PRIOR AUTHORIZATION POLICY

POLICY: Pheochromocytoma – Metyrosine and Phenoxybenzamine (Oral) Prior Authorization Policy
- Demser® (metyrosine capsules – Bausch Health, generic)
- Dibenzyline® (phenoxybenzamine capsules – Concordia, generic)

REVIEW DATE: 09/25/2024

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 AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. 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.

CIGNA NATIONAL FORMULARY COVERAGE:

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 2.2024 – August 01, 2024) 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.

POLICY STATEMENT

Prior Authorization is recommended for prescription 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.

Documentation: Documentation will be required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, prescription claims records, and prescription receipts.

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

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Pheochromocytoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A)** If brand Dibenzyline is requested, patient meets BOTH of the following (i and ii):
     - **i.** Patient has tried generic phenoxybenzamine; AND
     - **ii.** 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 **[documentation required]**; AND
   - **B)** The medication is prescribed by or in consultation with an endocrinologist or a physician who specializes in the management of pheochromocytoma.

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, and iii):

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.

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.

CONDITIONS NOT COVERED

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

is(are) considered experimental, investigational, or unproven for ANY other use(s).

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 2.2024 – August 01, 2024) © 2024 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org/. Accessed on September 11, 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	09/20/2023
Annual Revision	No criteria changes.	09/25/2024