DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020427/S-016
NDA 022006/S-018

SUPPLEMENT APPROVAL

Lundbeck Pharmaceuticals LLC
Attention: Gregg Pratt, PhD
Vice President, US Regulatory Affairs
Six Parkway North
Suite 400
Deerfield, IL 60015

Dear Dr. Pratt:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received November 2, 2016, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Sabril (vigabatrin) tablets and oral solution.

These Prior Approval supplemental new drug applications propose modifications to the approved risk evaluation and mitigation strategy (REMS) for Sabril to establish a single, shared system (SSS) REMS for vigabatrin products and updates to the approved Prescribing Information and Medication Guide to incorporate language reflecting the proposed SSS REMS.

APPROVAL & LABELING

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.

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information.

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, Medication Guide, and Instructions for Use), 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 that include labeling changes 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 these supplemental applications, 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.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Sabril was originally approved on August 21, 2009, and the most recent modification was approved on June 21, 2016. The REMS consists of elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS establish a SSS REMS for the elements to assure safe use and the implementation system required for the reference listed drug (RLD) Sabril and ANDAs referencing Sabril, called the Vigabatrin REMS Program.

Your proposed modified REMS, submitted on November 2, 2016, amended and appended to this letter, is approved. The modified REMS consists of elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

The timetable for submission of assessments of the REMS has been revised to be due annually from the date of the approval of the Vigabatrin REMS Program.

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

A. Program utilization
    1. Certification of healthcare providers (HCP)
        a. Number of new certifications of HCP; indicate whether previously certified or not
        b. Number of active HCP (have prescribed vigabatrin at least once during the reporting period) in outpatient pharmacy settings

2. Certification of pharmacies
    a. Number of new certified inpatient or outpatient pharmacies
    b. Number of active certified outpatient pharmacies (have filled or ordered at least one prescription for vigabatrin during the reporting period)
    c. For certified inpatient pharmacies, provide the number of orders shipped during the assessment period
3. Patient enrollment
    a. Number of new patients enrolled, stratified by age groups
    b. Number of active patients (have received at least one shipment of vigabatrin during the reporting period) in outpatient pharmacy settings stratified by age groups
4. Drug utilization
    a. Number of prescriptions by patient age for each reporting period and cumulatively
    b. Number of prescriptions by pharmacy type for each reporting period and cumulatively

B. Vigabatrin REMS Program Call center
1. Number of contacts by stakeholder type (patient/caregiver, prescriber pharmacy, other)
2. Summary of frequently asked questions (FAQ) by stakeholder type

C. Program performance/compliance
1. Audits: Summary of audit findings for audits conducted during the reporting period by pharmacy type, including any corrective and preventive actions (CAPA)
2. Number of prescribers and pharmacies de-certified and reasons for decertification
3. Number of vigabatrin prescriptions dispensed that were written by non-certified prescribers and any action taken and outcome of action (e.g., provision of educational program materials, prescriber became certified)
4. Number of prescriptions dispensed by non-certified pharmacies and the actions taken to prevent future occurrences
5. Number of times certified pharmacies either bypassed REMS authorization processes and dispensed vigabatrin OR did not receive authorization from the REMS to dispense the drug but dispensed it anyway
6. Number of shipments sent to non-certified pharmacies, sources of report, and actions taken to prevent future occurrences
7. Summary of any additional non-compliance, source of report, resulting corrective and preventive actions (CAPA)

D. Evaluation of knowledge through Knowledge, Attitude and Behavior (KAB) surveys
1. Prescribers

a. An evaluation of knowledge of certified prescribers of the increased risk of vision loss, the need to counsel patients and caregivers about the risk, and the need for periodic visual monitoring.
b. An evaluation of prescriber practice or behavior with regards to:
i. counseling patients and caregivers about the increased risk of vision loss, and the need for periodic visual monitoring
ii. documentation of counseling
iii. mitigation of potential vision loss (such as referring patients for periodic vision monitoring)

2. Patients
a. An evaluation of knowledge of patients or caregivers of the increased risk of vision loss, and the need for periodic visual monitoring.
b. An evaluation of patients' or caregivers' recall of counseling by prescriber on the risk of vision loss and the need for periodic visual monitoring as well as patients' recall of the frequency of their vision monitoring.

E. Overall Vigabatrin REMS Program evaluation
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.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any of goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of the FDCA. This assessment should include:

a) An evaluation of how the benefit-risk profile will or will not change with the new indication;
b) A determination of the implications of a change in the benefit-risk profile for the current REMS;
c) *If the new indication for use introduces unexpected risks*: A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.
d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use*: A statement about whether the REMS was meeting its goals at the time of the last assessment and if any modifications of the REMS have been proposed since that assessment.

e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.
f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including*: Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing REMS modifications*, provide a rationale for why the REMS does not need to be modified.

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 ###### 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.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Prominently identify any 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 ###### REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA ######/S-000/ SECONDARY TRACKING NUMBER
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA ######/S-000/ SECONDARY TRACKING NUMBER
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA ######/S-000/ SECONDARY TRACKING NUMBER
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABEL CHANGES SUBMITTED IN SUPPLEMENT XXX

or

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA ######/S-000/ SECONDARY TRACKING NUMBER
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISIONS FOR NDA ######

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

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 E. Andrew Papanastasiou, Regulatory Project Manager, via email at emilios.papanastasiou@fda.hhs.gov or by phone at (301) 796-1930.

Sincerely,

{See appended electronic signature page}

Alice Hughes, MD
Deputy Director for Safety
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/

ALICE HUGHES
04/27/2017