Clinical Policy Title:	midazolam
Policy Number:	RxA.668
Drug(s) Applied:	Nayzilam®
Original Policy Date:	03/09/2021
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Nayzilam® 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
midazolam (Nayzilam®)	Acute treatment of intermittent, stereotypic episodes of frequent seizure activity that are distinct from a patient's usual seizure pattern in patients with epilepsy 12 years of age and older	Initial Dose: Instill 1 spray (5 mg dose) into 1 nostril. Second Dose: 1 additional spray (5 mg dose) instilled into the opposite nostril may be administered after 10 minutes if the patient has not responded to the initial dose.	2 sprays per episode Max treatment: 1 episode per 3 days 5 episodes per month

Dosage Forms

- Single-dose nasal spray unit containing 5 mg midazolam per 0.1 mL solution.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Acute, intermittent, repetitive episodes of seizure activity outside of usual pattern of epilepsy (must meet all):

1. Diagnosis of epilepsy;
2. Documentation confirming diagnosis of acute repetitive seizures distinct from a patient's usual seizure pattern;
3. Prescribed by or in consultation with a neurologist;
4. Documentation of at least 1 current prophylactic antiepileptic drug (AED);
5. Member is age 12 years or older;

6. Member does not have acute narrow-angle glaucoma;
7. Dose prescribed does not exceed both of the following (a and b):
   a. 2 sprays per episode;
   b. 10 sprays per month.

Approval Duration
Commercial: 1 month
Medicaid: 1 month

II. Continued Therapy Approval

A. Acute, intermittent, repetitive episodes of seizure activity outside of usual pattern of epilepsy (must meet all):

1. Currently receiving medication that has been authorized by RxAdvance or documentation supports that member is currently receiving Nayzilam® for acute repetitive seizures;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets both of the following (a and b):
   a. 2 sprays per episode;
   b. 10 sprays per month.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
AED: antiepileptic drug

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
diazepam nasal spray (Valtoco®)	Dosage is dependent on the patient's age and weight. Initial Dose: 5 mg and 10 mg doses are administered as a single spray intranasally into 1 nostril. Administration of 15 mg and 20 mg doses requires 2 nasal spray devices, 1 spray into each nostril. Second Dose: When required, may be administered at least 4 hours after the initial dose. If administered, use a new blister pack.	2 sprays per episode Max treatment: 1 episode per 5 days 5 episodes per months

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Hypersensitivity to diazepam.

- Acute narrow-angle glaucoma.

- Boxed Warning(s):
  - Risk from concomitant use with opioids
    - Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death.
  - Abuse, misuse, and addiction
    - The use of benzodiazepines, including Nayzilam®, exposes users to risks of abuse, misuse, and addiction, which can lead to overdose or death. Before prescribing Nayzilam® and throughout treatment, assess each patient's risk for abuse, misuse, and addiction.
  - Dependence and withdrawal reactions
    - Although Nayzilam® is indicated only for intermittent use, if used more frequently than recommended, abrupt discontinuation or rapid dosage reduction of Nayzilam® may precipitate acute withdrawal reactions, which can be life-threatening. For patients using Nayzilam® more frequently than recommended, to reduce the risk of withdrawal reactions, use a gradual taper to discontinue Nayzilam®.

APPENDIX D: General Information
None.

References

1. Nayzilam® (midazolam) [prescribing information]. Plymouth, MN: Proximagen LLC; February 2021.
2. Valtoco® (diazepam intranasal) [prescribing information]. San Diego, CA: Neurelis Inc; February 2021.
3. UCB Biopharma S.P.R.L. A Randomized, Double-blind, Placebo-controlled Study of the Safety and Efficacy of Intranasal Midazolam (USL261) in the Outpatient Treatment of Subjects With Seizure Clusters. ARTEMIS-1: Acute Rescue Therapy in Epilepsy With Midazolam Intranasal Spray-1. Available from: https://clinicaltrials.gov/ct2/show/NCT01390220. NLM identifier: NCT01390220. Accessed February 15, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	03/09/2021	03/09/2021