

Clinical Policy: Iobenguane I-131 (Azedra)

Reference Number: ERX.SPA.420

Effective Date: 03.01.21

Last Review Date: 02.22

Line of Business: Commercial, Medicaid

[Revision Log](#)

See **Important Reminder** at the end of this policy for important regulatory and legal information.

Description

Iobenguane I-131 (Azedra®) injection is a radioactive agent.

FDA Approved Indication(s)

Azedra 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.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Azedra is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Pheochromocytoma and Paraganglioma (must meet all):

1. Diagnosis of pheochromocytoma or paraganglioma;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 12 years;
4. Tumor is unresectable, locally advanced, or metastatic;
5. Member currently receives medication to control tumor secretion of catecholamines (e.g., epinephrine, norepinephrine, dopamine) and related symptoms (e.g., hypertension, arrhythmia, hyperglycemia);
6. Documentation of positive metaiodobenzylguanidine (MIBG) scan;
7. Concurrent radiopharmaceuticals have not been prescribed (e.g., Lutathera® [lutetium lu-177 dotatate]);
8. Request meets one of the following (a or b):*
 - a. Dose does not exceed (i or ii):
 - i. Dosimetric dose (one dose only - dosimetry is used to calculate therapeutic dosing and must be administered first):
 - a) For member weight > 50 kg: 185 to 222 MBq (5 to 6 mCi);
 - b) For member weight \leq 50 kg: 3.7 MBq/kg (0.1 mCi/kg);
 - ii. Therapeutic dose (up to two doses at least 90 days apart):
 - a) For member weight > 62.5 kg: 18,500 MBq/kg (500 mCi);
 - b) For member weight \leq 62.5 kg: 296 MBq/kg (8 mCi/kg);
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 6 months (one dosimetric dose and up to two therapeutic doses)

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Pheochromocytoma and Paraganglioma (must meet all):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Azedra for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy as evidenced by but not limited to reduction or discontinuation of medication needed to control catecholamine-related symptoms (e.g., reduction in hypertension medication);
3. If request is for a dose increase, request meets one of the following (a or b):*
 - a. New dose does not exceed (i or ii):
 - i. Dosimetric dose (one dose only - dosimetry is used to calculate therapeutic dosing and must be administered first):
 - a) For member weight > 50 kg: 185 to 222 MBq (5 to 6 mCi);
 - b) For member weight ≤ 50 kg: 3.7 MBq/kg (0.1 mCi/kg);
 - ii. Therapeutic dose (up to two doses at least 90 days apart):
 - a) For member weight > 62.5 kg: 18,500 MBq/kg (500 mCi);
 - b) For member weight ≤ 62.5 kg: 296 MBq/kg (8 mCi/kg);
 - b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval duration: 6 months (one dosimetric dose and up to two therapeutic doses)

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

mCi: millicurie

MBq: megabecquerel

NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: Dosing Guidelines (Azedra Website and Prescribing Information)

- The manufacturer's website offers the following PDF dosing and administration resources (<https://azedra.com/site-setup-resources/>):
 - Dose preparation guide
 - Dosing and administration guide
 - Dosimetry guide

- Patient schedule and release instructions
- Patient treatment card
- Prescribing information:
 - Azedra is a radiopharmaceutical. Handle with appropriate safety measures to minimize radiation exposure. Use waterproof gloves and effective radiation shielding when handling Azedra. Radiopharmaceuticals, including Azedra, should be used by or under the control of physicians who are qualified by specific training and experience in the safe use and handling of radiopharmaceuticals, and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radiopharmaceuticals [i.e., Nuclear Regulatory Commission and state Health Departments].
 - Verify pregnancy status in females of reproductive potential prior to administering Azedra.
 - Do not administer if platelet count is less than 80,000/mcL or absolute neutrophil count is less than 1,200/mcL.
 - Block thyroid prior to administering Azedra.
 - 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 drugs that reduce catecholamine uptake or deplete catecholamine stores, such as those listed below, for at least 5 half-lives before administration of either the dosimetry or a therapeutic dose of Azedra. Do not administer these drugs until at least 7 days after each Azedra dose (see *Package Insert - Dosage and Administration (2.3) and Drugs that Reduce Catecholamine Uptake or Deplete Stores (7.1)*).
 - CNS stimulants or amphetamines (e.g. cocaine, methylphenidate, dextroamphetamine)
 - Norepinephrine and dopamine reuptake inhibitors (e.g. phentermine)
 - Norepinephrine and serotonin reuptake inhibitors (e.g. tramadol)
 - Monoamine oxidase inhibitors (e.g. phenelzine and linezolid)
 - Central monoamine depleting drugs (e.g. reserpine)
 - Non-select beta adrenergic blocking drugs (e.g. labetalol)
 - Alpha agonists or alpha/beta agonists (e.g. pseudoephedrine, phenylephrine, ephedrine, phenylpropanolamine, naphazoline)
 - Tricyclic antidepressants or norepinephrine reuptake inhibitors (e.g. amitriptyline, bupropion, duloxetine, mirtazapine, venlafaxine)
 - Botanicals that may inhibit reuptake of norepinephrine, serotonin or dopamine (e.g. ephedra, ma huang, St John's Wort, yohimbine)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Pheochromocytoma or paraganglioma	<p><u>Dosing regimen (see dosing guidelines at Appendix D):</u> Administer Azedra intravenously as a dosimetric dose followed by up to two therapeutic doses administered at least 90 days apart.</p> <ul style="list-style-type: none"> ● Recommended dosimetric dose: <ul style="list-style-type: none"> ○ Patients greater than 50 kg: 185 to 222 MBq (5 to 6 mCi) ○ Patients 50 kg or less: 3.7 MBq/kg (0.1 mCi/kg) ● Recommended therapeutic dose (adjust Azedra therapeutic dose(s) based on radiation dose estimates results from dosimetry): <ul style="list-style-type: none"> ○ Patients greater than 62.5 kg: 18,500 MBq (500 mCi) ○ Patients 62.5 kg or less: 296 MBq/kg (8 mCi/kg) 	See regimen

VI. Product Availability

Injection: 555 MBq/mL (15 mCi/mL) at TOC as a clear solution in a single-dose vial

Detailed description:

- Azedra injection, containing 555 MBq/mL (15 mCi/mL) of I-131 (as iobenguane I 131) and 0.006 mg/mL of iobenguane, is a sterile, clear, colorless to pale yellow solution for intravenous use supplied in a colorless Type 1 borosilicate glass 30 mL single-dose vial
- Azedra is supplied in dosimetric (2 mL) and therapeutic (22.5 mL) presentations:
 - Dosimetric: 1,110 MBq (30 mCi) of iobenguane I 131 at calibration time (NDC 71258-015-02)
 - Therapeutic: 12,488 MBq (337.5 mCi) of iobenguane I 131 at calibration time (NDC 71258-015-22)
- The product vial is in a lead shielded container placed in a re-sealable plastic bag. The product is shipped on dry ice in a USA DOT Type A Radioactive package. Store at -70°C (-94°F). The shelf life is 6 days post calibration time. Discard appropriately at 144 hours

VII. References

1. Azedra Prescribing Information. New York, NY: Progenics Pharmaceuticals, Inc.; March 2021. Available <https://azedra.com/full-prescribing-information.pdf>. Accessed September 14, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed September 14, 2021.
3. National Comprehensive Cancer Network. Neuroendocrine and Adrenal Tumors Version 3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed September 14, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	12.02.20	02.21
1Q 2022 annual review: no significant changes; updated Appendix D; references reviewed and updated.	09.14.21	02.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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