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: 09/20/2023

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.

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.

Automation: None.

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.

RECOMMENDED AUTHORIZATION CRITERIA

I. Coverage of phenoxybenzamine is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Pheochromocytoma.** Approve for 1 year if the patient meets 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.

II. Coverage of metyrosine is recommended in those who meet the following criteria:

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 RECOMMENDED FOR APPROVAL

Coverage of metyrosine and phenoxybenzamine is not recommended in the following situations:

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. 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.