DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202067

NDA APPROVAL

Lundbeck Inc.
Attention: Jenny Swalec
Sr. Director, Global Regulatory Affairs
Four Parkway North, Suite 200
Deerfield, IL 60015

Dear Ms. Swalec:

Please refer to your New Drug Application (NDA) dated December 23, 2010, received December 23, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Onfi (clobazam) oral tablets (5mg, 10mg, and 20mg).

We acknowledge receipt of your additional correspondence and amendments dated:

January 13, 2011	January 21, 2011	February 7, 2011	February 9, 2011
February 10, 2011	February 11, 2011	February 14, 2011	February 18, 2011
March 22, 2011	March 31, 2011	April 22, 2011	April 27, 2011
May 10, 2011	June 10, 2011	June 17, 2011	June 29, 2011
June 30, 2011	July 7, 2011	July 15, 2011	July 29, 2011
August 23, 2011	September 2, 2011	September 15, 2011	September 20, 2011
October 3, 2011	October 4, 2011	October 11, 2011	October 13, 2011
October 14, 2011	October 15, 2011	October 16, 2011	October 17, 2011
October 18, 2011	October 19, 2011	October 20, 2011	October 21, 2011

This new drug application provides for the use of Onfi (clobazam) Tablets for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome (LGS) for patients 2 years of age or older.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the 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, text for the instructions for use, Medication Guide). 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/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels submitted on October 17, 2011, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)." Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 202067**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the products with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

ADVISORY COMMITTEE

Your application for Onfi was not referred to an FDA advisory committee because the safety profile is similar to that of other drugs approved for this indication.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

As stated in our March 3, 2011 letter, because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess an unexpected serious risk of reproductive and developmental toxicity and carcinogenicity. The nonclinical studies provided in your application did not adequately assess these risks due to numerous deficiencies in their conduct and documentation.

For the dietary carcinogenicity studies in mouse and rat, these deficiencies include: early deaths (with replacement of high-dose animals with animals younger at initiation than the original animals) due to fighting-induced injury (mouse); group housing resulting in an inability to ensure accurate dosing; lack of data to document stability of drug in the diet; lack of toxicokinetic analysis; lack of documentation that a full battery of tissues was examined microscopically in any or all animals; and lack of a signed QA statement, study report or pathology report.

For the reproductive and developmental toxicity studies, deficiencies include: generally, a lack of evidence of toxicity in the F_0 generation or justification for dose selection; use of dietary administration (fertility studies in mouse and rat) with no documentation of stability of drug in diet or plasma exposure; inadequate dosing period (i.e., dosing only during gestation days 9 to 14 in rat, or gestations days 7 to 12 in mouse in the embryo-fetal studies; dosing only from gestation day 17 to postnatal day 21 in the pre [peri] and postnatal study); and/or the lack of complete individual animal line listings for all parameters.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

1827-1 A carcinogenicity study of orally administered clobazam in rats.

The timetable you submitted on October 17, 2011, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	05/2013
Study Completion:	03/2016
Final Report Submission:	07/2016

1827-2 A carcinogenicity study of orally administered clobazam in mice.

The timetable you submitted on October 17, 2011, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	08/2013
Study Completion:	06/2016
Final Report Submission:	10/2016

1827-3 A fertility and early embryonic development to implantation study in rats.

The timetable you submitted on October 17, 2011, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	11/2012
Study Completion:	05/2013
Final Report Submission:	10/2013

1827-4 An embryo-fetal development study of orally administered clobazam in rats.

The timetable you submitted on October 17, 2011, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	09/2012
Study Completion:	04/2013
Final Report Submission:	08/2013

1827-5 An embryo-fetal development study of orally administered clobazam in rabbits.

The timetable you submitted on October 17, 2011, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	11/2012
Study Completion:	04/2013
Final Report Submission:	08/2013

1827-6 A prenatal and postnatal development (including maternal function) study of orally administered clobazam in rats.

The timetable you submitted on October 17, 2011, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	09/2012
Study Completion:	03/2013
Final Report Submission:	08/2013

Submit the protocols to your IND, with a cross-reference letter to this NDA. Submit all final reports to your NDA. Prominently identify each submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **"Required Postmarketing Protocol Under 505(o)", "Required Postmarketing Final Report Under 505(o)", "Required Postmarketing Correspondence Under 505(o)"**.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

We acknowledge receipt of your submission dated December 23, 2010, of a proposed risk evaluation and mitigation strategy (REMS). We have determined that, at this time, a REMS is not necessary for Onfi to ensure that its benefits outweigh its risks. We will notify you if we become aware of new safety information and make a determination that a REMS is necessary.

CHEMISTRY MANUFACTURING AND CONTROLS

A shelf-life of 36 months at 20°C to 25°C (68°F to 77°F) with excursions permitted to 15°C to 30°C (59°F to 86°F) [USP Controlled Room temperature] is approved.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing,

Advertising, and Communications (DDMAC), see
http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

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

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at
http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm.

POST-ACTION FEEDBACK MEETING

New molecular entities and new biologics qualify for a post-action feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, call Su-Lin Sun, PharmD, Regulatory Project Manager, at (301) 796-0036.

Sincerely,

{See appended electronic signature page}

Ellis F. Unger, M.D.
Deputy Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling
Medication Guide

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

/s/

ELLIS F UNGER
10/21/2011