

Radioligand therapy (RLT) with ¹⁷⁷Lu-labeled compounds can be produced using either carrier-added or non-carrier-added methods.⁵ **¹⁷⁷Lu in BEXLUTRY is produced using the non-carrier-added approach.**⁴

Both methods provide ¹⁷⁷Lu, but differ in operational implications for treatment sites.⁵ The carrier-added production method coproduces a long-lived isotope, ^{177m}Lu, which has waste management and storage challenges due to its half-life. In contrast, the non-carrier-added method of manufacturing ¹⁷⁷Lu in BEXLUTRY eliminates this coproduct, reducing the radioactive waste burden.⁵

Although the carrier-added method has a production benefit (shorter processing time) for the manufacturer, the non-carrier-added method of manufacturing ¹⁷⁷Lu in BEXLUTRY benefits the treatment site through improved waste management, storage, and cost-effectiveness.^{4,6}

CARRIER-ADDED PRODUCTION^{4,6}

Begins with ¹⁷⁶Lu; neutron irradiation yields ¹⁷⁷Lu and ^{177m}Lu

irradiation



Total Processing
Time: 4 to 6 hours

NON-CARRIER-ADDED PRODUCTION OF BEXLUTRY^{4,6}

Begins with ¹⁷⁶Yb; neutron irradiation yields ¹⁷⁷Yb, which β- decays to ¹⁷⁷Lu, which is then chemically separated from ¹⁷⁷Yb

irradiation

¹⁷⁶Yb



¹⁷⁷Yb

β- decay



¹⁷⁷Lu

Total Processing
Time: 36 to 48 hours

Abbreviations: Lu, lutetium; Yb, ytterbium.

INDICATIONS AND USAGE

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

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Risk From Radiation Exposure:** Bexlutry contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk for cancer. These risks of radiation associated with the use of Bexlutry are greater in pediatric patients than in adults.

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

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Myelosuppression:** In NETTER-1, myelosuppression occurred more frequently in patients receiving lutetium Lu 177 dotatate injection with long-acting octreotide compared to patients receiving high-dose long-acting octreotide (all Grades/Grade 3 or 4): anemia (81%/0) versus (54%/1%); thrombocytopenia (53%/1%) versus (17%/0); and neutropenia (26%/3%) versus (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 nineteen 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 Bexlutry based on the severity of myelosuppression.

- **Secondary Myelodysplastic Syndrome (MDS) 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 lutetium Lu 177 dotatate injection with long-acting octreotide compared to no patients receiving high-dose long-acting octreotide.

In ERASMUS, 16 patients (2.0%) developed MDS and 4 (0.5%) developed acute leukemia. The median time to onset was 29 months (9 to 45 months) for MDS and 55 months (32 to 125 months) for acute leukemia.

- **Renal Toxicity:** In ERASMUS, 8 patients (< 1%) developed renal failure 3 to 36 months following lutetium Lu 177 dotatate injection. Two of these patients had underlying renal impairment or risk factors for renal failure (e.g., diabetes or hypertension) and required dialysis.

Administer the recommended amino acid solution before, during and after Bexlutry 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 the day after administration of Bexlutry.

Monitor serum creatinine and calculated creatinine clearance. Withhold dose, reduce dose, or permanently discontinue Bexlutry based on the severity of renal toxicity.

Patients with baseline renal impairment may be at increased risk of toxicity due to increased radiation exposure.

- **Hepatotoxicity:** In ERASMUS, 2 patients (< 1%) 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, serum albumin, and international normalized ratio (INR) during treatment. Withhold dose, reduce dose, or permanently discontinue Bexlutry based on the severity of hepatotoxicity.

- **Hypersensitivity Reactions:** Hypersensitivity reactions, including angioedema, occurred in patients treated with lutetium Lu 177 dotatate injection. Monitor patients closely for signs and symptoms of hypersensitivity reactions, including anaphylaxis, during and following Bexlutry administration for a minimum of 2 hours in a setting where 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 or 2 hypersensitivity reactions to Bexlutry before subsequent doses. Permanently discontinue Bexlutry in patients who experience Grade 3 or 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 lutetium Lu 177 dotatate injection 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 analogs, fluids, corticosteroids, and electrolytes as indicated.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Embryo-Fetal Toxicity:** Based on its mechanism of action, Bexlutry can cause fetal harm when administered to a pregnant woman. Verify pregnancy status of females of reproductive potential prior to initiating Bexlutry. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with Bexlutry and for 7 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with Bexlutry and for 4 months after the last dose.
- **Risk of Infertility:** Bexlutry may cause infertility in males and females. The recommended cumulative dose of 29.6 GBq of Bexlutry results in a radiation absorbed dose to the testes and ovaries within the range where 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 lutetium Lu 177 dotatate injection arm) reported in NETTER-1 were lymphopenia, increased GGT, vomiting, nausea, increased AST, increased ALT, hyperglycemia and hypokalemia.

With a median follow-up time of more than 4 years, the following rates of serious adverse reactions were reported in ERASMUS: myelodysplastic syndrome (2%), acute leukemia (1%), renal failure (2%), hypotension (1%), cardiac failure (2%), myocardial infarction (1%), and neuroendocrine hormonal crisis (1%).

DRUG INTERACTIONS

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

Glucocorticoids: Glucocorticoids can induce down-regulation of subtype 2 somatostatin receptors (SSTR2). Avoid repeated administration of high doses of glucocorticoids during treatment with Bexlutry.

USE IN SPECIFIC POPULATIONS

Lactation

Advise women not to breastfeed during treatment with Bexlutry and for 2.5 months after the last dose.

Pediatric Use

Somatostatin Receptor-Positive Gastroenteropancreatic Neuroendocrine Tumors: The risks of radiation exposure associated with Bexlutry are greater in pediatric patients than in adult patients due to longer life expectancy. The safety and effectiveness of Bexlutry have not been established in pediatric patients younger than 12 years old with somatostatin receptor-positive GEP-NETs.

Pediatric use information is approved for Advanced Accelerator Applications USA INC's LUTATHERA (lutetium Lu 177 dotatate) injection for intravenous use. However, due to Advanced Accelerator Applications USA Inc.'s marketing exclusivity rights, this drug product is not labeled with that pediatric information.

LUTATHERA® is a registered trademark of Advanced Accelerator Applications International SA.

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

 **Bexlutry**TM
(lutetium Lu 177 dotatate injection)
for intravenous use

OPERATIONAL AND LOGISTICAL IMPACT



BEXLUTRY

CARRIER-ADDED METHOD

Coproduction of ^{177}mLu impurity⁵	Does not coproduce ^{177}mLu impurity	Coproduces ^{177}mLu impurity
Specific activity⁴	High specific activity (70+ Ci/mg)	Low specific activity (20+ Ci/mg)
Storage considerations^{5,6}	^{177}Lu production without ^{177}mLu coproduction may reduce storage costs and free up storage space	^{177}Lu production resulting in ^{177}mLu coproduction may increase storage requirements and costs , limiting available space for other products
Waste considerations⁵⁻⁷	The half-life of ^{177}Lu is 6.65 days - Standard short-term decay-in-storage - Waste containing ^{177}Lu may be disposed of after a decay period of ~66 days, simplifying waste management	The half-life of the ^{177}mLu impurity is 160.4 days - Under US Nuclear Regulatory Commission rules, waste with a half-life of more than 120 days cannot undergo standard short-term decay-in-storage - Most sites cannot decay and dispose of waste materials on their own and require a third-party waste broker to collect waste

Non-carrier-added production of BEXLUTRY may simplify waste handling and storage, reducing operational burden and disposal costs for treatment sites.^{5,6}

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- Risk From Radiation Exposure (cont'd):** Radiation can be detected in the urine for up to 30 days following Bexlutry administration. Minimize radiation exposure to patients, medical personnel, and household contacts during and after treatment with Bexlutry 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](#).

References: 1. BEXLUTRY. Prescribing information. Curium US LLC; 2026. 2. US Food and Drug Administration. *Approved Drug Products With Therapeutic Equivalence Evaluations*. 44th ed. 2024. Accessed May 1, 2026. <https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book> 3. Lutathera. Prescribing information. Advanced Accelerator Applications USA Inc; 2024. 4. Data on file. Curium US LLC. 5. Cappon DJ, Fang S, Berry K, et al. Clinical best practices for radiation safety during lutetium-177 therapy. *Health Phys*. 2023;124(2):139-146. doi:10.1097/HP.0000000000001644 6. Dash A, Pillai MRA, Knapp FF Jr. Production of ^{177}Lu for targeted radionuclide therapy: available options. *Nucl Med Mol Imaging*. 2015;49(2):85-107. doi:10.1007/s13139-014-0315-z 7. Balzer M, Spiecker F, Bluemel S, Amthauer H, Brenner W, Spreckelmeyer S. Evaluation of the ^{177}mLu -concentration in in-house produced ^{177}Lu -radiopharmaceuticals and commercially available Lutathera®. *EJNMMI Radiopharm Chem*. 2023;8(1):37. doi:10.1186/s41181-023-00222-2

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CURIUM

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 **Bexlutry™**
(lutetium Lu 177 dotatate injection)
for intravenous use