Dear Healthcare Professional:

Lundbeck Inc. is writing to remind prescribers of the serious risks associated with SABRIL (vigabatrin), including vision loss, and to clarify which patients receiving SABRIL are exempt from the requirement for periodic vision assessment.

SABRIL® (vigabatrin), pronounced say-bril, is approved by the Food and Drug Administration (FDA) for the following indications: as adjunctive therapy in adult patients with refractory complex partial seizures (CPS) who have inadequately responded to several alternative treatments and as monotherapy for pediatric patients with infantile spasms (IS).

Decisions to use SABRIL to treat refractory CPS and IS must balance the potential benefits with the risks of therapy.

Three specific effects of SABRIL are highlighted below as well as a reminder of the timing of the mandatory benefit-risk that must occur. Copies of the full Prescribing Information and Medication Guide are enclosed for your reference.

**Vision Loss and Monitoring**

SABRIL causes permanent bilateral concentric constriction of the visual field in 30 percent or more of adult patients. Vision loss can range in severity from mild to severe, including tunnel vision to within about 10 degrees of visual fixation, and can result in disability. In some cases, SABRIL can also damage the central retina and may decrease visual acuity. The onset of vision loss from SABRIL is unpredictable. It can occur within weeks of starting treatment or at any time during treatment, even after months or years. There is no dose known to be free of the risk of vision loss, although the risk of vision loss may increase with increasing dose and cumulative exposure. The possibility that vision loss can worsen despite discontinuation of SABRIL has not been excluded.

Symptoms of vision loss from SABRIL are unlikely to be recognized by patients or caregivers before vision loss is severe; therefore, appropriate vision monitoring is needed for detection. Monitoring of vision by an ophthalmic professional (defined as having expertise in visual field interpretation and the ability to perform dilated indirect ophthalmoscopy of the retina) is required.

Vision monitoring is mandatory in adults receiving SABRIL for refractory CPS at baseline (no later than 4 weeks after starting SABRIL) and at least every 3 months while on therapy. Vision testing is also required about 3 to 6 months after the discontinuation of SABRIL therapy.

Assessing vision loss is difficult in children and therefore the frequency and extent of vision loss in infants and children is poorly characterized. Vision monitoring is required to the extent possible in infants receiving SABRIL at baseline (no later than 4 weeks after starting SABRIL) and at least every 3 months while on therapy. Vision testing is also required about 3 to 6 months after the discontinuation of SABRIL therapy. This assessment should include visual acuity and visual field testing whenever possible. Although the appropriate diagnostic approach should be individualized for the patient and clinical situation, attempts to monitor periodically must be documented under the SHARE program for all patients.

In those patients in whom vision testing is not possible, treatment may continue according to clinical judgment, with appropriate caregiver counseling, and with documentation in the SHARE program of the inability to test vision. Results from ophthalmic monitoring must be interpreted with caution, as reliability and predictive value are variable.

September 5, 2011
The prescriber may, with appropriate documentation and caregiver counseling, exempt certain patients from vision assessment, using the Ophthalmologic Assessment Form, if:

- The patient is blind (subsequent Ophthalmologic Forms do not need to be submitted to the REMS coordinating center)
- The patient’s general neurological and/or mental condition permanently precludes the need for visual assessment (subsequent Ophthalmologic Forms do not need to be submitted to the REMS coordinating center)
- The patient’s general neurological condition temporarily precludes the ability to assess visual function. The evaluation, however, may be performed at a later time as clinically appropriate
- The patient’s medical condition prevents visual assessment being performed safely
- For other reasons specified by the prescriber

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

Please read the full Prescribing Information for additional details.

**Other Safety Concerns**

Abnormal MRI signal changes characterized by increased T2 signal and restricted diffusion in a symmetric pattern involving the thalamus, basal ganglia, brain stem, and cerebellum have been observed in some infants treated with SABRIL. The potential for long-term clinical sequelae and the need for monitoring have not been adequately studied. In animals that received vigabatrin, similar MRI abnormalities were correlated histologically with microvacuoles, consistent with a process of intramyelitic edema in those animals. Vacuolar changes considered distinct from intramyelitic edema, as well as other neurotoxicity and neurobehavioral abnormalities have also been observed in animals.

Brain MRI abnormalities attributable to SABRIL have not been observed in older pediatric or adult patients treated with SABRIL for CPS.

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

Please read the full Prescribing Information for additional details regarding these safety concerns.
Support, Help And Resources for Epilepsy (SHARE) Program

Due to the risk of serious adverse events, particularly the risk of loss of vision, SABRIL is available only through a Risk Evaluation and Mitigation Strategy (REMS) program called the SHARE program. All physicians who prescribe SABRIL and all patients who take SABRIL must enroll in the SHARE program. Ophthalmic professionals do not need to be registered.

Please visit the Lundbeck SHARE website at www.LundbeckSHARE.com or call SHARE at 1-888-45-SHARE (1-888-457-4273) for registration information. Medical inquiries should be directed to the Medical Information Department at 1-866-402-8520. Adverse drug events or product complaints should be directed to the Patient Safety Department at 1-800-455-1141.

Sincerely,

Christopher F. Silber, MD
Lundbeck Inc.