PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 09/02/2020

OVERVIEW

Azedra is a radioactive therapeutic agent indicated for the treatment of adult and pediatric patients 12 years of age 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 infusion.[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.[1] 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.[5-7] 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.[5-8] Pheochromocytomas and paragangliomas release hormones, primarily adrenaline (epinephrine) and noradrenaline (norepinephrine) that cause episodic or persistent high blood pressure.[8] 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.[5,6,8,9]

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines for Neuroendocrine and Adrenal Tumors (version 2.2020 – July 24, 2020) note surgical resection as the mainstay of treatment for benign and malignant pheochromocytomas and paragangliomas.[10] 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 prescription benefit coverage of Azedra. 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

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

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

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Azedra is not recommended in the following situations:

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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4. Jimenez C. Treatment for patients with malignant pheochromocytomas and paragangliomas: a perspective from hallmarks of cancer. *Front Endocrinol*. 2018;9:277.
5. Pheochromocytoma. Available at: https://www.mayoclinic.org/diseases-conditions/pheochromocytoma/symptoms-causes/syc-20355367. Accessed on August 25, 2020.

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9. 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.
10. The NCCN Neuroendocrine and Adrenal Tumors Clinical Practice Guidelines in Oncology (Version 2.2020 – July 24, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on August 25, 2020.