SYSTEMATIC REVIEW FINDS INTRANASAL MIDAZOLAM COMPARABLE TO INTRAVENOUS OR RECTAL ADMINISTRATION OF DIAZEPAM FOR TREATMENT OF ACUTE SEIZURE EMERGENCIES IN PEDIATRIC PATIENTS

Findings Presented at 42nd Annual Child Neurology Society Meeting

MAPLE GROVE, MN - November 1, 2013 – A new systematic review found that when compared with intravenous or rectally administered diazepam, intranasal midazolam was equally effective and demonstrated comparable safety for the treatment of acute seizure emergencies in pediatric patients. Findings from the systematic review were presented at the 42nd Annual Child Neurology Society meeting in Austin, Texas, October 30 – November 2, 2013. The systematic review was supported by Upsher-Smith Laboratories, Inc. (Upsher-Smith).

Benzodiazepines are considered effective rescue therapies for seizure emergencies, and although rectal diazepam gel is approved by the U.S. Food and Drug Administration (FDA), some children may prefer an alternative form of administration. The systematic review of published literature suggests that intranasal midazolam may offer a convenient and socially acceptable alternative for children.

“Seizure emergencies, such as repetitive seizures or seizure clusters, typically require immediate action by a caregiver and often involve administering a rescue treatment,” said Jack Pellock, M.D., study author, Chairman, Division of Child Neurology, Virginia Commonwealth University. “Unfortunately, rescue treatment options for seizure clusters are very limited - the only FDA approved option is rectal diazepam, and this treatment may not be desirable for all age groups. Currently, there are other products in development, such as intranasal midazolam, which may address this unmet need for a non-invasive rescue therapy.”

The systematic review included the published results of randomized, prospective, active-comparator controlled, efficacy studies of intranasal midazolam studies in the treatment of acute seizure emergencies in pediatric patients. Seven identified studies evaluated intranasal midazolam in approximately 200 pediatric patients. All of the studies compared intranasal midazolam to diazepam delivered either intravenously (n=4) or by rectal administration (n=3). Intranasal administration was achieved by spraying (n=2) or dripping (n=5) midazolam intravenous solution into the nose. All studies demonstrated intranasal midazolam (0.2 mg/kg) was as effective as intravenous or rectal diazepam (0.2 – 0.5 mg/kg) in treating seizure emergencies with a rapid (<5 min) onset of action. Additionally, intranasal
midazolam and intravenous or rectal diazepam demonstrated similar safety profiles, with few reports of respiratory depression across all treatments.

About Epilepsy

Epilepsy is a medical condition that causes seizures affecting a variety of cognitive and physical functions. More than two million people in the U.S. are estimated to be affected by epilepsy with about 200,000 new cases of epilepsy diagnosed each year.1

About Seizure Clusters

Seizure clusters, also referred to as acute repetitive seizures or intermittent bouts of increased seizure activity, are multiple seizures which occur over a relatively brief period of time with a pattern distinguishable from the usual seizure pattern.2 Typically, there is recovery between seizures.3

Reports of seizure cluster prevalence vary, but it has been estimated that approximately 22% of the intractable epilepsy population (approximately 152,000 people) experience them.4,5,6,7

Inadequate treatment of seizure clusters may potentially impact the safety of an epilepsy patient, may result in emergency room visits, and/or may evolve into status epilepticus, a potentially life-threatening condition.8,9,10 Benzodiazepines are the treatment of choice for management of acute seizures.2 Prehospital treatment with benzodiazepines has been shown to reduce seizure activity significantly compared with seizures that remain untreated until the patient reaches the emergency department; however, currently available options are underused.2,11,12 It is important to treat seizure emergencies early for many reasons, including findings that patients treated within 30 minutes of seizure onset are more responsive to first-line treatment.13

Market research has shown that patients and caregivers would prefer a rescue medication for seizure clusters that could be administered in any setting and that provides effective and rapid seizure termination in an easy-to-use, non-invasive form of administration.14 Physicians, much like patients and caregivers, have expressed interest in a non-invasive rescue therapy for use outside of the hospital.15

Upsher-Smith’s Epilepsy Pipeline

Upsher-Smith’s clinical development pipeline includes three investigational drugs that are being studied for the management of seizure disorders. USL255 is an investigational once-daily, extended-release topiramate for the management of epilepsy. The pipeline also includes USL261, an investigational intranasal midazolam for the rescue treatment of seizures in patients who require control of intermittent bouts of increased seizure activity, often called seizure clusters, which is the subject of an ongoing international Phase 3 clinical trial (ARTEMIS1) with an open-label safety extension study. In addition, USL260 (tonabersat) is in early clinical development as a potential first-in-class neuronal gap junction modulator.

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About Upsher-Smith

Upsher-Smith, founded in 1919, is an independent and privately-owned specialty pharmaceutical company headquartered in Maple Grove, Minnesota that focuses on product growth and innovation for branded and generic pharmaceuticals. Upsher-Smith has a particular focus on providing therapies to assist people suffering from central nervous system diseases, and also markets products relating to cardiology, dermatology and women's health. For more information, visit www.upsher-smith.com.

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References