkage with LUTATHERA + 30 mg octreotide LAR compared with 9.3% of patients (7 of 75) with 60 mg octreotide LAR alone⁵

1ST radioligand therapy with **1st-line** evidence in newly diagnosed patients demonstrated in a phase 3 study^{1,4,6,*}

*In NETTER-2, 44 patients (19.5%) received prior treatment in the absence of progression, including CAPTEM (1 patient), everolimus (1 patient), and SSAs (42 patients, with the majority receiving 1 or 2 doses).^{4,5}
HR, hazard ratio; NE, not evaluable.

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.

3 Please see additional Important Safety Information throughout and full [Prescribing Information](#).

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injection, for intravenous use



NEWLY DIAGNOSED

AFTER SSA PROGRESSION

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SUMMARY

LUTATHERA can be used to treat SSTR+ GEP-NETs in the foregut, midgut, and hindgut²

LUTATHERA + SSA was studied in patients **AFTER SSA PROGRESSION**^{2,3,7}

NETTER-1 was a pivotal, phase 3, randomized, multicenter, open-label study of LUTATHERA with 30 mg octreotide LAR (n=116) vs 60 mg octreotide LAR (n=113) in patients with locally advanced, inoperable, or metastatic SSTR+ GEP-NETs. The primary end point of the study was centrally assessed PFS.^{2,3,6,*}

LUTATHERA is for patients with GEP-NETs after SSA progression^{2,3}

Consider these characteristics



Diagnosis^{2,3}

Well-differentiated, SSTR+, metastatic or locally advanced, inoperable GEP-NETs



Treatment stage^{2,3}

Any prior disease progression while on an SSA



Ki-67
≤20%
Grade 1/2³



Any GEP-NET
primary site²



Karnofsky
Performance Score
≥60³

*Defined as the time from randomization to first documented disease progression (centrally assessed according to RECIST v1.1) or death due to any cause.¹
2L, second line; 3L, third line.

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

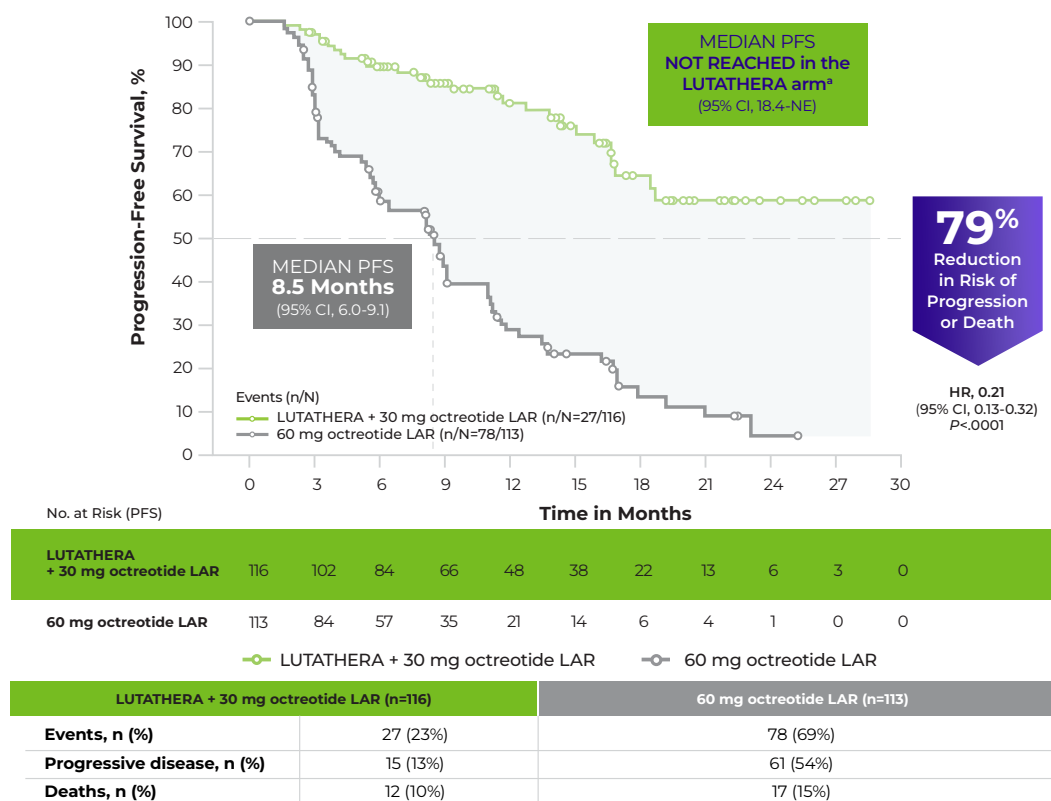
- **Renal Toxicity:** In ERASMUS, 8 patients (<1%) developed renal failure 3 to 36 months following LUTATHERA. Two of these patients had underlying renal impairment or risk factors for renal failure (eg, diabetes or hypertension) and required dialysis. Administer the recommended amino acid solution before, 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.

Superior PFS results with LUTATHERA after SSA progression²



LUTATHERA + SSA prolonged PFS for patients with **GRADE 1/2 GEP-NETs AFTER SSA PROGRESSION**^{2,3,7}

Statistically Significant Improvement in PFS (Primary End Point)²



^aAt primary analysis detailed in Prescribing Information for LUTATHERA.²

Primary PFS analysis

- PFS (as assessed by independent central review according to RECIST v1.1 by radiologists unaware of the treatment), defined as the time from randomization to documented disease progression or death from any cause^{3,8}
- The primary PFS analysis data cutoff was July 24, 2015. Median duration of follow-up was 14 months³

Early LUTATHERA + SSA: Enhancing the standard of care for your patients **AFTER SSA PROGRESSION**^{3,4}

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

- Renal Toxicity (continued):** 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.

LUTATHERA has a well-established safety profile across NETTER-1 and NETTER-2¹⁻⁴

- **In NETTER-2:** 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 + 30 mg octreotide LAR vs 60 mg octreotide LAR, respectively⁴
- **In NETTER-1:** The most common grade 3/4 adverse reactions with a higher incidence in the LUTATHERA arm were lymphopenia (44%), increased GGT (20%), vomiting (7%), nausea (5%), increased AST (5%), increased ALT (4%), hyperglycemia (4%), and hypokalemia (4%)²

No new safety signals were reported in the 5-year, long-term follow-up for NETTER-1^{9,*}

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 ⁹
Grade ≥3 Treatment-Related SAEs During the Entire Study	7 (6%) of 111 patients treated in the LUTATHERA arm ⁹
Incidence of Treatment-Related SAEs During the Long-Term Follow-Up Period	3 (3%) of 111 patients treated with LUTATHERA ⁹ — 2 (1.8%) patients experienced at least 1 grade ≥3 SAE (1 grade 5 MDS event) ⁹ — 1 (0.9%) patient experienced an SAE leading to study discontinuation ⁹
MDS or Acute Leukemia	No new cases were reported during long-term follow-up⁹ — 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 ^{2,9} — 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 ^{2,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 ⁹
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 ⁹

*Cutoff date for final analysis was January 18, 2021.⁹

^aERASMUS 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-positive tumors (neuroendocrine and other primaries). The median duration of follow-up was >4 years.²

AEs, adverse events; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; MDS, myelodysplastic syndrome; SSTR, somatostatin receptor.



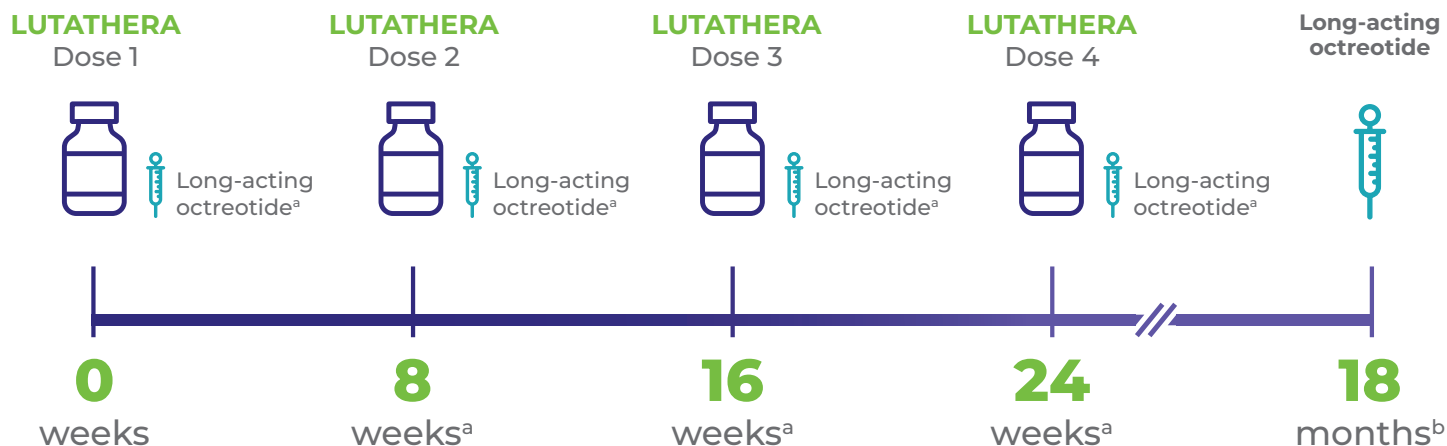
Find a LUTATHERA treatment center near your patients >

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.

Regardless of patient type, the dosing regimen for LUTATHERA remains the same²

Recommended Treatment Regimen With LUTATHERA²



During treatment, administer long-acting octreotide 30 mg IM between 4 to 24 hours after each dose of LUTATHERA

^aAdminister 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.²

^bContinue 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.²

IM, intramuscular.

BEFORE EACH DOSE OF LUTATHERA²

DO NOT ADMINISTER
LONG-ACTING SSAs FOR

**at least
4 WEEKS**

DO NOT ADMINISTER
SHORT-ACTING SSAs FOR

**at least
24 HOURS**

- LUTATHERA dosage should be modified based on hematologic, renal, hepatic, hypersensitivity, or other adverse reactions (see full Prescribing Information)²
- For reduced dose administration instructions, refer to section 2.5 (Preparation and Administration) of the full Prescribing Information

IN NETTER-2

88%

of patients completed all
4 doses of LUTATHERA⁴

IN NETTER-1

77%

of patients completed all
4 doses of LUTATHERA⁷

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

- **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. 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.

Novartis Patient Support

Support to help your patients start and stay on therapy

Designed to provide support in the following areas:



**Access &
Reimbursement**



Affordability



Acquisition



**Patient
Education**

Novartis Patient Support Co-pay Savings

We help make treatment more affordable for your patients through co-pay savings.

\$25
CO-PAY*

Eligible patients may pay as little as \$25 per dose.*

Enrollment in Novartis Patient Support is required to determine eligibility and participation.

*Limitations apply. Valid only for those 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 Enrollment Forms for details.



Here's How to Enroll

Simply download the Start Form at www.novartis-patientsupport.com/RLT, fill it out, and fax it to **1-844-638-7329** OR you can also access support by registering for our portal. Registration is required.

Have questions about the enrollment process? Call us at **1-844-638-7222**.



Additional Educational Support Is Available for Your Patients

After the decision to start LUTATHERA is made, our dedicated team of Patient Navigators can help answer some of the most common treatment questions. To put your patients in contact with one of our Patient Navigators, call **1-844-638-7222**.

Patients must be enrolled in Novartis Patient Support to be considered for financial support.

Visit our website www.novartis-patientsupport.com/RLT for more information.

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.
- **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 full [Prescribing Information](#).

References: 1. Data on file. Novartis Pharmaceuticals Corp; 2021. 2. Lutathera. Prescribing information. Novartis Pharmaceuticals Corp. 3. Strosberg J, El-Haddad G, Wolin E, et al; for the NETTER-1 trial investigators. Phase 3 trial of ^{177}Lu -dotatate for midgut neuroendocrine tumors. *N Engl J Med*. 2017;376(2):125-135. 4. Singh S, Halperin D, Myrehaug S, et al. [^{177}Lu]Lu-DOTA-TATE plus long-acting octreotide versus high-dose long-acting octreotide for the treatment of newly diagnosed, advanced grade 2-3, well-differentiated, gastroenteropancreatic neuroendocrine tumours (NETTER-2): an open-label, randomised, phase 3 study. *Lancet*. 2024;403(10446):2807-2817. 5. Data on file. CAAA601A22301 Clinical Study Report. Novartis Pharmaceuticals Corp; 2024. 6. US Food and Drug Administration. FDA approves new treatment for certain digestive tract cancers [press release]. Updated January 26, 2018. Accessed July 26, 2024. <https://www.fda.gov/news-events/press-announcements/fda-approves-new-treatment-certain-digestive-tract-cancers> 7. Strosberg J, El-Haddad G, Wolin E, et al; for the NETTER-1 trial investigators. Phase 3 trial of ^{177}Lu -dotatate for midgut neuroendocrine tumors. *N Engl J Med*. 2017;376(2)(suppl):125-135. 8. Strosberg J, El-Haddad G, Wolin E, et al; for the NETTER-1 trial investigators. Phase 3 trial of ^{177}Lu -dotatate for midgut neuroendocrine tumors. *N Engl J Med*. 2017;376(2)(protocol):125-135. 9. Strosberg JR, Caplin ME, Kunz PL, et al; NETTER-1 investigators. ^{177}Lu -dotatate plus long-acting octreotide versus high-dose long-acting octreotide in patients with midgut neuroendocrine tumours (NETTER-1): final overall survival and long-term safety results from an open-label, randomised, controlled, phase 3 trial. *Lancet Oncol*. 2021;22(12):1752-1763.

For your patients with SSTR+ GEP-NETs,¹⁻³

START STRONG WITH LUTATHERA: Enhance your standard of care^{2,4}

Statistically significant improvement in PFS demonstrated across a range of patients with SSTR+ GEP-NETs¹⁻⁴:

NEWLY DIAGNOSED^{1,4,5}

Explore Data 

Grade 2/3 SSTR+ GEP-NETs

72%
REDUCTION
in the risk of disease
progression or death

with LUTATHERA +
30 mg octreotide LAR (median
PFS, 22.8 months [95% CI, 19.4-NE])
vs 60 mg octreotide LAR (median
PFS, 8.5 months [95% CI, 7.7-13.8])
(HR, 0.28 [95% CI, 0.18-0.42]; $P < .0001$)

- ✓ Newly diagnosed (within last 6 months), well-differentiated SSTR+ GEP-NET
- ✓ **Karnofsky PS:** 90 to 100
- ✓ **Ki-67 index:** $\geq 10\%$ to $\leq 55\%$ (tumor grade 2/3)
- ✓ **Disease burden:** moderate to extensive

AFTER SSA PROGRESSION^{2,3,7}

Explore Data 

Grade 1/2 SSTR+ GEP-NETs

79%
REDUCTION
in the risk of disease
progression or death

with LUTATHERA +
30 mg octreotide LAR (median
PFS, not reached [95% CI, 18.4-NE])
vs 60 mg octreotide LAR (median
PFS, 8.5 months [95% CI, 6.0-9.1])
(HR, 0.21 [95% CI, 0.13-0.32]; $P < .0001$)

- ✓ Well-differentiated SSTR+ GEP-NET and progression on SSA
- ✓ **Karnofsky PS:** 75 to 95
- ✓ **Ki-67 index:** $< 10\%$ (tumor grade 1/2)

This is a representation of the typical patient in the NETTER-1 and NETTER-2 trials.
This list is NOT intended to be exhaustive of all inclusion/exclusion criteria.

PS, performance score.

LUTATHERA has a well-established safety profile across NETTER-1 and NETTER-2¹⁻⁴

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.

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

Which of your patients is ready to START WITH LUTATHERA?



Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

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