Safety and Tolerability of NRL-1, an Intransaminal Formulation of Diazepam, in Relationship to Usage Frequency With Subjects With Epilepsy: Results From a Phase 3, Open-label, Repeat Dose Study

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Diazepam nasal spray is a potential treatment option for subjects with epilepsy with reduced seizure frequency and tolerability for patients, with an increased incidence of TEAEs noted primarily in frequent users. The safety and tolerability with the nasal route was favorably matched with a low incidence of nasal irritation or olfactory complications. Identifying medical safety trends would be expected for diazepam nasal sprays.

Conclusion/Nursing Implications

Diazepam nasal spray provides a rapid, noninvasive route of rescue medication for seizure frequency effects on clinical or laboratory parameters. One hundred thirty-two patients on stable regimens had been enrolled in a clinical trial for three months. The 2274 seizure episodes treated with diazepam nasal sprays led to >2 doses/month in 95% patients. The noninvasive route of administering diazepam nasal spray had fewer adverse events, though there was an increased incidence of TEAEs noted primarily in frequent users. The safety and tolerability with the nasal route was favorably matched with a low incidence of nasal irritation or olfactory complications. Identifying medical safety trends would be expected for diazepam nasal sprays.

All patients or their legal representatives provided written informed consent.

A history of a clinically significant medical condition that would jeopardize the patient's ability to provide informed consent

- An intercurrent illness with clear alteration of awareness

Diazepam nasal spray was stored at 5, 10, 15, or 20 mg (weight-based), with a second dose administered, if needed, within 12 hours. Investigators could adjust the dose for safety.

This phase 3, repeat-dose, open-label study evaluated the safety of diazepam nasal spray (NRL-1, Valtoco®) in children and adults with epilepsy. A total of 132 patients were enrolled, administered diazepam nasal spray, and were included in the safety analysis with a mean follow-up of 18.6 months (Table 1).

- Patients were mostly female (53.3%), white (62.6%), and aged >65 years (47.7%).

- Among these patients, 2274 seizure episodes were treated with diazepam nasal sprays, 191 of which required a second dose.

- Overall, 91 patients (68.9%) had TEAEs (Table 1).

- The most common TEAEs were generally similar to the moderate and frequent use subgroups.

- The reports of nasal irritation were mild (maximum grade 1B, superficial mucosal erosion), and had a slightly greater incidence that was numerically higher in frequent users.

- The small tests showed minimal olfactory changes that did not appear to be related to usage frequency effects on clinical or laboratory parameters.

- The incidence of TEAEs was numerically higher with frequent use in comparison with less frequent use.

- The most common TEAEs generally had a numerically higher incidence among frequent users relative to moderate users (Table 2).

- There were relatively few treatment-related TEAEs overall, these events were transient, and the most common had an incidence that was numerically higher in frequent users relative to moderate users.

- No clinically relevant trends were observed for usage frequency effects on clinical or laboratory parameters.

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