



AZEDRA[®]

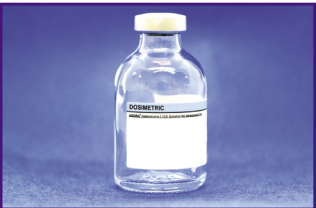
iobenguane | 131 injection for
intravenous use

DOSE PREPARATION GUIDE

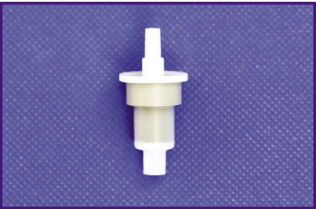
Please see Important Safety Information on page 6 and click here for full [Prescribing Information](#).

Supply List

Imaging Dose Preparation Components and Imaging Reference Standard



30 mL AZEDRA Vial
(2 mL fill)
Quantity: 1



Charcoal
Filter Unit
Quantity: 1



10 mL Luer-Lock
Syringe w/attached Needle
Quantity: 2



30 mL Luer-Lock Syringe w/
attached Needle
Quantity: 1



0.22 µm
Syringe Filter
Quantity: 1



20G x 1"
Luer-Lock Needle
Quantity: 1



40 mL of 0.9% Sodium
Chloride for Injection



1 mL Luer-Lock Syringe w/
attached Needle
Quantity: 1



10 mL Sterile
Empty Vial
Quantity: 1

Dose Instructions

Dosimetry Preparation

Preparation of a 1 mCi/mL Solution

Prepare both the dosimetric dose and the reference standard using a single 30 mL (2 mL fill) vial of AZEDRA® (iobenguane I 131).

1. Retrieve a frozen dosimetry vial of AZEDRA (2 mL fill) from $\leq -70^{\circ}\text{C}$ storage
2. Allow contents to thaw and come to room temperature in lead pot
 - a. Thawing takes approximately 90 minutes
 - b. Drug must be administered within 8 hours from the time it is removed from the freezer
 - c. Once thawed, swirl the vial to ensure homogeneity
 - d. Inspect visually for particulate matter and discoloration prior to administration whenever solution and container permit. Discard if particulate matter or discoloration is observed
3. Remove the vial from the lead shield and place in the dose calibrator to determine the current activity and the amount of radioactivity that will be present at the time of administration
4. Calculate the required amount of 0.9% sodium chloride for injection, USP [NaCl] for injection to reach a final radioactive concentration of 1 mCi/mL at the time of administration
5. Insert the venting unit into the vial to prevent pressurizing during dilution
6. Dilute the contents of the 30 mL (2 mL fill) vial with the required amount of 0.9% NaCl to reach a final radioactive concentration of 1 mCi/mL at the time of administration. Keep the vial in the lead pot during dilution to minimize exposure
7. Do not heat or refreeze. Discard unused medicinal product or waste material in accordance with local and federal laws

Preparation of the Dosimetric Dose

1. Place the 1 mCi/mL solution into the dose calibrator to determine the amount of radioactivity required to fill the patient dose at time of administration. Using this reading, calculate the volume (mL) of solution required to prepare the dosimetric dose that was ordered
2. Prepare the dosimetric dose in a 10 mL syringe and place in the dose calibrator to ensure that the activity concentration is within $\pm 10\%$ of the dose ordered (or as per institutional protocol)
3. Remove the needle from the 10 mL syringe, then cap the syringe with a Luer-Lock cap, label the syringe as "Dosimetric Dose" and measure the final activity in the dose calibrator
4. Place the capped syringe in a labeled lead shield for transport. The dosimetric dose should remain at room temperature and must be administered within 8 hours of the frozen product being taken out of storage at $\leq -70^{\circ}\text{C}$

Preparation of the Dosimetric Reference Standard

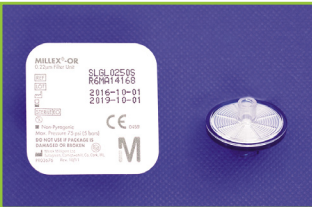
1. From the 1 mCi/mL solution, draw 100 uCi and dilute to create a reference standard. Measure the activity in a dose calibrator. Label "Reference Standard" and place in a shield for transport if applicable

Supply List

Therapeutic Dose Preparation System Component List



50 mL Sterile Empty Vial
Quantity: 1



0.22 µm Syringe Filter
Quantity: 3



48" Extension Set, M-F
Quantity: 1



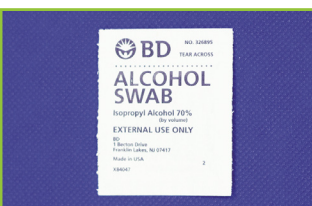
19G x 5" Aspirating Needle
Quantity: 2



20G x 1" Luer-Lock Needle
Quantity: 3



50 mL of 0.9% Sodium Chloride for Injection
Quantity: 1



Alcohol Swabs
Quantity: 1



30 mL AZEDRA Vial (22.5mL fill)
Quantity: 1



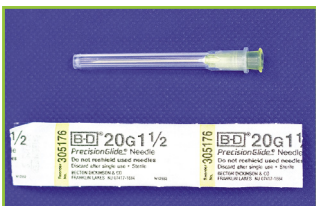
12" Extension Tubing, M-M
Quantity: 2



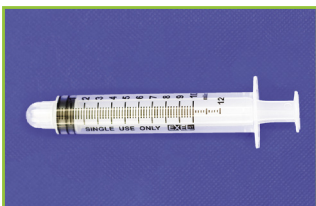
3-way Stopcock
Quantity: 1



60 mL Luer-Lock Syringe
Quantity: 2



20G x 1 1/2" Luer-Lock Needle
Quantity: 2



10 mL Syringe w/ 20G x 1 1/2" Needle
Quantity: 1



Charcoal Filter Unit
Quantity: 3

Therapeutic Instructions

1. Thaw the appropriate number of vials (2 or 3) to room temperature in lead pots. Do not heat or refreeze
2. Swirl AZEDRA® (iobenguane I 131) vial(s) to ensure homogeneity
3. Inspect visually for particulate matter and discoloration prior to administration whenever solution and container permit. Discard if particulate matter or discoloration is observed
4. Insert a venting unit into each AZEDRA vial to avoid pressurizing the contents of the vial during dilution
5. Insert a venting unit into a sterile 50-mL glass vial. Transfer the entire contents of the two therapeutic vial(s) into a 50-mL glass vial. Measure the radioactivity
 - a. If radioactivity in the 50-mL glass vial exceeds the therapeutic dose, withdraw and discard the appropriate volume using a shielded syringe. Add 0.9% Sodium Chloride Solution, USP to a total volume of 50 mL
 - b. If radioactivity in the 50-mL glass vial is less than the therapeutic dose, use a shielded syringe to withdraw the appropriate volume from a third AZEDRA vial and add to the 50-mL glass vial. Add 0.9% Sodium Chloride Solution, USP to a total volume of 50 mL
6. Swirl gently to ensure homogeneity
7. Remove the venting unit and place the 50-mL glass vial into a dose calibrator to ensure that the activity is within ± 10% of therapeutic dose
8. Maintain at room temperature and administer within 8 hours of retrieval from frozen storage
9. Do not heat or refreeze. Discard unused medicinal product or waste material in accordance with local and federal laws
10. If applicable, the patient dose should be transported in Department of Transportation-compliant shipping container for radioactive materials to the treating facility or department

Indication

AZEDRA® (iobenguane I 131) is indicated for the treatment of adult and pediatric patients 12 years and older with iobenguane scan positive, unresectable, locally advanced or metastatic pheochromocytoma or paraganglioma who require systemic anticancer therapy.

Important Safety Information

Warning and Precautions:

- **Risk from radiation exposure:** AZEDRA contributes to a patient's overall long-term radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk for cancer. These risks of radiation associated with the use of AZEDRA are greater in pediatric patients than in adults. Minimize radiation exposure to patients, medical personnel, and household contacts during and after treatment with AZEDRA consistent with institutional good radiation safety practices and patient management procedures.
- **Myelosuppression:** Severe and prolonged myelosuppression occurred during treatment with AZEDRA. Among the 88 patients who received a therapeutic dose of AZEDRA, 33% experienced Grade 4 thrombocytopenia, 16% experienced Grade 4 neutropenia, and 7% experienced Grade 4 anemia. Five percent of patients experienced febrile neutropenia. Monitor blood cell counts weekly for up to 12 weeks or until levels return to baseline or the normal range. Withhold and dose reduce AZEDRA as recommended in the prescribing information based on severity of the cytopenia.
- **Secondary myelodysplastic syndrome, leukemia, and other malignancies:** Myelodysplastic syndrome (MDS) and acute leukemias were reported in 6.8% of the 88 patients who received a therapeutic dose of AZEDRA. The time to development of MDS or acute leukemia ranged from 12 months to 7 years. Two of the 88 patients developed a non-hematological malignancy.
- **Hypothyroidism:** Hypothyroidism was reported in 3.4% of the 88 patients who received a therapeutic dose of AZEDRA. Initiate thyroid-blocking medications starting at least 1 day before and continuing for 10 days after each AZEDRA dose to reduce the risk of hypothyroidism or thyroid neoplasia. Evaluate for clinical evidence of hypothyroidism and measure thyroid-stimulating hormone (TSH) levels prior to initiating AZEDRA and annually thereafter.
- **Elevations in blood pressure:** Eleven percent of the 88 patients who received a therapeutic dose of AZEDRA experienced a worsening of pre-existing hypertension defined as an increase in systolic blood pressure to ≥ 160 mmHg with an increase of 20 mmHg or an increase in diastolic blood pressure to ≥ 100 mmHg with an increase of 10 mmHg. All changes in blood pressure occurred within the first 24 hours post infusion. Monitor blood pressure frequently during the first 24 hours after each therapeutic dose of AZEDRA.
- **Renal toxicity:** Of the 88 patients who received a therapeutic dose of AZEDRA, 7% developed renal failure or acute kidney injury and 22% demonstrated a clinically significant decrease in glomerular filtration rate (GFR) measured at 6 or 12 months. Monitor renal function during and after treatment with AZEDRA. Patients with baseline renal impairment may be at greater risk of toxicity; perform more frequent assessments of renal function in patients with mild or moderate impairment. AZEDRA has not been studied in patients with severe renal impairment.
- **Pneumonitis:** Fatal pneumonitis occurred 9 weeks after a single dose in one patient in the expanded access program. Monitor patients for signs and symptoms of pneumonitis and treat appropriately.
- **Embryo-fetal toxicity:** Based on its mechanism of action, AZEDRA can cause fetal harm. Verify pregnancy status in females of reproductive potential prior to initiating AZEDRA. Advise females and males of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment with AZEDRA and for 7 months after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 4 months after the final dose.
- **Risk of infertility:** Radiation exposure associated with AZEDRA may cause infertility in males and females. Radiation absorbed by testes and ovaries from the recommended cumulative dose of AZEDRA is within the range where temporary or permanent infertility can be expected following external beam radiotherapy.

Adverse Reactions:

The most common severe (Grade 3–4) adverse reactions observed in AZEDRA clinical trials ($\geq 10\%$) were lymphopenia (78%), neutropenia (59%), thrombocytopenia (50%), fatigue (26%), anemia (24%), increased international normalized ratio (18%), nausea (16%), dizziness (13%), hypertension (11%), and vomiting (10%). Twelve percent of patients discontinued treatment due to adverse reactions (thrombocytopenia, anemia, lymphopenia, nausea and vomiting, multiple hematologic adverse reactions).

Drug Interactions:

Based on the mechanism of action of iobenguane, drugs that reduce catecholamine uptake or that deplete catecholamine stores may interfere with iobenguane uptake into cells and therefore interfere with dosimetry calculations or the efficacy of AZEDRA. These drugs were not permitted in clinical trials that assessed the safety and efficacy of AZEDRA. Discontinue the drugs listed in the prescribing information for at least 5 half-lives before administration of either the dosimetry dose or a therapeutic dose of AZEDRA. Do not administer these drugs until at least 7 days after each AZEDRA dose.

For important risk and use information about AZEDRA, please click here for full [Prescribing Information](#).

To report suspected adverse reactions, contact Progenics Pharmaceuticals, Inc. at 844-668-3950 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Reference: AZEDRA® prescribing information. New York, NY: Progenics Pharmaceuticals, Inc.; 08 2018.