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Three-Year Data From Sabril® (vigabatrin) Registry Presented at American Epilepsy Society Annual Meeting

San Diego, Calif., Dec. 3, 2012 – Three-year vision data from Lundbeck's Sabril (vigabatrin) patient registry were presented as a late-breaking poster presentation at the annual meeting of the American Epilepsy Society (AES). The data set includes 4,292 patients enrolled as of August 22, 2012.[1] The U.S. Food and Drug Administration (FDA) requires a Risk Evaluation and Mitigation Strategy (REMS) because of the risk of Sabril-induced permanent vision loss, and includes an ongoing patient registry.

Sabril is indicated as adjunctive therapy for adult patients with refractory complex partial seizures (CPS) who have inadequately responded to several alternative treatments and for whom the potential benefits outweigh the risk of vision loss. Sabril is not indicated as a first-line agent for complex partial seizures.[2] Sabril is indicated as monotherapy for pediatric patients 1 month to 2 years of age with infantile spasms (IS) for whom the potential benefits outweigh the potential risk of vision loss.[3]

Of the total patients enrolled in the registry, 2,676 had IS and 1,354 had refractory CPS.[1] Because of the nature of the registry and vision testing variability, particularly among IS patients, a clear comparison cannot be drawn between registry data and clinical trial results.[1]

"Continued analyses of this data allow us to further our knowledge of Sabril, its potential benefits and the risk of permanent vision loss," said Robert C. Sergott, MD, lead author of the poster, director of neuro-ophthalmology at the Wills Eye Institute, and professor of ophthalmology, neurology and neurosurgery at Thomas Jefferson University Medical College. Dr. Sergott is also one of two expert neuro-opthalmologists who are part of the Sabril registry steering committee and who reviewed detailed vision test findings for technical adequacy and clinical significance. He added, "This registry data sheds light on Sabril use since it became available in the U.S. in 2009, including the number of patients who have received the therapy. It also reports why patients have discontinued Sabril use for reasons including completion of therapy, physician or patient choice, or vision loss clarified as a visual field defect."

A data subset of 718 patients with 1,125 sets of cumulative detailed vision results reviewed by the neuro-ophthalmologists were also included in the poster presentation.[1] This subset included all patients who voluntarily submitted vision results for expert analysis.

"Refractory complex partial seizures and infantile spasms present patients, their caregivers and physicians with numerous challenges, and considerations about potential adverse events associated with a particular medicine are just as important as a therapy's potential benefits," said John M. Pellock, MD, an author on the poster presentation and chairman of the Division of Child Neurology and professor of neurology, pediatrics and pharmacy and pharmaceutics at Virginia Commonwealth University. "This prospective, longitudinal Sabril data provide physicians with more information as they work with their patients to make informed choices."

About the Presentation

This study was presented at AES on Saturday, Dec. 1, 11:45 a.m. – 1:45 p.m., during Poster Session 1 at the San Diego Convention Center in Hall B, Ground Level.

About the Sabril Registry

All patients using Sabril are enrolled in a registry. The registry collects prescriber specialty, patient demographics, diagnosis, prior and concurrent anti-seizure medications, periodic ophthalmologic assessment data (i.e., the results of mandatory monitoring every three months), and the proportion of patients receiving Sabril for rCPS and IS who respond/do not respond to Sabril during the treatment initiation phase.

About Infantile Spasms
Infantile spasms is a difficult-to-treat epilepsy syndrome that usually strikes infants between four to eight months old.[4] Infants suffer spasms that typically last for one to five seconds[5] and occur in clusters of up to 100 spasms at a time.[4] An estimated 8,500 infants in the U.S. have been diagnosed with IS,[6] and each year approximately 2,500 new cases of IS are reported in the U.S. Sabril may not be appropriate for use in all patients with IS.

About Complex Partial Seizures
There are more than two million Americans (AP) affected by epilepsy,[7] and approximately 35 percent have CPS,[8] the single largest seizure type, which originates from a single region of the brain and can cause impaired consciousness.[8] Despite the availability of many antiepileptic treatment options, approximately 30 to 36 percent of adults with CPS continue to have seizures.[9,10,11]

About Sabril® (vigabatrin)[2,3]
Sabril is an oral antiepileptic drug developed in the United States by Lundbeck. Sabril is available in two formulations — in 500-mg tablets for use as add-on therapy for adults with refractory CPS and in 500-mg packets of powder for oral solution for infants with IS.

Indication
SABRIL is indicated as adjunctive therapy for adult patients with refractory complex partial seizures (CPS) who have inadequately responded to several alternative treatments and for whom the potential benefits outweigh the risk of vision loss. SABRIL is not indicated as a first line agent for complex partial seizures.

SABRIL is indicated as monotherapy for pediatric patients 1 month to 2 years of age with infantile spasms (IS) for whom the potential benefits outweigh the potential risk of vision loss.

Important Safety Information

WARNING: VISION LOSS
See full Prescribing Information for complete boxed warning

- SABRIL causes progressive and permanent bilateral concentric visual field constriction in a high percentage of patients. In some cases, SABRIL may also reduce visual acuity.
- Risk increases with total dose and duration of use, but no exposure to SABRIL is known that is free of risk of vision loss
- Risk of new and worsening vision loss continues as long as SABRIL is used, and possibly after discontinuing SABRIL
- Unless a patient is formally exempted, periodic vision assessment is required for patients on SABRIL. However, this assessment cannot always prevent vision damage
- Because of the risk of permanent vision loss, SABRIL is available only through a special restricted distribution program

SABRIL causes permanent vision loss in infants, children, and adults. Because assessing vision loss is difficult in children, the frequency and extent of vision loss in infants and children is poorly characterized.

In adults, SABRIL causes permanent bilateral concentric visual field constriction in 30% or more of patients that ranges in severity from mild to severe, including tunnel vision to within 10° of visual fixation, and can result in disability. In some cases, SABRIL also can damage the central retina and may decrease visual acuity. The onset of vision loss from SABRIL is unpredictable and can occur within weeks of starting treatment or sooner, or at any time during treatment, even after months or years. The lowest dose and shortest exposure to SABRIL should be used that is consistent with clinical objectives.

Because of the risk of permanent vision loss, SABRIL should be withdrawn from patients with IS who fail to show substantial clinical benefit within 2 to 4 weeks of initiation, or sooner if treatment failure becomes obvious, or adult patients treated for refractory CPS as adjunctive therapy who fail to show substantial clinical benefit within 3 months of initiation, or sooner if treatment failure becomes obvious. Patient response to and continued need for SABRIL should be periodically reassessed.

Unless a patient is formally exempted from periodic ophthalmologic assessment as documented in the SHARE program, vision assessment is required at baseline (no later than 4 weeks after starting SABRIL), at least every 3 months while on therapy and about 3-6 months after the discontinuation of SABRIL therapy. Once detected, vision loss is not reversible. It is expected that, even with frequent monitoring, some patients will develop severe vision loss. Drug discontinuation should be considered, balancing benefit and risk, if visual loss is documented.

Symptoms of vision loss from SABRIL are unlikely to be recognized by the patient, parent or caregiver before vision loss is severe. Vision loss of milder severity, although unrecognized by the patient, parent or caregiver may still adversely affect function. The possibility that vision loss from SABRIL may be more common, more severe, or have more severe functional consequences in infants and children than in adults, cannot be excluded.

SABRIL should not be used in patients with, or at high risk of, other types of irreversible vision loss or with other drugs associated with serious adverse ophthalmic effects such as retinopathy or glaucoma unless the benefits clearly outweigh the risks. The interaction of other types of irreversible vision damage with vision damage from SABRIL has not been well characterized, but is likely adverse.

In adult patients treated for CPS, dose adjustment is necessary in patients with renal impairment.

Abnormal MRI signal changes have been observed in some infants treated for IS with SABRIL. These changes generally resolved with discontinuation of treatment and in a few patients the lesion resolved despite continued use.

Antiepileptic drugs (AEDs), including SABRIL, increase the risk of suicidal thoughts or behavior. Adult patients should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior and/or any unusual changes in mood or behavior.

As with all AEDs, SABRIL should be discontinued gradually to avoid withdrawal seizures.

Vigabatrin is excreted in human milk and may cause serious adverse events in nursing infants. SABRIL should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus. ***Pregnancy Registry***: To provide information regarding the effects of in utero exposure to SABRIL, physicians are advised to recommend that pregnant patients taking SABRIL enroll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry. This can be done by calling the toll-free number 1-888-233-2334, and must be done by patients themselves. Information on the registry can also be found at the website http://www.aedpregnancyregistry.org/.

SABRIL has been shown to cause neurotoxicity, anemia, somnolence and fatigue, peripheral neuropathy, weight gain and edema. The most commonly observed adverse reactions reported in 2 add-on clinical studies of adults with refractory CPS treated with SABRIL as adjunctive therapy with the recommended dose of 3 g/day (≥10% and at least 5% greater than placebo, respectively) were dizziness (24% vs 17%), fatigue (23% vs 16%), somnolence (22% vs 13%), tremor (15% vs 8%), blurred vision (13% vs 5%), and arthralgia (10% vs 3%). A 6 g/day dose has not been shown to confer additional benefit compared to the 3 g/day dose and is associated with an increased incidence of adverse events.

The most common adverse events reported by >5% of infants taking SABRIL for IS occurring more frequently than placebo, respectively, in a randomized, placebo-controlled IS study with a 5-day double-blind treatment

phase (n=40) were somnolence (45% vs 30%), bronchitis (30% vs 15%), ear infection (10% vs 5%), and acute otitis media (10% vs 0%).

Oral Solution: For more information, please see the full Prescribing Information including Boxed Warning, Medication Guide and Dosing Instructions.

Solución oral: Para más información, vea por favor la información que prescribe completa incluyendo la advertencia encajonada, guía de la medicación y las instrucciones de la dosificación.

Tablets: For more information, please see the full Prescribing Information including Boxed Warning and Medication Guide.

Tabletas: Para más información, vea por favor la información que prescribe completa incluyendo la advertencia encajonada y guía de la medicación.

About Lundbeck in the U.S.
A wholly-owned subsidiary of H. Lundbeck A/S, Lundbeck in the U.S. is headquartered in Deerfield, Illinois, and is committed to accelerating our work in central nervous system (CNS) disorders, including challenging seizure disorders. Additionally, Lundbeck employees actively support and participate in hundreds of epilepsy awareness events each year as part of their ongoing commitment to make a difference for those impacted by epilepsy. For more information, please visit lundbeckus.com.

About Lundbeck
H. Lundbeck A/S (LUN.CO, LUN DC, HLUYY) is an international pharmaceutical company highly committed to improving the quality of life for people suffering from psychiatric and neurological disorders. For this purpose, Lundbeck is engaged in the research, development, production, marketing and sale of pharmaceuticals across the world. The company's products are targeted at disorders such as depression and anxiety, psychotic disorders, epilepsy and Huntington's, Alzheimer's and Parkinson's diseases.

Lundbeck was founded in 1915 by Hans Lundbeck in Copenhagen, Denmark. Today Lundbeck employs approximately 6,000 people worldwide. Lundbeck is one of the world's leading pharmaceutical companies working with psychiatric and neurological disorders. In 2011, the company's revenue was DKK 16.0 billion (approximately EUR 2.2 billion or USD 3.0 billion). For more information, please visit www.lundbeck.com.

Sources

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