Pharmacy Policy Bulletin

Title:	Acute Seizure Activity Agents
Policy #:	Rx.01.226

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **midazolam (Nayzilam®) nasal spray and diazepam (Valtoco®) nasal spray** as provided under the member's prescription drug benefit.

Description:

Seizures can result from a shift in the normal balance of excitation and inhibition within the CNS as well as abnormal brain function. Epilepsy is a chronic medical disorder when two or more unprovoked seizures occur that can't be explained by a medical condition. Abnormal, excessive, and hypersynchronous electrical discharge of neurons in the brain can manifest epileptic seizures. Seizure clusters, also known as acute repetitive seizures are frequent seizure activities that are distinct from a patient's usual seizure pattern. Benzodiazepines are used as a rescue medication for seizure clusters in an outpatient setting.

Midazolam (Nayzilam®) nasal spray is a benzodiazepine indicated 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 in patients with epilepsy **12 years of age and older**.

Diazepam (Valtoco®) nasal spray is a benzodiazepine indicated 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 in patients with epilepsy **6 years of age and older**.

The exact mechanism of action for Nayzilam® and Valtoco® is not fully understood, but it is thought to involve potentiation of GABAergic neurotransmission resulting from binding at the benzodiazepine site of the GABAA receptor.

Policy:

INITIAL CRITERIA: Midazolam (Nayzilam®) nasal spray is approved when ALL of the following inclusion criteria are met:

1. Diagnosis 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; AND
2. Member is 12 years of age or older; AND
3. Prescribed by or in consultation with a neurologist/epilepsy specialist

INITIAL CRITERIA: Diazepam (Valtoco®) nasal spray is approved when ALL of the following criteria are met:

1. Diagnosis 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; AND
2. Member is 6 years of age or older; AND

3. Prescribed by or in consultation with a neurologist/epilepsy specialist

Initial Authorization: 2 years

REAUTHORIZATION CRITERIA: Midazolam (Nayzilam®) nasal spray or diazepam (Valtoco®) nasal spray is reapproved when there is documentation of positive clinical response to therapy.

Reauthorization: 2 years

Black Box Warning as shown in the drug Prescribing Information:

Benzodiazepines (Nayzilam®, Valtoco®):

Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing of these drugs for patients for whom alternative treatment options are inadequate. Limit dosages and durations to the minimum required. Follow patients for signs and symptoms of respiratory depression and sedation. The use of benzodiazepines exposes users to risks of abuse, misuse, and addiction, which can lead to overdose or death. Abuse and misuse of benzodiazepines commonly involve concomitant use of other medications, alcohol, and/or illicit substances, which is associated with an increased frequency of serious adverse outcomes. Before prescribing Nayzilam or Valtoco and throughout treatment, assess each patient's risk for abuse, misuse, and addiction. The continued use of benzodiazepines may lead to clinically significant physical dependence. The risks of dependence and withdrawal increase with longer treatment duration and higher daily dose. Although Nayzilam and Valtoco is indicated only for intermittent use if used more frequently than recommended abrupt discontinuation or rapid dosage reduction may precipitate acute withdrawal reactions, which can be life-threatening. For patients using Nayzilam or Valtoco more frequently than recommended, to reduce the risk of withdrawal reactions, use a gradual taper to discontinue.

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Nayzilam® (midazolam nasal spray) [prescribing information]. Smyrna, GA: UCB Inc.; February 2021. Available from: https://www.ucb-usa.com/_up/ucb_usa_com_kopie/documents/Nayzilam_PI.pdf. Accessed April 1, 2021.

Valtoco® (diazepam nasal spray) [prescribing information]. San Diego, CA: Neurelis, Inc.; February 2021. Available from: https://www.valtoco.com/sites/default/files/Prescribing_Information.pdf. Accessed April 1, 2021.

Jafarpour, Saba & Hirsch, Lawrence & Gaínza-Lein, Marina & Kellinghaus, Christoph & Detyniecki, Kamil. (2018). Seizure cluster: Definition, prevalence, consequences, and management. Seizure. 68. 10.1016/j.seizure.2018.05.013.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand name	Generic name
Nayzilam®	Midazolam
Valtoco®	Diazepam

Cross References:

Off-Label Use Rx.01.33
Quantity Level Limits for Pharmaceuticals Covered Under the Prescription Drug Benefit Rx.01.76

P&T Approval Date:	March 18, 2021
Policy Effective Date:	July 01, 2021
Next Required Review Date:	March 18, 2022
