MONTHLY MINUTES

VALTOCO (Diazepam Nasal Spray) for Seizure Rescue Therapy

1. What is VALTOCO used for?

- VALTOCO 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 people with epilepsy 6 years of age and older.
- VALTOCO is the only nasal rescue medication approved for seizure clusters in adults and children ages 6 years and older.
- VALTOCO allows for individualized patient treatment with 5 mg, 10 mg, 15 mg and 20 mg doses based on age and weight.

2. Seizure clusters explained

- Seizure clusters or acute repetitive seizures are described as an increase in seizure frequency (≥ 2 within 24 hours) in patients with epilepsy who are typically on a maintenance anti-seizure medication.
- These types of seizure emergencies can be severe and life-threatening and can progress to prolonged seizures or status epilepticus if not adequately treated.
- When treating seizure cluster emergencies, the primary goals are to stop the initial seizure and prevent recurrence of seizure activity over a 24-hour period. Hence, seizure cluster rescue treatment is most effective when administered early.

3. Key clinical benefits of VALTOCO

- VALTOCO has been deemed by the FDA to be clinically superior to Diastat® rectal gel by providing a significantly improved ease of use.
- VALTOCO provides 97% absolute bioavailability relative to IV diazepam with consistent and reliable blood levels throughout the day.
- VALTOCO's pharmacokinetics were 2- to 4-fold less variable than Diastat.
- VALTOCO can be administered to actively seizing patients during cluster, with no active participation required from the patient.
- In a survey of patients (64) and care partners (84) who utilized VALTOCO:
  - The majority of both patients (88%) and care partners (88%) responded that they would prefer to exclusively use diazepam nasal spray versus rectal diazepam.
  - 59% of patients returned to their usual selves within 60 minutes of administration.

4. How to administer VALTOCO

Remove VALTOCO from the blister pack.

HOLD VALTOCO with your thumb on the bottom of the plunger and your first and middle fingers on either side of the nozzle.

DO NOT test or prime; each device sprays only one time.

INSERT the tip of the nozzle into 1 nostril until your fingers, on either side of the nozzle, are against the bottom of the person's nose.

For nasal use only.

PRESS the bottom of the plunger firmly with your thumb to give VALTOCO.

Throw away nasal spray device(s) after use.

If giving the **15 mg or 20 mg dose**, repeat the steps using the second device **in the other nostril** to give the full dose of VALTOCO.

Remember: If needed, a second dose may be given at least 4 hours after initial dose. Patients should not use more than 2 doses of VALTOCO to treat a single episode.[1] These are not the full Instructions for Use. Please see the complete Instructions for Use at VALTOCOHCP.com.

5. How to store VALTOCO

Store at room temperature between 68°F and 77°F (20°C to 25°C). Do not freeze. Protect from light.

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VALTOCO (Diazepam Nasal Spray) for Seizure Rescue Therapy, Continued

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6. Frequently asked questions

How frequently can VALTOCO be dosed?

It's recommended that VALTOCO be used to treat no more than 1 episode every 5 days and no more than 5 episodes per month.

If needed, a second dose may be given at least 4 hours after initial dose. Patients should not use more than 2 doses of VALTOCO to treat a single episode.

Does VALTOCO need to be primed?

No. Patients or their care partners SHOULD NOT test or prime VALTOCO. Each device sprays only one time.

Can patients carry VALTOCO with them?

Yes. With the small, portable, and discreet packaging of VALTOCO, patients can carry it with them in their backpack or purse—whenever, wherever. It does not need to be refrigerated and is designed for prompt administration by anyone.

7. Important safety information

WARNING: RISKS FROM CONCOMITANT USE WITH OPIOIDS; ABUSE, MISUSE, AND ADDICTION; and DEPENDENCE AND WITHDRAWAL REACTIONS

- Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death.
- The use of benzodiazepines, including VALTOCO, exposes users to risks of abuse, misuse, and addiction, which can lead to overdose or death.
- The continued use of benzodiazepines may lead to clinically significant physical dependence. Although VALTOCO is indicated only for intermittent use, if used more frequently than recommended, abrupt discontinuation or rapid dosage reduction of VALTOCO may precipitate acute withdrawal reactions, which can be life-threatening.

8. Adverse reactions

The most common adverse reactions (at least 4%) were somnolence, headache, and nasal discomfort.

Diazepam, the active ingredient in VALTOCO, is a Schedule IV controlled substance.

To report SUSPECTED ADVERSE REACTIONS, contact Neurelis, Inc. at 1-866-696-3873 or FDA at 1-800-FDA-1088 (www.fda.gov/medwatch).