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 (i.e., 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:
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

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

**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. Because of these risks, reserve concomitant prescribing of benzodiazepines and opioids for patients for whom alternative treatment options are inadequate. Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioids alone. If a decision is made to prescribe Nayzilam® or Valtoco® concomitantly with opioids, prescribe the lowest effective dosages and minimum durations of concomitant use, and follow patients closely for signs and symptoms of respiratory depression and sedation. Advise both patients and caregivers about the risks of respiratory depression and sedation when Nayzilam®, Valtoco® is used with opioids.

**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:**


**Applicable Drugs:**

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Generic name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nayzilam®</td>
<td>Midazolam</td>
</tr>
<tr>
<td>Valtoco®</td>
<td>Diazepam</td>
</tr>
</tbody>
</table>

**Cross References:**

Off-Label Use Rx.01.33

Quantity Level Limits for Pharmaceuticals Covered Under the Prescription Drug Benefit Rx.01.76

<table>
<thead>
<tr>
<th>Policy Version Number:</th>
<th>1.00</th>
</tr>
</thead>
<tbody>
<tr>
<td>P&amp;T Approval Date:</td>
<td>April 23, 2020</td>
</tr>
<tr>
<td>Policy Effective Date:</td>
<td>July 01, 2020</td>
</tr>
<tr>
<td>Next Required Review Date:</td>
<td>January 9, 2021</td>
</tr>
</tbody>
</table>

The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does
not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.