BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

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NAYZILAM® (midazolam) nasal spray

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.**

NAYZILAM® (midazolam) nasal spray

Criteria:

- **Criteria for initial therapy:** Nayzilam (midazolam) nasal spray is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in patient's diagnosis or is in consultation with a Neurologist

  2. Individual is 12 years of age or older

  3. A confirmed diagnosis of **epilepsy** on stable regimen of antiepileptic regimen and use is for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern

  4. Stereotypic episodes of frequent seizure activity occur **no more frequently than every 3 days**

  5. Individual has failure, intolerance, or contraindication to **ALL** the following preferred step therapy agents:
     - Diazepam rectal gel

  6. There are **NO** contraindications
     - Contraindications include:
       - Hypersensitivity to midazolam or any component of the formulation
       - Acute narrow-angle glaucoma

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Nayzilam (midazolam) nasal spray is 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 patient's diagnosis or is in consultation with a Neurologist

  2. Individual's condition responded or has worsened while on therapy [this can be modified or changed depending on drug or condition]
     - Response is defined as **TWO** of the following:
       - No evidence of disease progression
       - Reduction in number of recurrence stereotypic episodes seizure activity
       - Prolonged time to next stereotypic episodes seizure activity

  3. Individual has been adherent with the medication

  4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
     - Contraindications as listed in the criteria for initial therapy section
     - Significant adverse effect such as:

NAYZILAM® (midazolam) nasal spray

- Profound sedation
- Profound respiratory depression
- Profound cognitive dysfunction
- Coma
- Increased or emergent signs and symptoms of suicidal ideation and/or behaviors

5. Stereotypic episodes of frequent seizure activity occur **no more frequently than every 3 days**

6. There are no significant interacting drugs

Renewal duration: 12 months

Description:

Nayzilam (midazolam) nasal spray is indicated for acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy ≥ 12 years of age.

Midazolam binds to stereospecific benzodiazepine receptors on the postsynaptic gamma aminobutyric acid (GABA) neuron at several sites within the central nervous system, including the limbic system, reticular formation. GABA is the chief inhibitory neurotransmitter in the developmentally mature mammalian central nervous system. Its principal role is reducing neuronal excitability throughout the nervous system. Enhancement of the inhibitory effect of GABA on neuronal excitability results by increased neuronal membrane permeability to chloride ions. This shift in chloride ions results in hyperpolarization (a less excitable state) and stabilization. Benzodiazepine receptors and effects appear to be linked to the GABA-A receptors. Benzodiazepines do not bind to GABA-B receptors.

Diazepam rectal gel is a gel formulation of diazepam intended for rectal administration in the management of selected, refractory, patients with epilepsy, on stable regimens of AEDs, who require intermittent use of diazepam to control bouts of increased seizure activity. Evidence to support the use of diazepam rectal gel was adduced in two controlled trials. The trials enrolled patients with partial onset or generalized convulsive seizures who were suffering intermittent and periodic episodes of markedly increased seizure activity were characteristic and deemed to be of a kind for which a benzodiazepine would ordinarily be administered acutely. The clusters of seizure activity were not only stereotypic but were judged by those conducting and participating in these studies to be distinguishable from other seizures suffered by that patient.

Resources:

Nayzilam (midazolam) nasal spray product information accessed 10-09-19 at DailyMed