Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 02/01/2021**
Policy Number: PA.CP.PHAR.459	**Effective Date: 10/2020** **Revision Date: 01/2021**
Policy Name: Iobenguane I-131 (Azedra)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

1Q 2021 annual review: no significant changes; references reviewed and updated.

Name of Authorized Individual (Please type or print): **Auren Weinberg, MD**	**Signature of Authorized Individual:** 

Clinical Policy: Iobenguane I-131 (Azedra)

Reference Number: PA.CP.PHAR.459
Effective Date: 10/2020
Last Review Date: 01/2021

Coding Implications
Revision Log

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 health plans affiliated with 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)**:**

1. Diagnosis of pheochromocytoma or paraganlioma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 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. Metaiodobenzylguanidine (MIBG) scan is positive;
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 ≤ 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. 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 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.LTSS.PHAR.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):
         b. 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 PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.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	mCi: millicurie
MBq: megabecquerel	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
- 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	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): 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)	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.; August 2018. Available https://azedra.com/full-prescribing-information.pdf. Accessed November 10, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 10, 2020.
3. National Comprehensive Cancer Network. Neuroendocrine and Adrenal Tumors Version 2.2020. Available at:

https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed November 10, 2020.

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
A9699, A4641	Iobenguane I 131 injection, for intravenous use (Azedra®)

Reviews, Revisions, and Approvals	Date
Policy created.	10/2020
1Q 2021 annual review: no significant changes; references reviewed and updated.	01/2021