DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020427/S-005
NDA 022006/S-006

SUPPLEMENT APPROVAL
REMS MODIFICATION

Lundbeck LLC
Attention: Mahlaqa Patel
Director, Regulatory Affairs
Four Parkway North, Suite 200
Deerfield, IL 60015

Dear Ms. Patel:

Please refer to your Supplemental New Drug Applications (sNDA) dated February 25, 2011, received February 25, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for:

Application	Product Name
NDA 020427	Sabril (vigabatrin) tablets
NDA 022006	Sabril (vigabatrin) powder for oral solution

We also acknowledge receipt of your proposed risk evaluation and mitigation strategy (REMS) modifications dated November 8, 2011, January 10 and 17, 2012, February 10 and 23, 2012 and October 17, 2012; and your REMS assessment dated February 25, 2011.

These "Prior Approval" sNDAs provide for revisions to the prescribing information and proposed modifications to the approved REMS primarily to clarify that certain patients may be exempted from periodic vision assessments, and that such assessments are not always required in order to receive Sabril. We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content

of labeling must be identical to the enclosed labeling (text for the package insert and text for the Medication Guide), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

Under 21 CFR 208.24(d), you are responsible for ensuring that the label of each container or package includes a prominent and conspicuous instruction to authorized dispensers to provide a Medication Guide to each patient to whom the drug is dispensed, and states how the Medication Guide is provided.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Sabril (vigabatrin) was originally approved on August 21, 2009, and a REMS modification was approved on January 18, 2011. The REMS consists of a Medication Guide, communication plan, elements to assure safe use, implementation system, and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consist of revisions to the Ophthalmologic Assessment Form, the Medication Guide, the REMS document, the Patient/Parent/Legal Guardian Physician Agreement Form, the Prescriber Enrollment and Agreement Form, the Treatment Initiation Form, and the Dear Healthcare Provider Letter. As discussed above, the revisions to the REMS primarily serve to clarify the REMS requirements and procedures related to vision assessments. The timetable for submission of assessments was also revised to add precise submission dates.

Your proposed modified REMS, submitted on February 23, 2012, and appended to this letter, is approved.

The REMS assessment plan should include, but is not limited to, the following:

1. Registration and drug distribution data
2. Medication Guide assessment data
    a. Patients' understanding of the serious risks of Sabril (vigabatrin)
    b. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
    c. A report on failures to adhere to distribution and dispensing requirements and corrective actions taken to address noncompliance
3. Report of mandatory benefit-risk assessments prior to entering maintenance therapy, including how many patients completed the mandatory benefit-risk assessment, and how many patients did not complete the mandatory benefit-risk assessment
4. Vision Monitoring, including information on vision monitoring (including missed and completed monitoring and patients exempted from monitoring), narrative summary and analysis of information collected on Ophthalmologic Assessment Forms, and narrative summary and assessments of reports of vision loss
5. Patient/Parent or Legal Guardian Knowledge, Attitude and Behavior (KAB) Surveys
6. Ophthalmic professional KAB Surveys
7. Prescriber KAB Surveys
8. An analysis of all spontaneously reported vision adverse events; to the extent possible, these reports should be linked to the reports of vision loss reported through the REMS so that the assessment report includes the total number of reports of vision loss reported for Sabril, from all sources.
9. Reasons for discontinuation for patients who discontinued Sabril therapy

The requirements for assessments of an approved REMS under section 505-1(g)(3) include, with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether 1 or more such goals or such elements should be modified.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the

submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

> **NDA 20427 / 22006 REMS CORRESPONDENCE**
> **(insert concise description of content in bold capital letters, e.g.,**
> **UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY)**

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

Prominently identify the submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

> **NDA 20427 / 22006 REMS ASSESSMENT**
>
> **NEW SUPPLEMENT FOR NDA 20427 / 22006**
> **PROPOSED REMS MODIFICATION**
> **REMS ASSESSMENT**
>
> **NEW SUPPLEMENT (NEW INDICATION FOR USE)**
> **FOR NDA 20427 / 22006**
> **REMS ASSESSMENT**
> **PROPOSED REMS MODIFICATION (if included)**

If you do not submit electronically, please send 5 copies of REMS-related submissions.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, contact Fannie Choy, RPh, Regulatory Project Manager, by phone or email at (301) 796-2899 or fannie.choy@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Russell G. Katz, M.D.
Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURES:
Content of Labeling
REMS

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

RUSSELL G KATZ
12/11/2012