

PRIOR AUTHORIZATION POLICY

POLICY: Antiepileptics – Valtoco® (diazepam nasal spray – Neurelis)

DATE REVIEWED: 02/05/2020

OVERVIEW

Valtoco, a benzodiazepine, is 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.¹ The exact mechanism of action is not fully understood, but it is thought to involve potentiation of gamma-aminobutyric acid (GABA)ergic neurotransmission resulting from binding at the benzodiazepine site of the GABA_A receptor. The maximum plasma diazepam concentrations after nasal administration of Valtoco is reached in approximately 1.5 hours, and the mean elimination half-life of diazepam is about 49.2 hours. The recommended dose is 0.2 mg/kg or 0.3 mg/kg, depending on the patient's age and weight. Recommended doses are 5 mg, 10 mg, 15 mg, and 20 mg. The 5 mg and 10 mg doses are administered as one spray in one nostril, and the 15 mg (using two 7.5 mg devices) and 20 mg (using two 10 mg devices) doses are administered as one spray in each nostril. A second dose, when required, may be administered ≥ 4 hours after the initial dose. Do not use more than two doses of Valtoco to treat a single episode. It is recommended that Valtoco be used to treat no more than one episode every five days and no more than five episodes per month. Valtoco is available in 5 mg, 7.5 mg, and 10 mg strengths; each nasal spray device contains 0.1 mL solution. Valtoco is a ready-to-use nasal spray device. Valtoco nasal spray delivers its entire contents upon activation. Do not prime or attempt to use for more than one administration per device.

Disease Overview

Patients with epilepsy can experience acute repetitive seizures or seizure clusters.² Patients with severe and/or poorly controlled epilepsy are more likely to experience seizure clusters. No consensus definition of a seizure cluster has been agreed upon, and seizure cluster is not listed in the International League Against Epilepsy commission on classification and terminology. A broad definition of seizure clusters has been proposed to be "acute episodes of deterioration in seizure control". More specifically, they could be defined as a series of grouped seizures that have short interictal periods. However, the number of seizures and the interictal period are the subject of controversy. Seizure clusters can result in increased emergency room visits or hospitalization, and they can disrupt the daily life, studies, and work of patients and caregivers. They are particularly concerning because of their association with status epilepticus, a potentially life-threatening condition. Benzodiazepine rescue medication is the primary acute therapy for management of seizure clusters, helping to abort clusters and reduce emergency department visits.

The prevalence of epilepsy in the US is approximately 3.4 million people, and of these patients, an estimated 36% of patients have uncontrolled disease, a significant risk factor for seizure clusters.^{3,4} Seizure clusters are estimated to occur in approximately 15% of adults with uncontrolled epilepsy.⁵ Based on this information, it has been estimated that more than 150,000 people in the US with uncontrolled epilepsy also experience seizure clusters.⁶

Safety

Valtoco is contraindicated in patients with acute narrow angle glaucoma or with known hypersensitivity to diazepam.¹ Similar to other benzodiazepines, Valtoco has a Boxed Warning with regard to the risk of concomitant use with opioids. Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death. Of note, Valtoco is not approved for use in neonates or infants because it contains the preservative benzyl alcohol. Serious and fatal adverse reactions including “gasping syndrome” can occur in neonates and low birth weight infants treated with benzyl alcohol-preserved drugs, including Valtoco.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Valtoco. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Valtoco is recommended in those who meet the following criteria:

FDA-Approved Indications

- 1. Intermittent Episodes of Frequent Seizure Activity (i.e., seizure clusters, acute repetitive seizures).** Approve for 1 year if the patient meets the following criteria (A and B):
 - A)** Patient is currently receiving maintenance antiepileptic medication(s); AND
 - B)** Valtoco is prescribed by or in consultation with a neurologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Valtoco has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

- 1.** Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Valtoco[®] nasal spray [prescribing information]. San Diego, CA: Neurelis, Inc.; January 2020.
 2. Jafarpour S, Hirsch LJ, Gaínza-Lein M, et al. Seizure cluster: Definition, prevalence, consequences, and management. *Seizure*. 2019;68:9-15.
 3. Zack M, Kobau R. National and state estimates of the numbers of adults and children with active epilepsy - United States, 2015. *MMWR Morb Mortal Wkly Rep*. 2017;66(31):821-825. Available at: <https://www.cdc.gov/mmwr/volumes/66/wr/mm6631a1.htm>. Accessed on January 29, 2020.
 4. Chen B, Choi H, Hirsch LJ, et al. Prevalence and risk factors of seizure clusters in adult patients with epilepsy. *Epilepsy Res*. 2017;133:98-102.
 5. Chen Z, Brodie MJ, Liew D, et al. Treatment outcomes in patients with newly diagnosed epilepsy treated with established and new antiepileptic drugs: a 30-year longitudinal cohort study. *JAMA Neurol*. 2018;75(3):279-286.
 6. Data on file. Clinical and economic evidence supporting formulary consideration of Nayzilam[®] CIV (Midazolam Nasal Spray) for seizure clusters. UCB, Inc.; June 24, 2019.
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