The Usability of Diazepam Buccal Film as an Oral Rescue Treatment in Adult Patients with Epilepsy


Aquestive Therapeutics Inc, Warren, NJ, USA; Clinical and Medical Affairs, Cognex, "Safety Monitoring Unit, Results from an American Registry for Epilepsy Care Centers Dataset," Greenwich, CT, USA; Department of Medicine, Neurology, University of Alabama at Birmingham School of Medicine, Huntsville, AL, USA; Aquestive Epilepsy Care Centers, Austin, TX, USA;

*Multisite epilepsy and sleep centers, Bethesda, MD, USA; Department of Neurology, University of Pennsylvania, Philadelphia, PA, USA; Departments of Neurology and Pharmacology, School of Medicine, University of California, Davis, Sacramento, CA, USA; Pharrma Study Design LLC, Woodbridge, CT, USA.

ABSTRACTS

The Usability of Diazepam Buccal Film as an Oral Rescue Treatment in Adult Patients with Epilepsy

BACKGROUND

Seizure clusters, also termed acute repetitive seizures, commonly occur in patients with drug refractory epilepsy. Benzodiazepines such as diazepam are the mainstay of rescue therapy for seizure clusters. Diazepam buccal film (DBF, formerly DBEP) is a novel dosing form of diazepam under development as an alternative approach for the management of seizure clusters. The intended target population is selected patients with refractory epilepsy who require intermittent use of diazepam to control episodes of increased seizure activity. The purpose was to be the first orally administered treatment for this indication and would provide an alternative to rectal diazepam gel. DBF is administered by placing the film against the inner aspect of the cheek, where it adheres, dissolves, and releases drug onto the buccal mucosa. This phase 2 study assessed the safety, pharmacokinetics, and usability of DBF in adult patients with epilepsy under interictal (Treatment A) and ictal/perispiral (Treatment B) conditions.

OBJECTIVE

• To assess the usability of DBF in adult patients with epilepsy under interictal conditions (Treatment A) and ictal/perispiral conditions (Treatment B) conditions

METHODS

STUDY SUBJECTS

• Adult men and women ages 17-65 years with poorly controlled tonic-clonic seizures or focal seizures with impaired awareness
• Subjects had on average ≥1 seizure every 3 days or ≥10 seizures/month
• The subjects were receiving at least one antiseizure drug
• Baseline medications were adjusted according to clinical judgement
• Eligibility was established at a screening visit within 28 days of the first study drug administration

STUDY DESIGN

• This was a single-dose crossover study in which subjects were investigated while undergoing a clinical epilepsy monitoring unit (EMU) evaluation (Treatment B) and on an interictal-only visit (Treatment A), with the visits separated by in most cases 2 weeks (but not <14 days)
• Treatment A and Treatment B could occur in either order

STUDY PROCEDURES

• DBF was administered by placing the film against the inner aspect of the cheek, where it adhered, dissolved and released drug onto the buccal mucosa

STUDY OUTCOMES

• Usability endpoints for investigator placement of DBF included:
  1. Whether successful placement was achieved
  2. Whether more than one attempt was needed to successfully insert the film
  3. Whether the subject spit or blew out the film

• Usability endpoints for patient investigator placement of DBF included:

  1. Whether successful placement was achieved
  2. Whether more than one attempt was needed to successfully insert the film
  3. Whether the subject spat or blew out the film

• Usability endpoints for investigator placement of DBF included:

  1. Whether successful placement was achieved
  2. Whether more than one attempt was needed to successfully insert the film
  3. Whether the subject spit or blew out the film

• Usability outcomes:

  Results from usability endpoints for investigator placement of DBF are summarized in Table 2

SAFETY AND TOLERABILITY

• Subjects were monitored for adverse events (AE) throughout the study

RESULTS

SUBJECTS

• A total of 35 subjects received at least one dose of DBF and are included in the safety population. The demographic characteristics of these subjects are summarized in Table 1

PROCEDURES

• DBF was administered during a clinically indicated event
• Successful placement of film, n (%) 33 (100%) 33 (100%)
• Swallowed film, n (%) 2 (6.1%) 1 (3.0%)
• Spat or blew out film, n (%) 0 1 (3.0%)
• Declined to use film, n (%) 0 1 (2.9%)

SAFETY AND TOLERABILITY

• Majority of treatment-emergent adverse events (TEAEs) were classified as probably related to study drug and no patient withdrew because of an AE

CONCLUSIONS

• DBF is safe and well tolerated
• In the EMU setting, DBF was successfully placed and generally used without difficulty in both interictal and ictal/perispiral states
• There was 1 event of angina pectoris considered unrelated to study drug and 1 event of tachycardia considered unlikely to be related to study drug

ACKNOWLEDGEMENTS

Support in preparing this paper was provided by Nate Connors, PhD, and Abhijit Khan, PhD, of ACCESS Medical, LLC, and funded by Aquestive Therapeutics.

FUNDING AND DISCLOSURES

Financial support for this study was provided by Aquestive Therapeutics. All authors contributed to the development of the poster and maintained control over the final content.

Allen H. Heller and Michael A. Rogawski are consultants to Aquestive Therapeutics. Cassie Jung, Stephen Wargacki, and Rikin Mehta are employees of Aquestive Therapeutics.

REFERENCE