Effective Date 12/15/2024
Coverage Policy Number IP0450

Metyrosine

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for the following products:

- **Demser**® (metyrosine capsules)
- **metyrosine** capsule

Medical Necessity Criteria

Metyrosine products (Demser and metyrosine capsules) are considered medically necessary when the following are met:

Pheochromocytoma. Individual meets **ALL** of the following criteria:
A. **ONE** of the following:
i. Individual is currently receiving metyrosine
ii. Documented failure, contraindication, or intolerance to **BOTH** of the following:
a. **ONE** selective alpha blocker (for example, doxazosin, terazosin or prazosin)
b. phenoxybenzamine

B. The medication is prescribed by, or in consultation with, an endocrinologist or a physician who specializes in the management of pheochromocytoma

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Reauthorization Criteria

Continuation of metyrosine products (Demser and metyrosine capsules) are considered medically necessary for pheochromocytoma when the above medical necessity criteria are met **AND** there is documentation of beneficial response.

Authorization Duration

Initial and reauthorization approval duration: up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

Background

OVERVIEW
Metyrosine, a tyrosine hydroxylate inhibitor, is indicated for the treatment of patients with **pheochromocytoma** for the following uses:[1]

- Preoperative preparation of patients for surgery.
- Management of patients when surgery is contraindicated.
- Chronic treatment of patients with malignant pheochromocytoma.

Phenoxybenzamine, a long-acting, adrenergic, alpha-receptor blocking agent, is indicated for the treatment of **pheochromocytoma** to control episodes of hypertension and sweating. If tachycardia is excessive, it may be necessary to use a beta-blocking agent concomitantly.[2]

Guidelines
A clinical practice guideline was published in 2014 from the Endocrine Society regarding pheochromocytoma and paraganglioma.[3] The guidelines recommend a preoperative alpha$_1$-adrenergic receptor blocker as the first choice to control blood pressure and prevent a hypertensive crisis. Both selective and non-selective alpha-blockers have been used (e.g., phenoxybenzamine, doxazosin, prazosin, and terazosin). Calcium channel blockers are the most often used add-on drug class to further improve blood pressure control in patients already treated with alpha-adrenergic receptor blockers. Preoperative co-administration of a beta-adrenergic receptor blocker (e.g., atenolol, metoprolol, and propranolol) is utilized to control tachycardia after administration of an alpha-adrenergic receptor blocker. Metyrosine may be used in combination with an alpha-adrenergic receptor blocker 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 guidelines for neuroendocrine and adrenal tumors (version 1.2023 – August 02, 2023) address pheochromocytoma and paragangliomas.[4] Alpha blockade (e.g., terazosin, doxazosin, and prazosin) is recommended first-line for all hormone-secreting pheochromocytomas and paragangliomas. After alpha blockade, if additional blood pressure support is required, the additional of

dihydropyridine calcium channel blockers can be considered. Metyrosine can be used in addition to alpha blockade to stabilize blood pressure.

References

1. Demser® capsules [prescribing information]. Bridgewater, NJ: Bausch Health; July 2021.
2. Dibenzyline® capsules [prescribing information]. St. Michael, Barbados: Concordia; August 2021.
3. Lenders JWM, Duh QY, Eisenhofer G, et al. Pheochromocytoma and paraganglioma: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2014;99(6):1915-1942.
4. The NCCN Neuroendocrine and Adrenal Tumors Clinical Practice Guidelines in Oncology (version 1.2023 – August 02, 2023) © 2023 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org/. Accessed on September 18, 2023.

Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	No criteria changes	12/15/2024

The policy effective date is in force until updated or retired.