

Oscar Clinical Guideline: Benzodiazepines for Acute Repetitive Seizures or Seizure Clusters (PG181, Ver. 1)

## Benzodiazepines for Acute Repetitive Seizures or Seizure Clusters

- Diazepam rectal gel (Diastat, Diastat AcuDial)
- Nayzilam (midazolam) nasal spray
- Valtoco (diazepam nasal spray)

### Disclaimer

*Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.*

*Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.*

### Summary

Acute repetitive seizures (ARS) or seizure clusters are episodic flare-ups of frequent seizure activity distinct from a patient's typical seizure pattern. Seizure clusters are a common complication of epilepsy, a chronic neurological disorder characterized by recurrent, unprovoked seizures caused by abnormal electrical activity in the brain. Patients with epilepsy often experience acute repetitive seizure episodes, or clusters of seizures occurring closely together over a period of hours to days, interspersed with recovery of consciousness. Compared to a patient's usual seizure pattern, these acute repetitive seizures represent a marked increase in seizure frequency over a short time.

Acute repetitive seizures can progress to life-threatening status epilepticus if prolonged. Seizure clusters also negatively impact patient quality of life and place a significant burden on patients with epilepsy. Rescue therapy commonly involves the administration of rapid-acting benzodiazepines, either intravenously or rectally, to stop acute repetitive seizure activity. Three benzodiazepine formulations used for this purpose are:

1. Diazepam rectal gel - for acute repetitive seizure treatment in patients with epilepsy ages 2 years and older.
2. Valtoco (diazepam nasal spray) - for acute repetitive seizure treatment in patients with epilepsy ages 6 years and older.
3. Nayzilam (midazolam) nasal spray - for acute repetitive seizure treatment in patients with epilepsy ages 12 years and older.

These provide minimally invasive rescue therapy options for rapid cessation of acute repetitive seizures across different age groups. The diazepam rectal gel allows treatment in young pediatric epilepsy patients starting at age 2, while the nasal spray formulations offer alternatives for older childhood and adolescent populations who may prefer a nasal route of administration over rectal.

## Definitions

**“Acute Repetitive Seizures”**, also known as seizure clusters, are episodes of increased seizure activity distinct from a patient's usual seizure pattern. Acute repetitive seizures involve serial seizures occurring within a short time frame, often with incomplete recovery between seizures.

**“Rescue Therapy”** refers to the use of a rapidly acting medication for the purpose of terminating an ongoing seizure or stopping a seizure cluster/acute repetitive seizure episode.

**“Seizure Cluster”** are multiple seizures occurring over a relatively brief period of time with interictal recovery between seizures. This represents an acute change from a patient’s typical baseline seizure pattern. Also referred to as acute repetitive seizures.

**“Status Epilepticus”** is a prolonged seizure or recurrent seizures without complete recovery between events. It is an urgent neurologic condition which can lead to permanent neuronal injury or death without prompt treatment.

**“Usual Seizure Pattern”** refers to the typical seizure frequency and characteristics established over time specific to an individual patient.

## Clinical Indications

### Medical Necessity Criteria for Initial Authorization

The Plan considers **Valtoco (diazepam nasal spray), Nayzilam (midazolam nasal spray), or Diastat (diazepam rectal gel)** medically necessary when **ALL** of the following criteria are met:

1. The medication is prescribed by or in consultation with a neurologist; **AND**
2. Safety and efficacy of the requested medication has been established for the member's age as evidenced by FDA-approved labeling (Use in Specific Populations); **AND**
  - a. Valtoco (diazepam nasal spray): 6 years of age and older.
  - b. Nayzilam (midazolam nasal spray): 12 years of age and older.
  - c. Diastat (diazepam rectal gel): 2 years of age and older.
3. The member has a diagnosis of epilepsy; **AND**
4. The member experiences intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures<sup>1</sup>) that are distinct from the member's usual seizure pattern; **AND**

<sup>1</sup>*also referred to as serial, cyclic, cluster, breakthrough, or crescendo seizures*
5. The member is currently on a stable regimen of anti-epileptic drugs (AEDs); **AND**
6. Valtoco (diazepam nasal spray), Nayzilam (midazolam nasal spray), or Diastat (diazepam rectal gel) is prescribed at a dose and frequency that is within FDA approved labeling.
  - a. Valtoco (diazepam nasal spray), Diastat (diazepam rectal gel): do not exceed maximum treatment frequency of 1 episode every 5 days and 5 episodes per month.
  - b. Nayzilam (midazolam nasal spray): do not exceed maximum treatment frequency of 1 episode every 3 days and treatment of 5 episodes in 1 month.

**If the above prior authorization criteria are met, the requested product will be authorized for up to 12 months.**

### Medical Necessity Criteria for Reauthorization

Reauthorization for 12 months will be granted if the member has recent (within the last 3 months) clinical chart documentation demonstrating **ALL** of the following criteria:

1. The requested medication is prescribed by or in consultation with a neurologist; **AND**
2. The member has experienced clinical benefit from Valtoco, Nayzilam, or Diastat (documentation required), demonstrated by:
  - a. A decrease in the frequency or duration of acute repetitive seizure episodes; **OR**
  - b. A reduction in seizure-related hospitalizations; **OR**

- c. Improved quality of life per clinical notes; **AND**
3. Valtoco (diazepam nasal spray), Nayzilam (midazolam nasal spray), or Diastat (diazepam rectal gel) is prescribed at a dose and frequency that is within FDA approved labeling.
  - a. Valtoco (diazepam nasal spray), Diastat (diazepam rectal gel): do not exceed maximum treatment frequency of 1 episode every 5 days and 5 episodes per month.
  - b. Nayzilam (midazolam nasal spray): do not exceed maximum treatment frequency of 1 episode every 3 days and treatment of 5 episodes in 1 month.

#### **Additional Doses for Travel**

The plan will cover up to 2 additional doses of **Valtoco (diazepam nasal spray), Nayzilam (midazolam nasal spray), or Diastat (diazepam rectal gel)** per 365 days for travel purposes.

#### **Additional Doses for School/Work**

The plan will cover up to 2 additional doses of **Valtoco (diazepam nasal spray), Nayzilam (midazolam nasal spray), or Diastat (diazepam rectal gel)** per 365 days to be stored at a school or work location.

#### **Experimental or Investigational / Not Medically Necessary**

Valtoco (diazepam nasal spray), Nayzilam (midazolam nasal spray), or Diastat (diazepam rectal gel) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven.

#### **References**

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#### Clinical Guideline Revision / History Information

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