

Clinical Policy: Iobenguane I-131 (Azedra)

Reference Number: LA.PHAR.459

Effective Date: 09.29.23Last Review Date: 05.09.23 04.05.24

Line of Business: Medicaid

[Coding Implications](#)[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

****Please note:** This policy is for medical benefit**

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.

It is the policy of Louisiana Healthcare Connections[®] 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 dotate]);
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);

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- b) For member weight ≤ 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 (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

II. Continued Therapy

A. Pheochromocytoma and Paraganglioma (must meet all):

1. Currently receiving medication via Louisiana Healthcare Connections benefit, 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND

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criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

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 policies – LA.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration	NCCN: National Comprehensive Cancer Network
MBq: megabecquerel	
mCi: millicurie	

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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.

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- 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></p> <p>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

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VI. Product Availability

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

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

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VII. References

1. Azedra Prescribing Information. New York, NY: Progenics Pharmaceuticals, Inc.; March 2021. Available <https://azedra.com/full-prescribing-information.pdf>. Accessed October 25, 2022 13, 2023.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed October 25, 2022 November 15, 2023.
3. National Comprehensive Cancer Network. Neuroendocrine and Adrenal Tumors Version 1. 2022 2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed October 25, 2022 November 21, 2023.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPSC Codes	Description
A9590	Iodine I-131, iobenguane 1 millicurie

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Reviews, Revisions, and Approvals	Date	LDH Approval Date
Policy created.	05.09.23	08.28.23
Annual review: no significant changes; references reviewed and updated.	04.05.24	

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Important Reminder

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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. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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