Nayzilam® (midazolam) – New orphan drug approval

- On May 20, 2019, UCB announced the FDA approval of Nayzilam (midazolam), for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (ie, 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.
    - Nayzilam is a Schedule IV controlled substance.
- It is estimated that more than 150,000 people in the U.S. with uncontrolled epilepsy also experience seizure clusters. Rescue treatment of seizure clusters is critical because when left untreated, seizure clusters can increase the risk of physical injury, neurological damage, prolonged seizures, and status epilepticus.
- Midazolam, a benzodiazepine, is also available generically as an injection and oral syrup.
    - Injectable midazolam is indicated for preoperative sedation/anxiolysis/amnesia; sedation/anxiolysis/amnesia prior to or during diagnostic, therapeutic or endoscopic procedures; induction of general anesthesia; and sedation of intubated and mechanically ventilated patients.
    - Midazolam oral syrup is indicated for pediatric patients for sedation/anxiolysis/amnesia prior to diagnostic, therapeutic or endoscopic procedures or before induction of anesthesia.
- The efficacy of Nayzilam was established in a study of 201 patients 12 years of age and older with epilepsy. Patients treated a single seizure cluster episode with either a dose of Nayzilam or placebo. If the seizure activity persisted or recurred, patients in both groups had the option to receive a subsequent unblinded dose of Nayzilam to be used between 10 minutes and 6 hours after administration of the initial blinded dose of study drug. The primary efficacy endpoint 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.
    - Treatment success was achieved in 53.7% (95% CI: 45.3, 62.2) and 34.3% (95% CI: 23.0, 45.7) of patients receiving Nayzilam and placebo, respectively (p = 0.011).
- Nayzilam carries a boxed warning for risks from concomitant use with opioids.
- Nayzilam is contraindicated in patients with known hypersensitivity to midazolam and patients with acute narrow-angle glaucoma.
- Additional warnings and precautions for Nayzilam use include risks of cardiorespiratory adverse reactions; central nervous system (CNS) depression from concomitant use with other CNS depressants, or moderate or strong CYP3A4 inhibitors; suicidal behavior and ideation; impaired cognitive function; glaucoma; and other adverse reactions (when midazolam is used for sedation, reactions such as agitation, involuntary movements, hyperactivity, and combativeness have been reported).
- The most common adverse reactions (≥ 5%) with Nayzilam use were somnolence, headache, nasal discomfort, throat irritation, and rhinorrhea.

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- The recommended initial dosage of Nayzilam is one spray (5 mg dose) into one nostril. One additional spray (5 mg dose) into the opposite nostril may be administered after 10 minutes if the patient has not responded to the initial dose.
    - A second dose of Nayzilam should not be administered if the patient has trouble breathing or if there is excessive sedation that is uncharacteristic of the patient during a seizure cluster episode.
    - The maximum dosage of Nayzilam is two doses to treat a seizure cluster. It is recommended that Nayzilam be used to treat no more than one episode every three days and treat no more than five episodes per month.
- UCB's launch plans for Nayzilam are pending. Nayzilam will be available as a single-dose nasal spray unit containing 5 mg of midazolam in 0.1 mL solution.