Drug Coverage Policy

Effective Date..... 12/1/2025
Coverage Policy Number IP0450
Policy Title..... Metyrosine and Phenoxybenzamine (Oral)

Pheochromocytoma – Metyrosine and Phenoxybenzamine (Oral)

- Demser® (metyrosine capsules – Bausch Health, generic)
- Dibenzyline® (phenoxybenzamine capsules – Concordia, generic)

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. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. 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

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 2.2025 – May 28, 2025) 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.

Coverage Policy

Prior Authorization is required for benefit coverage of metyrosine and phenoxybenzamine. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with metyrosine and phenoxybenzamine as well as the monitoring required for adverse events and long-term efficacy, approval requires metyrosine and phenoxybenzamine to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Employer and Individual and Family Plans:

I. Metyrosine products are considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Pheochromocytoma.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 1 year if the patient meets ALL of the following (i, ii, iii and iv):
     - **i.** Patient has tried a selective alpha blocker (e.g., doxazosin, terazosin, or prazosin); AND
     - **ii.** Patient has tried phenoxybenzamine (brand or generic); AND
     - **iii.** The medication is prescribed by, or in consultation with, an endocrinologist or a physician who specializes in the management of pheochromocytoma; AND
     - **iv.** Preferred product criteria is met for the product(s) as listed in the below table(s).
   - **B)** Patient is Currently Receiving Metyrosine. Approve for 1 year if prescribed by or in consultation with an endocrinologist or a physician who specializes in the management of pheochromocytoma.

Product	Criteria
Demser (metyrosine 250 mg capsule)	**1.** Approve if the patient meets ALL of the following (A, B and C): A. Patient meets the above criteria; AND B. Patient has tried generic metyrosine 250 mg capsule; AND C. Patient cannot continue to use generic metyrosine 250 mg capsule due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the brand and the bioequivalent generic product which, according to the prescriber, would result in a significant allergy or a serious adverse reaction.

Individual and Family Plans:

II. Dibenzyline is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Pheochromocytoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Preferred product criteria is met for the product(s) as listed in the below table(s); AND
   B) The medication is prescribed by or in consultation with an endocrinologist or a physician who specializes in the management of pheochromocytoma.

Product	Criteria
Dibenzyline (phenoxybenzamine capsules)	**1.** Approve for 1 year if the patient meets BOTH of the following (A and B): **A.** Patient has tried generic phenoxybenzamine; AND **B.** Patient cannot continue to use generic phenoxybenzamine due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the brand and the bioequivalent generic product which, according to the prescriber, would result in a significant allergy or a serious adverse reaction

Conditions Not Covered

Metyrosine products and phenoxybenzamine for any other use is considered not medically necessary. Criteria will be updated as newly published data are available.

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 2.2025 – May 28, 2025) © 2025 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org/. Accessed on September 09, 2025.

Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	No criteria changes	12/15/2024
Annual Revision	**Policy Title:** **Updated** from "Metyrosine" to "Pheochromocytoma-Metyrosine and Phenoxybenzamine (Oral)." **Added** Preferred Product Criteria Table for brand use of Demser to coverage policy. **Added** phenoxybenzamine criteria for Individual and Family Plan Benefit Plans to coverage policy.	12/1/2025

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