BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

DEMSER® (metyrosine) oral
Metyrosine oral

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require precertification is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Demser (metyrosine) and generic metyrosine is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist or Endocrinologist.

2. Individual is 12 years of age or older.

3. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Patient with pheochromocytoma and **ANY** of the following:
        i. Preoperative preparation for surgery
        ii. Management of patients with pheochromocytoma when surgery is contraindicated

iii. Chronic treatment of patients with malignant pheochromocytoma

b. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A.

4. Individual has symptoms consistent with pheochromocytomas such as hypertension, episodic headache, nausea, tachycardia, sweating, and syncope.

5. Use is **NOT** intended for the treatment of essential hypertension.

6. The individual has received and completed **ONE** of the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
   a. Free metanephrine in plasma
   b. 24-hour urine fractionated metanephrines and normetanephrines with or without a serum and/or 24-hour urine fractionated catecholamines

7. Documented failure, contraindication per FDA label, intolerance, or not a candidate to the following:
   a. **ONE** selective alpha 1 blockader (such as terazosin, doxazosin, or prazosin)
   b. Phenoxybenzamine (brand or generic)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Demser (metyrosine) and generic metyrosine is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy**):

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist or Endocrinologist.

2. Individual's condition has responded while on therapy with response defined as ALL of the following:
   a. No evidence of disease progression
   b. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

3. Individual has been adherent with the medication.

4. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
   a. Significant hypotension
   b. Life threatening arrhythmia
   c. Crystalluria and urolithiasis

Renewal duration: 12 months

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- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-Cancer Medications**

  2. **Off-Label Use of Cancer Medications**

Description:

Demser (metyrosine) is indicated in the treatment of patients with pheochromocytoma for: 1) preoperative preparation of patients for surgery; 2) management of patients when surgery is contraindicated; and 3) chronic treatment of patients with malignant pheochromocytoma. Demser (metyrosine) is not recommended for the control of essential hypertension.

Demser (metyrosine) inhibits tyrosine hydroxylase, the enzyme that catalyzes the first transformation in catecholamine biosynthesis, i.e., the conversion of tyrosine to dihydroxyphenylalanine (DOPA). Because the first step is also the rate-limiting step, blockade of tyrosine hydroxylase activity results in decreased endogenous levels of catecholamines, usually measured as decreased urinary excretion of catecholamines and their metabolites.

In patients with pheochromocytoma, who produce excessive amounts of norepinephrine and epinephrine, administration of Demser (metyrosine) reduces catecholamine biosynthesis as measured by the total excretion of catecholamines and their metabolites (metanephrine and vanillylmandelic acid). The maximum biochemical effect usually occurs within two to three days, and the urinary concentration of catecholamines and their metabolites usually returns to pretreatment levels within three to four days after Demser (metyrosine) is discontinued. Alpha-1 selective blockers (terazosin, doxazosin, prazosin) or non-selective alpha blockade (phenoxybenzamine) are recommended 7-14 days prior to surgery. After adequate alpha blockade is achieved, a beta blocker is started 2-3 days prior to surgery. Intravenous phentolamine can be used intraoperatively. Alpha blockade is first-line therapy for all hormonally secreting pheochromocytomas. After alpha blockade, if further blood pressure control is needed, the addition of a dihydropyridine calcium channel blocker can be used. Metyrosine can also be used with alpha blockers for blood pressure control. Beta blockers can be added to alpha blockers for tachycardia. Beta-1 selective agents on no-selective beta blockers can be used.

Resources:

Demser (metyrosine) product information, revised by Bausch Health US, LLC. 07-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 08, 2022.

Metyrosine product information, revised by Oceanside Pharmaceuticals. 07-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 08, 2022.

Young WF. Clinical presentation and diagnosis of pheochromocytoma. In: UpToDate, Nieman LK, Martin KA (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on May 02, 2022. Accessed June 18, 2022.

Young WF, Kebebew E. Treatment of pheochromocytoma in adults. In: UpToDate, Nieman LK, Carty SE, Martin KA, Chen W (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on February 12, 2021. Accessed June 18, 2022.

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National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Neuroendocrine and Adrenal Tumors Version 1.2022 – Updated May 23, 2022. Available at https://www.nccn.org. Accessed June 18, 2022.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.