

POLICY: Oncology – Azedra® (iobenguane I 131 injection, for intravenous use – Progenics Pharmaceuticals, Inc.)

DATE REVIEWED: 08/28/2019

OVERVIEW

Azedra is a radioactive therapeutic agent 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.¹

Azedra, a high-specific iodine-131-metaiodobenzylguanidine (I-131 MIBG) product, is produced by a manufacturing process, Ultratrace®.² Compared with conventional I-131 MIBG, Azedra has little to no unlabeled MIBG. Theoretical advantages of using a high-specific activity product are improved targeting, greater tumor concentration, and decreased potential for side effects.^{3,4}

The recommended Azedra regimen consists of one dosimetric dose and two therapeutic doses; the doses are administered via intravenous infusions.¹ Three scans are recommended after the dosimetric dose. Administration of the therapeutic doses may need to be reduced or delayed based on dosimetry data or adverse events (e.g., myelosuppression, pneumonitis). In one of the studies, patients received the first therapeutic dose 7 to 28 days after the dosimetric dose.² The two therapeutic doses should be separated by a minimum of 90 days.¹

The administration of Azedra requires the use of pre- and concomitant medications. Inorganic iodine therapy should be initiated before Azedra therapy and continued for 10 days after each Azedra dose. Fluid intake should be increased before Azedra therapy and continued for 1 week after each Azedra dose. Drugs that reduce catecholamine uptake or deplete catecholamine stores should be discontinued before Azedra therapy and should not be re-initiated for at least 7 days after each Azedra dose. Antiemetics are recommended before each Azedra dose.

Disease Overview

Pheochromocytoma is a rare tumor that develops in chromaffin cells in the central part of the adrenal glands. Paraganglioma also develops in chromaffin cells, but outside of the adrenal glands.⁵⁻⁸ Most pheochromocytomas and paragangliomas are benign, but approximately 10% to 15% of pheochromocytomas and 20% to 50% of paragangliomas are malignant; cancer cells often migrate to the lymph nodes, bones, liver, or lungs.^{5,6,8,9} Pheochromocytomas and paragangliomas release hormones, primarily adrenaline (epinephrine) and noradrenaline (norepinephrine) that cause episodic or persistent high blood pressure.⁹ Hypertensive crisis can lead to cardiac arrhythmias, myocardial infarction, and death. Surgery is the standard of care for patients with localized or regional pheochromocytomas and paragangliomas.^{5-7,9,10}

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines for Neuroendocrine and Adrenal Tumors (version 1.2019 – March 5, 2019) note surgical resection as the primary treatment of pheochromocytomas and paragangliomas.¹¹ Azedra or other I-131 MIBG therapy (requires positive MIBG scan) is recommended (among other therapies) for unresectable tumors or in the presence of distant metastases.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Azedra. Approval is recommended for those who meet the Criteria and Dosing for the listed indications. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Azedra as well as the monitoring required for adverse events and long-term efficacy, approval requires Azedra to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Azedra is recommended in those who meet the following criteria:

FDA-Approved Indications

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- 1. Pheochromocytoma.** Approve for 6 months if the patient meets the following criteria (A, B, and C):
- A) The patient is ≥ 12 years of age; AND
 - B) The patient has iobenguane scan positive, unresectable, locally advanced or metastatic pheochromocytoma; AND
 - C) Azedra is prescribed by, or in consultation with, an oncologist or radiologist.

Dosing. Approve the following dosing regimens (A and B):

- A) Approve the following weight-based dosimetric dose (i or ii):
 - i. ≤ 50 kg: approve up to 3.7 MBq/kg (0.1 mCi/kg) for one dose; OR
 - ii. > 50 kg: approve up to 222 Mbq (6 mCi) for one dose; AND
- B) Approve the following weight-based therapeutic dose (i or ii):
 - i. ≤ 62.5 kg: approve up to 296 MBq/kg (8 mCi/kg) per dose for up to two doses; OR
 - ii. > 62.5 kg: approve up to 18,500 Mbq (500 mCi) per dose for up to two doses.

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- 2. Paraganglioma.** Approve for 6 months if the patient meets the following criteria (A, B, and C):
- A) The patient is ≥ 12 years of age; AND
 - B) The patient has iobenguane scan positive, unresectable, locally advanced or metastatic paraganglioma; AND
 - C) Azedra is prescribed by, or in consultation with, an oncologist or radiologist.

Dosing. Approve the following dosing regimens (A and B):

- A) Approve the following weight-based dosimetric dose (i or ii):
 - i. ≤ 50 kg: approve up to 3.7 MBq/kg (0.1 mCi/kg) for one dose; OR
 - ii. > 50 kg: approve up to 222 Mbq (6 mCi) for one dose; AND
- B) Approve the following weight-based therapeutic dose (i or ii):
 - i. ≤ 62.5 kg: approve up to 296 MBq/kg (8 mCi/kg) per dose for up to two doses; OR
 - ii. > 62.5 kg: approve up to 18,500 Mbq (500 mCi) per dose for up to two doses.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Azedra has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-

coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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5. Pheochromocytoma. Available at: <https://www.mayoclinic.org/diseases-conditions/pheochromocytoma/symptoms-causes/syc-20355367>. Accessed on August 22, 2019.
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10. Lenders JWM, Duh QY, Eisenhofer G, et al. Pheochromocytoma and paraganglioma: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2014;99:1915-1942.
11. The NCCN Neuroendocrine and Adrenal Tumors Clinical Practice Guidelines in Oncology (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on August 21, 2019.

HISTORY

Type of Revision	Summary of Changes	Approval Date
New Policy	--	08/15/2018
Revision	Revised with new NCCN Neuroendocrine and Adrenal Tumors Clinical Practice Guidelines in Oncology (version 3.2018).	09/21/2018
Annual Revision	No criteria changes.	08/28/2019