Nayzilam (midazolam)

NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Nayzilam
- **Generic name:** Midazolam
- **Pharmacological class:** Benzodiazepine
- **Strength and Formulation:** 5mg per 0.1mL; solution
- **Manufacturer:** UCB
- **How supplied:** Nasal spray unit—2
- **Legal Classification:** CIV

Nayzilam


Nayzilam®
(midazolam) nasal spray
5 mg
FOR NASAL USE ONLY
2 Nasal Spray Units
(1 dose per unit)
NDC 50474-500-14
Rx only
PEEL HERE
Nayzilam®
(midazolam) nasal spray 5 mg
FOR NASAL USE ONLY
Each dose contains 5 mg of midazolam in 0.1 mL of nasal spray.
1 spray per unit.
DO NOT test or prime before use.
Do not use if the nasal spray unit appears damaged.
WARNING: Keep out of reach of children.
USUAL DOSAGE: See package insert for dosage information and for full prescribing information.
Store at controlled room temperature 20°C to 25°C (68°F to 77°F), excursions permitted to 15°C to 30°C (59°F to 86°F).
EXP:
1 Dose

Indication

- Acute treatment of intermittent, stereotypic episodes of frequent seizure activity (eg, seizure clusters, acute repetitive seizures) that are distinct from a patient’s usual seizure pattern in those with epilepsy

Dosage and Administration

- Consider **prior to initiation**:
  - For patients at increased risk of respiratory depression from benzodiazepines, administration under healthcare professional supervision should be considered prior to treatment; this administration may be performed in the absence of a seizure episode
  - Instruct individual administering Nayzilam on how to identify seizure clusters and use the product appropriately

Dosage and Administration

- Give as single spray into 1 nostril; if no response after 10 minutes, may give additional spray into opposite nostril; max 2 sprays/episode
- **Max treatment**: 1 episode every 3 days or 5 episodes/month
- <12yrs: not established

Considerations for Special Populations

- **Pregnancy:** observe newborns exposed to Nayzilam *in utero* during later stages of pregnancy for symptoms of withdrawal and manage accordingly
- **Nursing mothers**: breastfed infants of mothers taking benzodiazepines may have effects of lethargy, somnolence, and poor sucking
- **Pediatric**: <12 years: not established
- **Geriatric:** studies did not include sufficient number of patients ≥65 years; possible prolonged drug exposure
- **Renal impairment:** moderate or severe impairment may result in prolonged drug exposure
- **Congestive heart failure:** slower elimination may result in prolonged drug exposure

Contraindications

- **Acute narrow-angle glaucoma**
  - Benzodiazepines can increase intraocular pressure in patients with glaucoma

Boxed Warnings

- Risks from **concomitant use with opioids**
  - Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death

Warnings/Precautions

- Increased risk of drug-related mortality from concomitant use with opioids
- Decreased pulmonary reserve
- COPD
- Monitor for the emergence or worsening of depression, suicidal thoughts/behavior, and/or unusual changes in mood or behavior
- Open-angle glaucoma

Warnings/Precautions

- Impaired cognitive function
- Obesity
- CHF
- Avoid abrupt cessation
- Drug or alcohol abuse
- Hepatic or moderate to severe renal impairment
- Elderly
- Debilitated
- Labor & delivery
- Neonatal withdrawal and floppy infant syndrome

Interactions

- Increased risk of profound sedation, respiratory depression, coma, and death with **opioids or other CNS depressants** (eg, other benzodiazepines, sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, alcohol); reserve concomitant use in those for whom alternative options are inadequate; limit dosages/durations to minimum required; monitor
- Avoid concomitant with **moderate/strong CYP3A4 inhibitors** (eg, erythromycin, diltiazem, verapamil, ketoconazole, itraconazole, clarithromycin)
- Caution with concomitant **mild CYP3A inhibitors**

Adverse Reactions

- **Most common (≥5%)**:somnolence, headache, nasal discomfort, throat irritation, rhinorrhea
- **Others:** severe cardiorespiratory reactions, agitation, involuntary movements (including tonic/clonic movements and muscle tremor), hyperactivity, combativeness

Mechanism of Action

- The exact mechanism of action for midazolam is not fully understood, but it is thought to involve potentiation of GABAergic neurotransmission resulting from binding at the benzodiazepine site of the $GABA_A$ receptor

Clinical Trials

- Effectiveness established in randomized, double-blind, placebo-controlled trial
- Patients with epilepsy on a stable regimen of antiepileptic drugs who were identified by their physicians as having intermittent, stereotypic episodes of frequent seizure activity that were distinct from patient's usual seizure pattern
- Conducted in 2 phases: open-label Test Dose Phase followed by randomized, double-blind, placebo-controlled Comparative Phase

Clinical Trials

- **Test Dose Phase**
  - Tolerability assessed in 292 patients who, in the absence of a seizure, received two 5mg doses of Nayzilam (10mg total dosage) separated by 10 minutes
  - Patients excluded from Comparative Phase if they failed to meet pre-defined blood pressure, heart rate, sedation, electrocardiogram, and peripheral oxygen saturation criteria

Clinical Trials

- **Comparative Phase**
  - 201 patients treated a single seizure cluster episode in an outpatient setting with either a blinded dose of Nayzilam 5mg (n=134) or placebo (n=67)
  - If seizure activity persisted or recurred, patients in both groups had the option to receive a subsequent unblinded dose of Nayzilam 5mg to be used between 10 minutes and 6 hours after administration of the initial blinded dose of study drug

Clinical Trials

- **Primary efficacy end point** was treatment success, defined as the termination of seizures within 10 minutes after the initial blinded dose of study drug and the absence of a recurrence of seizures within 6 hours of the initial blinded dose of study drug
- A statistically significantly higher percentage of Nayzilam-treated patients met the primary end point
  - 53.7% of Nayzilam-treated patients vs 34.3% of placebo-treated patients (*P* =.011)

Clinical Trials

- Numerical differences in favor of Nayzilam were observed on each of the components of the treatment success responder definition; termination of seizure(s) within 10 minutes after initial dose of study drug (80.6% vs 70.1%) and the absence of seizure recurrence between 10 minutes and 6 hours after the initial dose of study drug (58.2% vs 37.3%)

Clinical Trials

- Occurrence and time to next seizure after the initial blinded dose of study drug was also evaluated
- A smaller proportion of Nayzilam-treated patients experienced the next seizure within 24 hours after the initial blinded dose of study drug (37.3% vs 46.3%)
- Nayzilam-treated patients experienced a statistically longer time-to-next-seizure than the placebo group

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/nayzilam/