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

ADMINISTRATION GUIDE

Step-by-step instructions and important considerations

This guide is intended to be an educational tool for all staff members involved in the administration of BEXLUTRY and includes the following:

- BEXLUTRY dosing schedule and infusion timing
- Administration preparation for before, during, and after treatment
- Quick administration summary

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

- **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.

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

CURIUM
LIFE FORWARD

WHAT IS BEXLUTRY?

- BEXLUTRY (lutetium Lu 177 dotatate injection) is a radioligand equivalent (RLE) that delivers targeted radiation to treat adults with somatostatin receptor (SSTR)–positive (SSTR+) gastroenteropancreatic neuroendocrine tumors (GEP-NETs)[1-3]
- BEXLUTRY should be used only by or under the supervision of healthcare providers who are qualified and licensed by the appropriate governmental agency for the safe use and handling of radioligand therapies[1]

Follow your institution's radiation safety practices, patient management procedures, Nuclear Regulatory Commission patient-release guidance, and patient follow-up instructions for radiation protection at home.[1]

This guide will provide practical information about the administration of BEXLUTRY, including **BEFORE**, **DURING**, and **AFTER** treatment requirements and recommendations.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **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.

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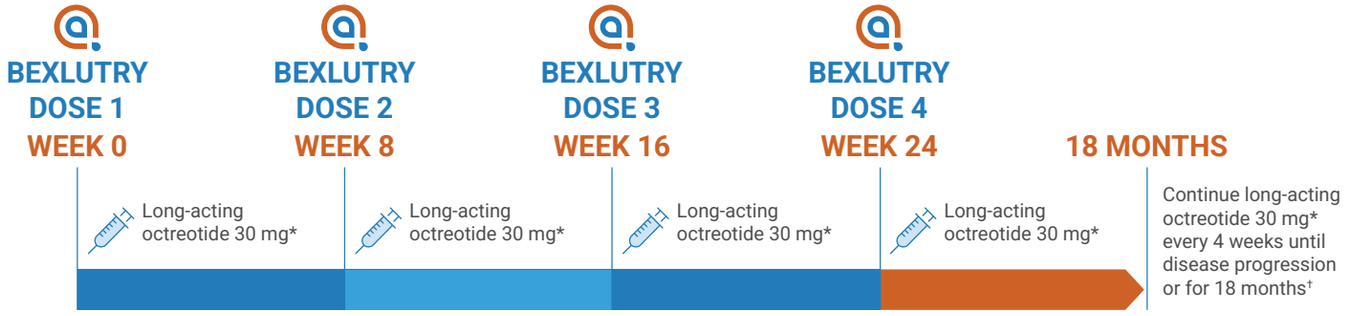
BEXLUTRY DOSING OVERVIEW

The recommended dosage of BEXLUTRY is 7.4 GBq (200 mCi) given intravenously every 8 weeks (± 1 week), for a total of 4 administrations.[1]



Before each dose of BEXLUTRY

*Administer long-acting octreotide 30 mg intramuscularly (IM) between 4 and 24 hours after each administration of BEXLUTRY. Do not administer long-acting octreotide within 4 weeks prior to each subsequent dose of BEXLUTRY.[1]

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

Prior to the first dose of BEXLUTRY, check labs, creatinine clearance, and Karnofsky performance status, as well as verify pregnancy status of patients with reproductive potential.[1,4]

Radiation dose measurement: BEXLUTRY, containing 370 MBq/mL (10 mCi/mL) of lutetium Lu 177 dotatate at time of calibration, is a sterile, preservative-free, clear, colorless-to-yellow solution. It is supplied in a clear, colorless, Type I glass, 30-mL single-dose vial containing 7.4 GBq (200 mCi) ± 10% of lutetium Lu 177 dotatate at the time of injection. The solution volume in the vial ranges between 23 and 25 mL to provide a total of 7.4 GBq (200 mCi) of radioactivity.[1]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **Renal Toxicity (cont'd):** 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.

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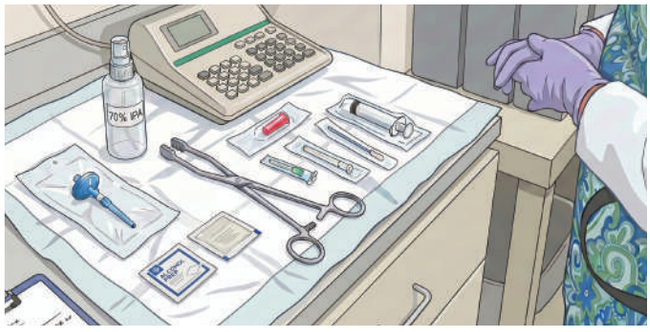
BEFORE ADMINISTRATION OF BEXLUTRY

Consider the following guidance for medical personnel to minimize radiation exposure.

Supplies and equipment

Ensure the following items are available prior to infusion with BEXLUTRY:



Pharmaceuticals[1]

- 500 mL of 0.9% sterile sodium chloride (NaCl)
- 0.9% NaCl for priming the lines
- L-lysine and L-arginine amino acid solution
- Antiemetics
- **IV somatostatin analogs (SSAs), fluids, corticosteroids, and electrolytes in case of neuroendocrine hormonal crisis**

Radiopharmaceuticals[1]

- BEXLUTRY is in a shielded container

Equipment

- Tongs to handle BEXLUTRY vials[1]
- Infusion pole[5]
- 2.5-cm (1-in), 20-gauge needle (short needle) and 9-cm (3.5-in), 18-gauge needle (long needle)[1]
- Syringe for 0.9% NaCl flush[1]
- Male-to-male adaptor[6]
- 3-way stopcock[1]
- Peristaltic or syringe pump when appropriate for IV administration method
- Waterproof gloves and disposable lab coats and shoe covers[1,7]
- Waste container for contaminated items[7]
- Radiation detection survey meter[7]
- CPR medication and equipment[1]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **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.

  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.

BEFORE ADMINISTRATION OF BEXLUTRY (CONT'D)

Safe handling of BEXLUTRY

Staff protection from radiation[1,8]

- Ensure that all staff are aware of safety protocols to reduce radiation exposure, including **time, distance,** and **shielding**
- Set up radiation safety measures with proper signage
- Use personal protective equipment (PPE) and dosimeter, and segregate radioactive waste
- Track staff exposures and ensure that they remain below regulatory limits
- Follow established protocols to respond quickly to spills, contamination, and/or extravasation

Proper technique[1]

- Use aseptic technique and shielding when handling BEXLUTRY
- Use tongs when handling the vial

Inspection[1]

- Inspect the vial through a shielded window for particulate matter and discoloration

Dose verification[1]

- Verify activity using a radioactivity dose calibrator
- Using the radioactivity dose calibrator, ensure BEXLUTRY dose is the correct activity per written directive for the correct patient
- Ensure expiration/BUD is documented according to the label and administration occurs before that time

Proper disposal

- Dispose radiopharmaceutical waste as required by law and institutional SOPs[1]
- Minimize storage demands with Curium's lead safe retrieval service

What should I do if a radiation spill occurs?

If a radiation spill occurs, you should always follow the guidance of your institution's radiation safety department. Refer to the Nuclear Regulatory Commission for additional considerations at www.nrc.gov.[7]

Abbreviations: BUD, beyond-use date; SOP, standard operating procedure.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **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.

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BEFORE ADMINISTRATION OF BEXLUTRY (CONT'D)

Patient preparation and room setup

Patient preparation and guidance

- Offer hospital scrubs or gowns to help avoid potential contamination of personal belongings[9]
- Provide instructions to sit on the toilet to urinate, close the toilet lid prior to flushing, and double flush after each use[9]
- Provide disposable undergarments if urinary incontinence is a concern. The use of routine bladder catheterization is not recommended[9]
- Discuss instructions on radiation precautions, visitor restrictions, and what to expect[8]

Premedication and infusion setup

- Confirm the patient has discontinued SSAs prior to infusion[1]
- Prepare the infusion room with disposable pads, shielded waste containers, and a spill kit[5,7]
- Prepare amino acid solution[1]
- Verify correct patient, treatment, and BEXLUTRY activity prior to infusion
- Establish IV access for amino acid solution and BEXLUTRY using one of the following methods[1]
  - Use a 3-way valve on the same venous access for both solutions
  - Establish separate IV access in the patient's other arm (one for amino acids, one for BEXLUTRY)
- Flush IV line with ≥10 mL 0.9% sodium chloride, USP, to ensure patency and reduce extravasation risk[1]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **Hepatotoxicity (cont'd):** 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.

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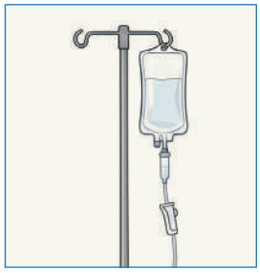
BEFORE ADMINISTRATION OF BEXLUTRY (CONT'D)

Administration options

There are 3 different infusion methods for administration of BEXLUTRY—the gravity method, peristaltic pump method, and syringe pump method.[1] Please refer to the Prescribing Information (Section 2.5) for full instructions on the gravity, peristaltic pump, and syringe pump methods.



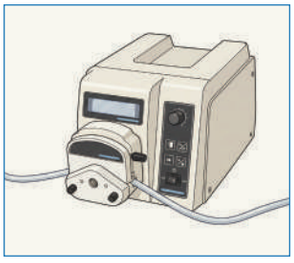
Administration of the gravity method[1]

The gravity method may be used for the administration of the prescribed activity. Infuse BEXLUTRY directly from its original container.

If using the gravity method for reduced-activity BEXLUTRY, activity must be adjusted before administration to avoid incorrect volume delivery.[1]

Administration instructions for other methods

The **peristaltic pump method** (left) or the **syringe pump method** (right) may also be used for BEXLUTRY administration. These pump methods may be used to administer either full- or reduced-activity BEXLUTRY following a dosage modification for an adverse reaction.[1]



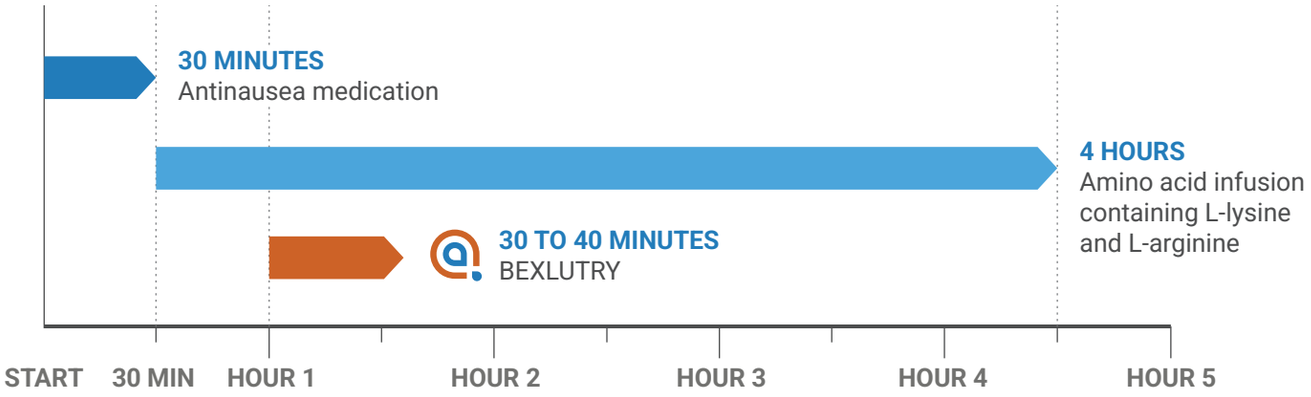
IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **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.

DURING ADMINISTRATION OF BEXLUTRY

Recommended timing for the administration of premedications, concomitant medications, and BEXLUTRY[1]



- ✓ **Confirm the patient has discontinued SSAs** prior to infusion[1]
- ✓ **Verify a dated and signed written directive** per 10 CFR 35.40[10]
- ✓ **Confirm the amount of radioactivity** of BEXLUTRY administered to the patient with an appropriate dose calibrator prior to and after each dose[1]
- ✓ **Administer antiemetics** before the amino acid solution to prevent nausea and vomiting[1]
- ✓ **Administer amino acid solution** containing L-lysine and L-arginine intravenously **30 minutes before** administering BEXLUTRY. **Continue the infusion during** and for at least **3 hours after** the infusion of BEXLUTRY. Do not decrease the dose of the amino acid solution if the dose of BEXLUTRY is reduced[1]
- ✓ **Administer BEXLUTRY** infusion (approximately **30 to 40 minutes**)[1]
  - **Same venous access:** Co-administer amino acids and BEXLUTRY via a 3-way stopcock
  - **Different venous access:** Use separate lines, administering amino acids in one arm and BEXLUTRY in the other

Abbreviation: CFR, Code of Federal Regulations.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **Hypersensitivity Reactions (cont'd):** 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.

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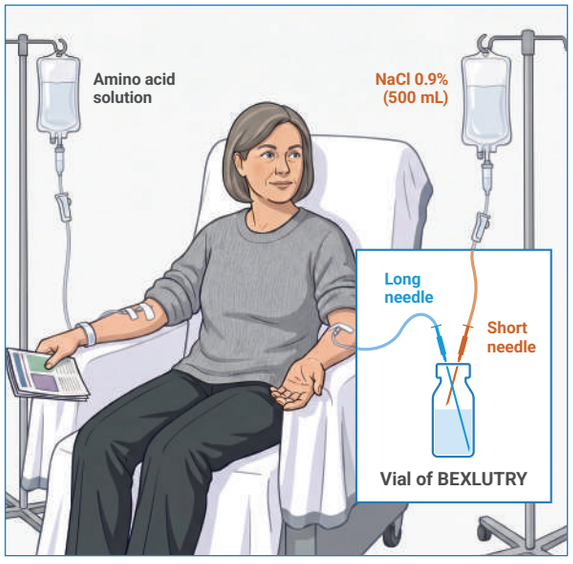
DURING ADMINISTRATION OF BEXLUTRY (CONT'D)

Administration instructions for the gravity method

The following are not inclusive of every step. Please refer to the Prescribing Information (Section 2.5) for full administration instructions.

Short- and long-needle instructions[1]



1
- Insert the 2.5-cm (1-in), 20-gauge needle **(short needle)** into the vial of BEXLUTRY
- Ensure that the short needle does not touch the solution of BEXLUTRY inside the vial
- **Do not** connect the short needle directly to the patient

2
- Connect the short needle to the 500 mL 0.9% sterile NaCl solution via a catheter
- **Do not** allow 0.9% NaCl solution to flow into the BEXLUTRY vial prior to the start of the infusion
- **Do not** inject BEXLUTRY directly into the 0.9% NaCl solution

3
- Insert the 9-cm (3.5-in), 18-gauge needle **(long needle)** into the vial of BEXLUTRY
- The long needle must touch and be secured to the bottom of the vial during the entire infusion

4
- Connect the long needle to the patient by an IV catheter
- The catheter should be prefilled with 0.9% NaCl solution and used exclusively for infusion of BEXLUTRY into the patient; amino acid solution may be administered concurrently through the same line using a 3-way stopcock

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **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.

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DURING ADMINISTRATION OF BEXLUTRY (CONT'D)

Administration instructions for the gravity method (cont'd)

Additional administration instructions[1]

- **Infuse in 2 phases:** Use a clamp or an infusion pump to regulate the flow of the NaCl solution via the short needle into the BEXLUTRY injection vial at a rate of 50 to 100 mL/hour for 5 to 10 minutes and then 200 to 300 mL/hour for an additional 25 to 30 minutes
- The NaCl solution entering the vial through the short needle will carry the BEXLUTRY solution from the vial to the patient via the IV catheter connected to the long needle over a total duration of 30 to 40 minutes
- During the infusion, ensure that the level of solution in the vial of BEXLUTRY remains constant
- Disconnect the vial from the long needle line and clamp the NaCl 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 NaCl solution through the IV to the patient
- Assay the vial with a radioactivity dose calibrator to confirm the amount of BEXLUTRY activity administered

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **Neuroendocrine Hormonal Crisis (cont'd):** 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.

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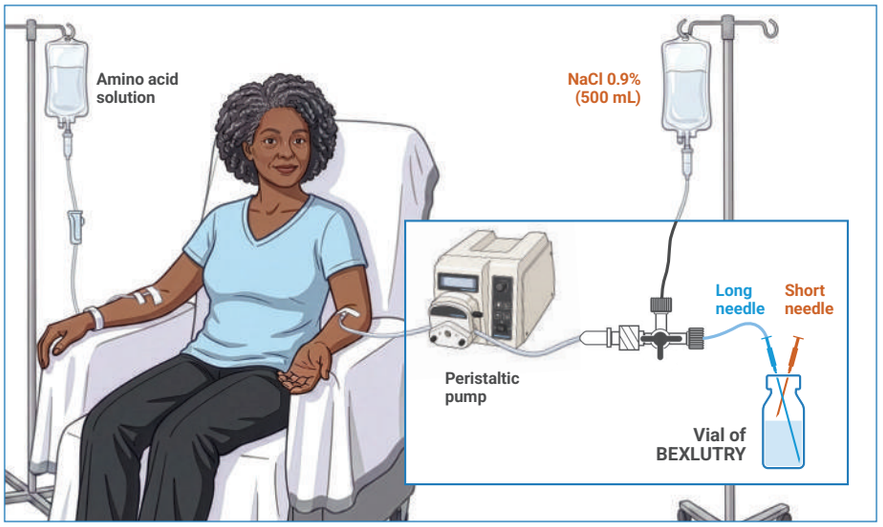
DURING ADMINISTRATION OF BEXLUTRY (CONT'D)

Administration instructions for the peristaltic pump method[1]

Short- and long-needle instructions[1]



The following are not inclusive of every step. Please refer to the Prescribing Information (Section 2.5) for full administration instructions.

1
- Insert the filtered 2.5-cm (1-in), 20-gauge needle **(short venting needle)** into the BEXLUTRY vial
- Ensure that the short needle does not touch the BEXLUTRY inside the vial
- **Do not** connect the short needle directly to the patient or to the peristaltic pump

2
- Insert the 9-cm (3.5-in), 18-gauge needle **(long needle)** into the vial of BEXLUTRY
- The long needle must touch and be secured to the bottom of the vial during the entire infusion
- Connect the long needle and a 0.9% NaCl solution to a 3-way stopcock valve via appropriate tubing

3
- Connect the output of the 3-way stopcock valve to tubing installed on the input side of the peristaltic pump according to manufacturer's instructions

4
- Prime the line by opening the 3-way stopcock valve and pumping the BEXLUTRY solution through the tubing until it reaches the exit of the valve

5
- Prime the IV catheter that will be connected to the patient by opening the 3-way stopcock valve to the 0.9% NaCl solution and pumping the solution until it exits the end of the catheter tubing

6
- Connect the primed IV catheter to the patient and set the 3-way stopcock valve such that the BEXLUTRY solution is in line with the peristaltic pump. Infuse an appropriate volume of BEXLUTRY solution over a total duration of **30 to 40 minutes** to deliver the desired radioactivity

7
- When the desired radioactivity has been delivered, stop the peristaltic pump and then change the position of the 3-way stopcock valve so that the peristaltic pump is in line with the 0.9% NaCl solution
- Restart the peristaltic pump and infuse an IV flush of 25 mL of 0.9% NaCl solution through the IV catheter to the patient
- Assay the vial with a radioactivity dose calibrator to confirm the amount of BEXLUTRY activity administered

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **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.

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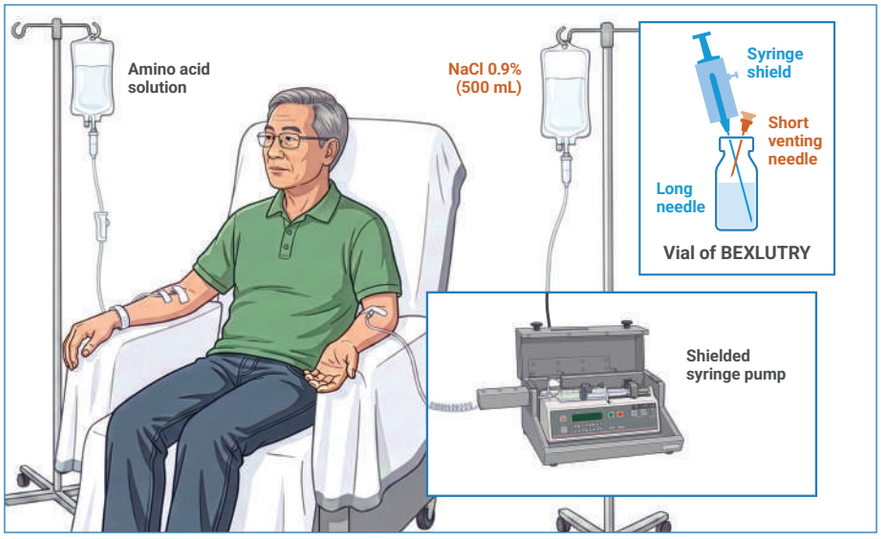
DURING ADMINISTRATION OF BEXLUTRY (CONT'D)

Administration instructions for the syringe pump method[1]

Short- and long-needle instructions[1]



The following are not inclusive of every step. Please refer to the Prescribing Information (Section 2.5) for full administration instructions.

1. • Withdraw an appropriate volume of BEXLUTRY solution to deliver the desired radioactivity by using a disposable syringe fitted with a syringe shield and a disposable sterile needle that is 9-cm (3.5-in), 18-gauge **(long needle)**

2. • To aid the withdrawal of the solution, a filtered 2.5-cm (1-in), 20-gauge needle **(short venting needle)** can be used to reduce the resistance from the pressurized vial
   • Ensure that the short needle does not touch the BEXLUTRY solution in the vial

3. • Fit the syringe into the shielded pump and include a 3-way stopcock valve between the syringe and an IV catheter prefilled with 0.9% NaCl solution and used for BEXLUTRY administration to the patient

4. • Infuse an appropriate volume of BEXLUTRY solution over a total duration of **30 to 40 minutes** to deliver the desired radioactivity

5. • When the desired radioactivity has been delivered, stop the syringe pump and then change the position of the 3-way stopcock valve to flush the syringe with 25 mL of 0.9% NaCl solution
   • Restart the syringe pump

6. • After the flush of the syringe has been completed, perform an IV flush with 25 mL of 0.9% NaCl solution through the IV catheter to the patient
   • Assay the vial with a radioactivity dose calibrator to confirm the amount of BEXLUTRY activity administered

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **Embryo-Fetal Toxicity (cont'd):** 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.

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MONITORING AND MANAGEMENT OF ADVERSE REACTIONS DURING BEXLUTRY TREATMENT

Hematologic reactions[1]

Thrombocytopenia

MONITOR

- CBC with differential before each dose
- Signs of bone marrow suppression

ACTION

If **first occurrence** of grade 2-4:

- **Withhold** dose until complete or partial resolution (grade 0-1)
  - **Resume** dose at 3.7 GBq (100 mCi) with complete or partial resolution; if no grade 2-4 event with reduced dose, give 7.4 GBq (200 mCi) as next dose
  - **Permanently discontinue** for grade ≥2 requiring a dosing interval >16 weeks

If **recurrent** grade 2-4:

- **Permanently discontinue**

Anemia/neutropenia

MONITOR

- CBC with differential before each dose
- Signs of bone marrow suppression

ACTION

If **first occurrence** of grade 3-4:

- **Withhold** dose until complete or partial resolution (grade 0-2)
  - **Resume** dose at 3.7 GBq (100 mCi) with complete or partial resolution; if no grade 3-4 event with reduced dose, give 7.4 GBq (200 mCi) as next dose
  - **Permanently discontinue** for grade ≥3 requiring a dosing interval >16 weeks

If **recurrent** grade 3-4:

- **Permanently discontinue**

Abbreviation: CBC, complete blood count.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **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.

MONITORING AND MANAGEMENT OF ADVERSE REACTIONS DURING BEXLUTRY TREATMENT (CONT'D)

Renal and hepatic reactions[1]

Renal toxicity

MONITOR

- Serum creatinine and calculated creatinine clearance prior to each dose
- Signs of renal dysfunction

ACTION

If **first occurrence***:

- **Administer** amino acids as prescribed
- **Withhold** dose until resolution or return to baseline
  - **Resume** dose at 3.7 GBq (100 mCi) with resolution or return to baseline; if no renal toxicity with reduced dose, give 7.4 GBq (200 mCi) as next dose
  - **Permanently discontinue** if renal toxicity requires a dosing interval >16 weeks

If **recurrent**:

- **Permanently discontinue**

Hepatotoxicity

MONITOR

- Transaminases, bilirubin, serum albumin, and INR during treatment
- Signs of hepatic impairment

ACTION

If **first occurrence**†:

- **Withhold** dose until resolution or return to baseline
  - **Resume** dose at 3.7 GBq (100 mCi) with resolution or return to baseline; if no hepatotoxicity with reduced dose, give 7.4 GBq (200 mCi) as next dose
  - **Permanently discontinue** if hepatotoxicity requires a dosing interval >16 weeks

If **recurrent**:

- **Permanently discontinue**

*Creatinine clearance less than 40 mL/min calculated using Cockcroft-Gault formula with actual body weight, 40% increase from baseline serum creatinine, or 40% decrease from baseline creatinine clearance calculated using Cockcroft-Gault formula with actual body weight.

†Bilirubinemia greater than 3 times the upper limit of normal (grade 3 or 4) or serum albumin less than 30 g/L with INR >1.5.

Abbreviation: INR, international normalized ratio.

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS

The most common Grade 3-4 adverse reactions (≥ 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.

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MONITORING AND MANAGEMENT OF ADVERSE REACTIONS DURING BEXLUTRY TREATMENT (CONT'D)

Infusion reactions and hormonal crisis[1]*

Hypersensitivity

MONITOR

- During infusion and ≥2 hours after; have emergency medications/supplies available
- Signs of allergic reaction

ACTION

- **Premedicate** prior to subsequent doses for grade 1 or 2 reactions
- **Discontinue** infusion at the first sign of a severe hypersensitivity reaction and initiate appropriate therapy
- **Permanently discontinue** for grade 3 or 4 reactions

Neuroendocrine hormonal crisis

MONITOR

- During infusion and shortly after for signs of hormonal release (flushing, diarrhea, hypotension, bronchoconstriction)

ACTION

- **Administer** IV SSAs, fluids, corticosteroids, and electrolytes as indicated

Stop infusion immediately if

- Severe hypersensitivity occurs[1]
- Carcinoid crisis develops[11†]

Please see Prescribing Information (Section 2.4 Dosage Modifications for Adverse Reactions) for more information.[1]

The administered activity of BEXLUTRY should be modified based on hematologic, renal, hepatic, hypersensitivity, and other adverse reactions.[1]

*Other common grade 3-4 infusion reactions include nausea, vomiting, and electrolyte changes.[1]

†A patient in carcinoid crisis requires the immediate administration of an IV bolus of octreotide as needed until stabilized. Alert the intensive care unit, monitor vital signs, and consider supportive care.[11]

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS (cont'd)

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%).

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

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

EDUCATING PATIENTS AND CAREGIVERS ON IMPORTANT RADIATION SAFETY GUIDANCE

Review these precautions with patients before they leave the clinic. Encourage patients to follow recommendations as best they can, based on what's practical for their situation.

For the first 3 DAYS after infusions

Hydration

- Drink plenty of liquids and urinate often to remove BEXLUTRY from the body[12,13]

Bathroom use

- Sit down when using the toilet to avoid splashing[13,14]
- Flush 2 times with lid closed after each use[12,13]
- Clean any spills right away[13]
- Wash hands well with soap and water[12,13]
- **For Caregivers:** Wear disposable gloves when helping with bathroom needs or handling bodily fluids, and dispose of in a separate bag[12,13]

Close contact with others

- Stay at least 3 feet away from other people and pets[13]
- Do not use public transportation[13]
- Wait 3 days before returning to work in person[13]

It's important to educate patients about radiation safety to help minimize risks during treatment with BEXLUTRY.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

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EDUCATING PATIENTS AND CAREGIVERS ON IMPORTANT RADIATION SAFETY GUIDANCE (CONT'D)

For the first 7 DAYS after infusions

Personal hygiene

- Take a shower every day to help remove radioactive skin contamination[12,15]
- Wash clothing, towels, and bedding separately from other household members[16]

Sleeping and personal space

- Sleep alone to limit radiation exposure to others, including children and pets[12,13]
- Avoid sexual activity[12]
- Limit close physical contact[8]

Close contact with others

- In general, maintain 3-foot distance from children and pregnant people[13]
- Avoid close contact in crowded public places[8]

Additional safety measures around pregnancy

- Do not share a bed with a pregnant person for **up to 15 days after infusions**[12,13]

Safety for people of reproductive potential

- Use effective birth control during treatment and for **7 months after the final dose**[1]
- Do not breastfeed during treatment and for **2.5 months after the final infusion**[1]
  - During this time, continue expressing breast milk to maintain lactation; milk should be discarded or stored until safe for use per your doctor's or care team's direction[17]

IMPORTANT SAFETY INFORMATION (cont'd)

DRUG INTERACTIONS (cont'd)

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

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

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AT-A-GLANCE ADMINISTRATION SUMMARY

BEFORE administration

- **Discontinue long-acting SSAs** (≥4 weeks before infusion)[1]
- Administer short-acting SSA as needed[1]
- **Discontinue short-acting SSAs** (≥24 hours before infusion)[1]
- Check labs, creatinine clearance, and performance status[4]
- Verify pregnancy status of patients with reproductive potential[1]
- Prepare patient information, including visitor restrictions[8]

Safe handling

- **Follow radiation safety protocols** (time/distance/shielding)[8]
- Confirm administration method[1]
- **Use aseptic technique** when handling or administering BEXLUTRY[1]
- Use tongs when handling the vial[1]
- Inspect vial for particulate matter and discoloration[1]
- Verify activity with radioactivity dose calibrator[1]
- Dispose of unused product or waste material[1]

Patient and room setup

- Prepare infusion room[5]
- Establish IV access[1]
- Flush IV line[1]
- Prepare amino acid solution[1]
- **Prepare radiation safety setup** (signage, PPE, shielding)[8]

Do not initiate treatment until...

the treating provider reviews labs, performance status, and Prescribing Information guidance.[18]

IMPORTANT SAFETY INFORMATION (cont'd)

USE IN SPECIFIC POPULATIONS

Lactation

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

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

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

AT-A-GLANCE ADMINISTRATION SUMMARY (CONT'D)

DURING administration

- **Verify a dated and signed written directive** per 10 CFR 35.40[10]
- **Verify correct patient, treatment, and BEXLUTRY activity** prior to infusion
- **Administer antiemetics** before amino acid solution[1]
- **Administer amino acid solution** (30 min prior to infusion)[1]
- **Administer BEXLUTRY**[1]

Monitoring

- Observe patient for hypersensitivity reactions[1]
- Check IV lines periodically[5]
- Continue amino acid solution during and for at least 3 hours after infusion[1]

If a patient becomes nauseated…

Administer antiemetics as directed to relieve nausea and prevent vomiting.[4] If additional management is needed, follow institutional guidelines or prescribing physician's direction.

AFTER administration

- Stop infusions and flush IV lines[1]
- Secure radioactive waste[8]
- Provide post-treatment instructions for patient[8]
- Document dose completion[8]
- Monitor lab tests as necessary[1]
- Schedule next infusion and follow-up labs/dosimetry
- **Administer long-acting SSA between 4 and 24 hours after each administration** of BEXLUTRY. Do not administer long-acting SSA within 4 weeks prior to each subsequent dose of BEXLUTRY[1]
- **Continue long-acting SSA every 4 weeks after completing BEXLUTRY** until disease progression or for 18 months following treatment initiation, at the discretion of the physician[1]

What to do about unused or delayed doses…

Contact Curium Connects™ at 1-844-287-2628 about unused doses, delayed doses, or patient cancellations.

For more details on how to monitor for adverse reactions, see pages 13-15.

IMPORTANT SAFETY INFORMATION (cont'd)

USE IN SPECIFIC POPULATIONS (cont'd)

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™
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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 June 4, 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. Becx MN, Minczeles NS, Brabander T, de Herder WW, Nonnekens J, Hofland J. A clinical guide to peptide receptor radionuclide therapy with ^{177}Lu-DOTATATE in neuroendocrine tumor patients. *Cancers.* 2022;14(23):5792. doi:10.3390/cancers14235792
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. 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. doi:10.2967/jnmt.118.221846
7. Attachment 1, Item 19, Emergency Procedures. Nuclear Regulatory Commission. Accessed June 4, 2026. https://www.nrc.gov/docs/ML0827/ML082750235.pdf
8. Hosono M, Ikebuchi H, Nakamura Y, et al. Manual on the proper use of lutetium-177-labeled somatostatin analogue (Lu-177-DOTA-TATE) injectable in radionuclide therapy (2nd ed.). *Ann Nucl Med.* 2018;32(3):217-235. doi:10.1007/s12149-018-1230-7
9. Hope TA, Abbott A, Colucci DL, 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. doi:10.2967/jnumed.118.230607
10. *Code of Federal Regulations.* Title 10–Energy, Chapter I–Nuclear Regulatory Commission, Part 35–Medical Use of Byproduct Material, Subpart B–General Administrative Requirements, CFR §35.40. National Archives. Accessed June 4, 2026. https://www.ecfr.gov/current/title-10/chapter-I/part-35/subpart-B/section-35.40
11. Laudicella R, Faggiano A, Pirro V, et al. AIMN, ITANET, SIE joint position paper for the recognition, prevention and management of NET carcinoid syndrome and crises during peptide receptor radionuclide therapy. *Eur J Nucl Med Mol Imaging.* 2026;53(3):1445-1457. doi:10.1007/s00259-025-07596-2
12. Ladrière T, Faudemer J, Levigoureux E, Peyronnet D, Desmonts C, Vigne J. Safety and therapeutic optimization of Lutetium-177 based radiopharmaceuticals. *Pharmaceutics.* 2023;15(4):1240. doi:10.3390/pharmaceutics15041240
13. Radiation safety patient instructions: LUTATHERA (Lu-177 dotatate). Dartmouth Health. Accessed June 4, 2026. https://geiselmed.dartmouth.edu/radiology/wp-content/uploads/sites/47/2024/09/LUTATHERA-radiation-safety.pdf
14. Levart D, Kalogianni E, Corcoran B, Mulholland N, Vivian G. Radiation precautions for inpatient and outpatient ^{177}Lu-DOTATATE peptide receptor radionuclide therapy of neuroendocrine tumours. *EJNMMI Phys.* 2019;6(1):7. doi:10.1186/s40658-019-0243-1
15. Hendifar AE, Mehr SH, McHaffie DR. Best practices for the coordinated care of patients with neuroendocrine tumors undergoing peptide receptor radionuclide therapy. *Pancreas.* 2022;51(3):213-218. doi:10.1097/MPA.0000000000002002
16. Radioligand therapy. International Neuroendocrine Cancer Alliance. Accessed June 4, 2026. https://incalliance.org/wp-content/uploads/2020/12/What-is-RadioLigandTherapy_EN.pdf
17. Dilsizian V, Palestro C, Zanzonico P. *Advisory Committee on Medical Uses of Isotopes (ACMUI) Sub-Committee on Nursing Mother Guidelines for the Medical Administration of Radioactive Materials.* Nuclear Regulatory Commission. Updated January 31, 2019. Accessed June 5, 2026. https://www.nrc.gov/docs/ML1903/ML19038A498.pdf
18. Soulek DK, Martin ME, Mastascusa NJ, Graves SA. Practical considerations for implementation of ^{177}Lu-DOTATATE neuroendocrine tumor treatment programs. *J Nucl Med Technol.* 2022;50(3):195-202. doi:10.2967/jnmt.122.263813

ADMINISTRATION OF BEXLUTRY: KEY TAKEAWAYS

BEFORE administration

- Discontinue long-acting SSAs at least 4 weeks before infusion[1]
- Discontinue short-acting SSAs at least 24 hours before infusion[1]
- Check labs, creatinine clearance, and performance status[4]
- Verify pregnancy status[1]
- Follow radiation safety handling and room setup protocols[1,8]

DURING administration

- Verify correct patient, treatment, and BEXLUTRY activity
- Select gravity, peristaltic pump, or syringe pump method for BEXLUTRY infusion[1]
- Administer antiemetics prior to amino acid solution containing L-lysine and L-arginine[1]
- Administer amino acid solution 30 minutes before, during, and for at least 3 hours after BEXLUTRY infusion[1]
- Administer BEXLUTRY for 30 to 40 minutes[1]
- Observe patient for hypersensitivity reactions[1]

AFTER administration

- Document dose completion[8]
- Provide radiation safety instructions for patient[8]
- Monitor lab tests as necessary[1]
- Schedule next infusion and follow-up labs/dosimetry

Recommended dosing and calibration[1]

7.4 GBq (200 mCi) every 8 weeks (± 1 week), for a **total of 4 doses**

Consistent calibration time at 5:00 PM ET for 200 mCi, expiring 3 hours later at 8:00 PM ET

Please see the full guide for complete instructions on the administration of BEXLUTRY.

Learn more at BEXLUTRYHCP.com

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **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.

CURIUM

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