Pharmacy Policy Bulletin: J-1292 Demser (metyrosine) – Commercial and Healthcare Reform	
Number: J-1292	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Other Managed Prior Authorization = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1292-003	**Original Date:** 06/07/2023
Effective Date: 04/25/2025	**Review Date:** 04/09/2025

Drugs Product(s):	• Demser (metyrosine)

FDA-Approved Indication(s):	• Treatment of patients with pheochromocytoma for:
	  ○ Preoperative preparation of patients for surgery.
	  ○ Management of patients when surgery is contraindicated.
	  ○ Chronic treatment of patients with malignant pheochromocytoma.

Background:	• Demser (metyrosine) inhibits tyrosine hydroxylase, which acts as a catalyst in catecholamine biosynthesis. Through blocking tyrosine hydroxylase activity, endogenous catecholamine levels are decreased. • A pheochromocytoma is a catecholamine secreting tumor present in the adrenal glands. Due to excessive amounts of norepinephrine and epinephrine, symptoms of pheochromocytoma include high blood pressure, heavy sweating, headache, tachycardia, pallor, and dyspnea. Surgery is considered the mainstay of treatment for both benign and malignant pheochromocytomas. • The Pheochromocytoma and Paraganglioma: An Endocrine Society Clinical Practice Guideline recommends perioperative alpha-adrenergic receptor blockers as the first choice to reduce the risk of hypertensive crisis and to control blood pressure. Metyrosine may be used in combination with alpha-adrenergic receptor blockers for a short period before surgery to further stabilize blood pressure to reduce blood loss and volume depletion during surgery. • The National Comprehensive Cancer Network Neuroendocrine and Adrenal Tumors guidelines state that alpha blockade is necessary treatment for all hormonally secreting pheochromocytomas and paragangliomas regardless of clinical symptoms. The guidelines state that metyrosine can be used in addition to alpha blockade to stabilize blood pressure. • The clinical practice guidelines state that there is compelling evidence that measurements of plasma free or urinary fractionated metanephrines are superior to other tests of catecholamine excess for diagnosis. A pheochromocytoma can be diagnosed by one of the following: ○ Plasma fractionated metanephrines:

	▪ Normetanephrines > 0.6 nmol/L ▪ Metanephrine > 0.3 nmol/L ○ 24-hour urine fractionated metanephrines and catecholamines: ▪ Normetanephrine > 900 mcg/24 hours ▪ Metanephrine > 400 mcg/24 hours ▪ Norepinephrine > 170 mcg/24 hours ▪ Epinephrine > 35 mcg/24 hours ▪ Dopamine > 700 mcg/24 hours • Prescribing Considerations: ○ Demser is not recommended for the control of essential hypertension.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Demser (metyrosine) may be approved when all of the following criteria are met **(A. through D.)**:

A. The member has a diagnosis of pheochromocytoma (ICD-10: C74.10) defined by one (1) of the following **(1. or 2.):**
- **1.** Elevated metanephrines in plasma or urine
- **2.** Tumor evidence from CT scan or MRI

B. The member meets one (1) of the following criteria **(1., 2., or 3.):**
- **1.** The member has a planned resection surgery.
- **2.** Resection surgery is contraindicated.
- **3.** The member has malignant pheochromocytoma.

C. The member has experienced therapeutic failure, contraindication, or intolerance to one (1) of the following **(1., 2., or 3.):**
- **1.** doxazosin
- **2.** prazosin
- **3.** terazosin

D. If the request is for brand Demser, the member has experienced therapeutic failure or intolerance to generic metyrosine.

II. Reauthorization

When a benefit, reauthorization of Demser (metyrosine) may be approved when all of the following criteria are met **(A. and B.)**:

A. The member meets one (1) of the following criteria **(1., 2., or 3.)**:
- **1.** The member experienced an incomplete response to tumor resection.
- **2.** Resection surgery is contraindicated.
- **3.** The member has malignant pheochromocytoma.

B. The member has experienced a positive clinical response to therapy (for example, symptom improvement, reduction in hypertensive episodes).

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Demser [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals International, Inc.; July 2021.
2. Mayo Clinic. Diseases and Conditions: Pheochromocytoma. Available at: https://www.mayoclinic.org/diseases-conditions/pheochromocytoma/symptomscauses/syc-20355367. Accessed February 28, 2025.
3. Lenders JWM,Duh QY, Eisenhofer G. Pheochromocytoma and paraganglioma: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2014;99(6):1915-1942.
4. Nölting S, Bechmann N, Taieb D, et al. Personalized management of pheochromocytoma and paraganglioma. *Endocr. Rev.* 2021;43(2):199-239.
5. National Comprehensive Cancer Network. NCCN Guidelines Version 4.2024 Neuroendocrine and Adrenal Tumors. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed February 28, 2025.