I. GOAL(S):

The goals of the REMS are:

1) To reduce the risk of a Sabril-induced vision loss while delivering benefit to the appropriate patient populations;

2) To ensure that all patients receive a baseline ophthalmologic evaluation unless a patient is formally exempted from vision testing; 50% of patients will receive the evaluation within 2 weeks of starting Sabril and 100% within 4 weeks;

3) To discontinue Sabril therapy in patients who experience an inadequate clinical response;

4) To detect Sabril-induced vision loss as early as possible;

5) To ensure regular vision monitoring to facilitate ongoing benefit-risk assessments; and

6) To inform patients/parent or legal guardian of the serious risks associated with Sabril, including vision loss and increased risk of suicidal thoughts and behavior.
II. REMS ELEMENTS

A. Medication Guide
Lundbeck will ensure that a Medication Guide is dispensed with each prescription of Sabril and in accordance with 21CFR 208.24. The Medication Guide will be included in the Sabril Starter Kit to be reviewed with the patient/parent or legal guardian by the physician prior to starting the patient on Sabril therapy.

Please see appended Medication Guide.

B. Communication Plan
At product launch (that is, during the first 6 months after product approval) and yearly for 3 years thereafter Lundbeck will send a Dear Healthcare Professional Letter via direct mail to all registered ophthalmologists. The Sabril package insert will accompany the letter. Additionally, Lundbeck field representatives will call on neuro-ophthalmologists and/or ophthalmologists at key epilepsy centers at product launch to disseminate the Sabril package inserts.

The Dear Healthcare Professional Letter is part of the REMS and is appended. The final distribution date of this letter was August 31, 2012.

C. Elements To Assure Safe Use
1) Healthcare providers who prescribe Sabril will be specially certified under 505-1 (f)(3)(A).
   a) Lundbeck will ensure that prescribers enrolled in the REMS program are specially certified. Lundbeck will ensure that, to become certified, prescribers attest to their understanding of the REMS program requirements and the risks associated with Sabril, and that prescribers commit to the following:
      i) Reading the full prescribing information (PI) and Medication Guide;
      ii) Having knowledge of the approved indications for Sabril;
      iii) Having experience in treating epilepsy;
      iv) Having knowledge of the risks of Sabril, especially vision loss;
      v) If prescribing for infantile spasms, having knowledge of the risk of MRI abnormalities with use of Sabril;
      vi) Assessing the effectiveness of Sabril within 2-4 weeks in infants and children (<3 years of age) and within 12 weeks in children (≥3 years of age), adolescent, and adults; in the case that insufficient clinical benefit has occurred, Sabril will be discontinued; for patients discontinuing Sabril at this evaluation, a Treatment Maintenance Form will not be completed; for patients
continuing treatment, a Treatment Maintenance Form will be completed and faxed to the REMS coordinating center;

vii) Ordering and reviewing visual assessment at the time of initiation of Sabril using the Ophthalmologic Assessment Form (with the baseline assessment to be conducted within 4 weeks of starting Sabril), and every 3 months after initiating Sabril therapy; the Ophthalmologic Assessment Form will be faxed to the REMS coordinating center;

viii) Educating patients on the risks and benefits of Sabril;

ix) Enrolling all patients who take Sabril in the REMS program by completing and submitting the Treatment Initiation Form and the Patient/Parent/Legal Guardian-Physician Agreement Form;

x) Reviewing the Sabril Medication Guide with every patient;

xi) Counseling the patient if the patient is not complying with the required vision monitoring beyond the baseline test, and removing the patient from therapy if the patient still fails to comply with required vision monitoring;

(1) Should discontinuation be required, discontinuation will be accomplished by tapering the patient from therapy as described in the Dear HCP Medication Taper Letter; and

xii) Reporting to the Sponsor at 1-800-455-1141 any serious adverse events with Sabril and providing all known details of the event.

b) The prescriber may exempt certain patients from vision assessment, using the Ophthalmologic Assessment form, if:

i) The patient is blind (subsequent Ophthalmologic Forms do not need to be submitted to the REMS coordinating center)

ii) 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)

iii) The patient’s general neurological condition temporarily precludes the need for visual assessment

iv) The patient’s medical condition prevents visual assessment being performed safely, documented by the prescriber.

v) For other reasons documented by the prescriber.

c) The following materials are part of the REMS and are appended

(1) Dear Healthcare Professional (HCP) Letter

(2) Dear HCP Medication Taper Letter

(3) Prescriber Enrollment and Agreement Form

(4) Treatment Initiation Form
Lundbeck will maintain a database of certified prescribers in the REMS program. Lundbeck will ensure that prescribers comply with the requirements of the REMS and may de-enroll noncompliant prescribers.

2) Pharmacies that dispense Sabril are specially certified by Lundbeck under 505-1(f)(3)(B).

   Lundbeck will ensure that to be certified, each pharmacy does the following; pharmacies not complying may be de-enrolled by Lundbeck:

   a) designates a representative who is trained on the REMS program
   b) dispenses Sabril only to patients who are enrolled in the REMS program, and whose continued eligibility has been established within the REMS
   c) obtains treatment forms and prescriptions only from the REMS coordinating center.
   d) obtains a dispensing authorization from the REMS coordinating center before dispensing the first Sabril prescription and before dispensing each refill.
   e) trains pharmacy staff on the REMS program procedures and REMS materials for dispensing
   f) agrees that the certified pharmacy may be audited by the FDA, Lundbeck, or a third party designated by Lundbeck.

3) Sabril will be dispensed to patients with evidence or other documentation of safe-use conditions under 505-1(f)(3)(D):

   a) Lundbeck will ensure that each patient treated with Sabril is enrolled in the Sabril REMS before Sabril is dispensed to him or her. Lundbeck will ensure that, to become enrolled, each patient or parent/legal guardian must sign a Patient/Parent/Legal Guardian-Physician Agreement Form indicating that:
      i) they have read the Medication Guide;
      ii) the prescriber has explained the risk of visual loss;
      iii) vision loss, should it occur, is irreversible;
      iv) that prescribed vision assessments must be obtained unless exempt by C(1)(b) above;
      v) periodic vision assessment, although not protective from all vision loss, is required for the duration of therapy, and even after stopping Sabril; and
vi) response to Sabril will be assessed after a short trial period (3 months for complex partial seizures and 1 month for infantile spasms); should the patient’s response to Sabril be insufficient, therapy with Sabril will be stopped

b) The following materials are part of the REMS and are appended

(1) Patient/Parent/Legal Guardian-Physician Agreement
(2) Treatment Maintenance Form
(3) Ophthalmologic Assessment Form

4) Each patient using the drug is enrolled in a registry under 505-1(f)(3)(F)
   The registry will collect prescriber specialty, patient demographics, diagnosis, prior and concurrent anti-seizure medications, periodic ophthalmologic assessment data (i.e., the results of every 3-month monitoring), and the proportion of patients receiving Sabril for refractory complex partial seizures and infantile spasms who respond/do not respond to Sabril during the treatment initiation phase.

D. Implementation System

The Implementation System will include the following. Lundbeck will:

1) maintain a validated and secured (21 CFR Part 11 compliant) database of certified pharmacies, certified prescribers and enrolled patients.

2) monitor distribution data to ensure that only certified pharmacies are distributing and dispensing Sabril.

3) train all personnel working for the REMS coordinating center (TheraCom) directly responsible for the Sabril REMS program and site managers at all certified pharmacies. Lundbeck will audit all certified pharmacies and the REMS coordinating center on an annual basis.

4) ensure that the REMS coordinating center receives each enrolled patient’s completed Treatment Maintenance Form documenting an assessment of risk-benefit prior to authorizing the maintenance phase of therapy.

5) ensure that the REMS coordinating center obtains an initial completed Ophthalmologic Assessment Form for all registered patients and subsequent forms for those who are not exempt at 3-month intervals (plus a 90-day grace period, as detailed in the REMS Supporting Document) prior to authorizing continued dispensing of refills

6) ensure that certified pharmacies dispense Sabril only if they receive authorization for each dispense from the REMS coordinating center.

7) ensure that patients who are not exempted from vision assessment [see (C)(1)(b)] and who do not comply with the vision monitoring requirements of the REMS are tapered from Sabril.

8) monitor and evaluate the implementation of the elements provided for under Sections C1, C.2, C.3, and C.4, above, in the manner described in the REMS supporting
document, and take reasonable steps to work to improve implementation of these elements.

E. Timetable for Submission of Assessments

Lundbeck will submit REMS assessments to the FDA every 6 months for 1 year from the date of the original approval of the REMS (August 21, 2009), and then annually thereafter on October 21. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment report should conclude no earlier than 60 days before the submission date for that assessment. Lundbeck will submit each assessment so that it will be received by the FDA on or before the due date.