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SABRIL® REGISTRY CHARACTERIZES VISION LOSS ASSOCIATED WITH VIGABATRIN THERAPY

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Background: Vigabatrin was approved in the United States in August 2009 as adjunctive therapy for adult patients with refractory complex partial seizures (rCPS) who had responded inadequately to several alternative treatments and as monotherapy for patients 1 month to 2 years of age with infantile spasms (IS). An important safety issue for vigabatrin is the risk of vision loss, which needs further characterization.

Objectives: To manage this risk appropriately, the FDA and Lundbeck Inc. require a comprehensive Risk Evaluation and Mitigation Strategy (REMS), including an ongoing patient registry, which was designed to assess incidence, prevalence, time to onset, progression, and severity of vision loss.

Methods: Sabril prescribers and patients are enrolled in the —SHARE program (Support, Help and Resources for Epilepsy). Participation in SHARE and the registry is mandatory for both prescribers and their patients. Data on prescriber specialty/location, patient demographics, and clinical characteristics are collected. Patients are assigned unique identifiers, and all data are associated with these identifiers. Regular vision assessments are required throughout vigabatrin therapy — at baseline (≤ 4 weeks after therapy initiation), at least every 3 months during therapy, and 3–6 months after discontinuation. Visual results are entered into the database. If formal perimetry or optical coherence tomography (OCT) is conducted, copies of reports are requested to be submitted to SHARE. Spontaneous adverse events are not collected via the registry, but rather are treated as post-marketing reports and triaged and submitted to the FDA, as appropriate. Visual assessment data are considered outcome measures, and are summarized in REMS assessments for the FDA, as required. Mandatory benefit/risk assessments are conducted by treating physicians early in therapy (within 2–4 weeks for patients < 3 years of age, and within 3 months for patients ≥ 3 years). For each patient, if the benefit of vigabatrin therapy exceeds the risk, the prescriber submits the appropriate SHARE form, and the patient then continues in the maintenance phase. Outcomes of benefit/risk assessments are entered into the database, and data are collected as long as patients receive vigabatrin. A steering committee of external experts in epileptology, neuro-ophthalmology, and epidemiology, and Lundbeck staff, finalized the registry protocol and is overseeing its conduct. The committee periodically reviews registry visual function data and spontaneously reported visual function adverse events and serious adverse events. The external experts advise the sponsor on data analysis, and execution of the overall REMS. Analyses were completed every 6 months during the first year of the registry (2009–10), and are now being conducted annually for 6 years.

Results: As of June 22, 2010, 1,690 patients had enrolled, of which, 1,047 had IS, 557 had rCPS, and 81 had other diagnoses (as determined by treating physicians). At enrollment, 38.3% had previously received or were currently receiving vigabatrin. Kaplan-Meier analyses of time in the registry for all patients enrolled indicate that 947 (97.6%) of patients with IS had remained in the registry beyond 1 month, and 341 (86.8%) of patients with rCPS had remained in the registry beyond 3 months. Similarly, Kaplan-Meier analyses of time in the registry for Sabril-naive patients enrolled indicate that 518 (96.5%) of patients with IS had remained in the registry beyond 1 month, and 99 (74.5%) of patients with rCPS had remained in the registry beyond 3 months.

Conclusions: The registry provides information on vision monitoring results, including risk factors, which may guide treatment decisions.