PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 08/19/2021
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ARCHIVE DATE:

DEMSER® (metyrosine) oral
Metyrosine oral

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Demser (metyrosine) and generic metyrosine are considered ***medically necessary*** and will be approved when **ALL** of 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. 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 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, tachycardia, sweating, and syncope

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

  6. **ALL** of the following **baseline tests** have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     a. Free metanephrine in plasma or 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)

  8. There are no significant interacting drugs

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Demser (metyrosine) and generic metyrosine are considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

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

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2. Individual's condition has responded
    a. Response is defined as:
        i. No evidence of disease progression
        ii. 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
    a. Significant adverse effect such as:
        i. Significant hypotension
        ii. Life threatening arrhythmia
        iii. Crystalluria and urolithiasis

5. There are no significant interacting drugs

Renewal duration: 12 months

- 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 a Non-cancer Medications**

    2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

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. 07-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on July 30,2021.

Metyrosine product information, revised by Amneal Pharmaceuticals NY, LLC. 07-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on August 06, 2021.

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. Accessed on August 06, 2021.

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. Accessed on August 06, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Neuroendocrine and Adrenal Tumors Version 2.2021 – Updated June 18, 2021. Available at https://www.nccn.org. Accessed on August 06, 2021.

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. Accessed on August 07, 2021.

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.