Clinical Policy: Iobenguane I-131 (Azedra)

Reference Number: PA.CP.PHAR.459
Effective Date: 10/2020
Last Review Date: 01/2025

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.

*** Progenics Pharmaceuticals, a subsidiary of Lantheus Holdings, announced they will no longer be producing Azedra due to lack of commercial demand** (*see Appendix E*).

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 PA Health & Wellness® that Azedra is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Pheochromocytoma and Paraganglioma (must meet all)**:**
Authorization is not permitted. Member may not initiate therapy with Azedra. If member is currently using Azedra proceed to section II.A. Pheochromocytoma and Paraganglioma for continued therapy (*see Appendix E).* **Approval duration: Not applicable**

B. Other diagnoses/indications
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Pheochromocytoma and Paraganglioma (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
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*).

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 PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
MBq: megabecquerel
mCi: millicurie
NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: Dosing Guidelines (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)

Appendix E: Azedra Manufacturer Discontinuation

- Progenics Pharmaceuticals, a subsidiary of Lantheus Holdings, will no longer be producing Azedra due to lack of commercial demand. Lantheus will continue to manufacturer Azedra into the first quarter of 2024, to the extent feasible, with the goal of providing doses of Azedra to current patients so they can complete their treatment regimen.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Pheochromocytoma or paraganglioma	Dosing regimen (see dosing guidelines at Appendix D): Administer Azedra intravenously as a dosimetric dose followed by up to two therapeutic doses administered at least 90 days apart. • Recommended dosimetric dose: o Patients greater than 50 kg: 185 to 222 MBq (5 to 6 mCi) o 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):	See regimen

Indication	Dosing Regimen	Maximum Dose
	o Patients greater than 62.5 kg: 18,500 MBq (500 mCi) o Patients 62.5 kg or less: 296 MBq/kg (8 mCi/kg)	

VI. Product Availability

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

VII. References

1. Azedra Prescribing Information. New York, NY: Progenics Pharmaceuticals, Inc.; May 2021. Available https://azedra.com/full-prescribing-information.pdf. Accessed November 7, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 7, 2024.
3. National Comprehensive Cancer Network. Neuroendocrine and Adrenal Tumors Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed November 7, 2024.
4. Latest news. Important update: Azedra (iobenguane I-131). Available at: https://pheopara.org/2023/08/important-update-azedra-iobenguane-i-131. Accessed November 7, 2024.

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.

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

Reviews, Revisions, and Approvals	Date
Policy created.	10/2020
1Q 2021 annual review: no significant changes; references reviewed and updated.	01/2021
1Q 2022 annual review: updated Appendix D and HCPCS code; references reviewed and updated.	01/2022
1Q 2023 annual review: no significant changes; references reviewed and updated.	01/2023
1Q 2024 annual review: no significant changes; references reviewed and updated.	01/2024
1Q 2025 annual review: removed initial approval criteria due to manufacturer discontinuation; added information regarding manufacturer discontinuation to Appendix E; references reviewed and updated.	01/2025