

PRIOR AUTHORIZATION POLICY

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

APPROVAL DATE: 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; Azedra is administered intravenously.¹ Three scans are recommended after the dosimetric dose; the therapeutic doses may need to be reduced based on dosimetry data. 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 Administration of the second therapeutic dose may need to be delayed due to myelosuppression.

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 spread 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 prescription benefit coverage of Azedra. 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 an oncologist. All approvals are provided for the duration listed below.

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) 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.
- 2. Paraganglioma.** Approve Azedra for 6 months if the patient meets ALL of the following conditions (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.

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

1. Azedra® I 131 injection [prescribing information]. New York, NY: Progenics Pharmaceuticals, Inc.; August 2018.
2. Noto RB, Pryma DA, Jensen J, et al. Phase 1 study of high-specific-activity I-131 MIBG for metastatic and/or recurrent pheochromocytoma or paraganglioma. *J Clin Endocrinol Metab.* 2018;103:213-220.
3. Carrasquillo JA, Pandit-Taskar N, Chen CC. I-131 metaiodobenzylguanidine therapy of pheochromocytoma and paraganglioma. *Semin Nucl Med.* 2016;46:202-214.
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 22, 2019.
6. Pheochromocytoma. Available at: <https://emedicine.medscape.com/article/124059-overview>. Updated August 10, 2018. Accessed on August 22, 2019.
7. Pheochromocytoma (adrenaline-producing adrenal tumor). Available at: <http://endocrinediseases.org/adrenal/pheochromocytoma.shtml>. Accessed on August 22, 2019.
8. Pappachan JM, Raskauskiene D, Sriraman R, et al. Diagnosis and management of pheochromocytoma: a practical guide to clinicians. *Curr Hypertens Rep.* 2014;16:442.
9. Pheochromocytoma and paraganglioma treatment (PDQ) – health professional version. Available at: <https://www.cancer.gov/types/pheochromocytoma/hp/pheochromocytoma-treatment-pdq/>. Updated February 8, 2018. Accessed on August 22, 2019 July 25, 2018.
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 22, 2019.