DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020789/S-024 and S-026 **SUPPLEMENT APPROVAL**

Eisai Inc.
Attention: Martina Struck, PhD
Senior Director Regulatory Operations
300 Tice Boulevard
Woodcliff Lake, New Jersey 07677

Dear Dr. Struck:

Please refer to your supplemental new drug applications dated March 17, 2009, received March 18, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zonegran (zonisamide) capsules.

We acknowledge receipt of your additional submissions dated August 17, 2009 (S-024) and August 27, 2009 (S-026), January 25, 2010 (S-026), and January 28, 2010 (S-026).

We note that your submission dated August 27, 2009 stated that it is too early to provide a meaningful REMS assessment at this time.

The "Changes Being Effected" supplemental new drug application, S-024, provides for revisions to the labeling for Zonegran (zonisamide) that add information pertaining to the risk for metabolic acidosis. Specifically, the labeling revisions strengthen the WARNINGS and PRECAUTIONS sections of the Zonegran (zonisamide) prescribing information by adding safety-related language regarding metabolic acidosis as well as modifying the patient-related, pharmacology/toxicology, and CLINICAL PHARMACOLOGY sections in a corresponding manner.

The "Prior Approval" supplement, S-026, provides for proposed modifications to the approved Risk Evaluation and Mitigation Strategy (REMS) as described below.

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

Within 14 days from the date of this letter, please amend all pending supplemental applications for this NDA, including pending "Changes Being Effected" (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 structured product labeling (SPL) format that includes the changes approved in this supplemental application.

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

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for Zonegran (zonisamide) was originally approved on April 23, 2009. The REMS consisted of a comprehensive Medication Guide and a timetable for submission of assessments of the REMS.

Your proposed modified REMS, submitted on January 28, 2010 and appended to this letter, is approved. The proposed modified REMS contains a revised Medication Guide which includes language regarding the risk of metabolic acidosis as well as revisions to the timetable for submission of assessments to specify the submission dates.

The REMS assessment plan will remain the same as that approved on April 23, 2009.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include, in section 505-1(g)(3)(B) and (C), requirements for information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)vii and including any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

We remind you that 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 the FDCA.

Prominently identify future submissions containing the REMS assessment or proposed REMS modification with the following appropriate wording in bold capital letters at the top of the first page of the submission:

NDA 020789 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 020789
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT FOR (NEW INDICATION FOR USE) FOR NDA 020789
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

PROMOTIONAL MATERIALS

All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions to your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the following address or by facsimile at 301-847-8444:

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

In addition, as required under 21 CFR 314.81(b)(3)(i), you must submit your updated final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA-2253, directly to the above address. 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.

LETTERS TO HEALTH CARE PROFESSIONALS

We recommend that you issue a letter communicating the new important safety related information described in the revised label about this drug product (i.e., a "Dear Health Care Professional" letter). Prior to issuing such a letter, we request that you submit a draft of this letter to the Division of Neurology Products (DNP) for review and await feedback/comment, and that you also propose a list of the Health Care Professionals to whom you plan to send this letter. We request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
5600 Fishers Lane, Room 12B05
Rockville, MD 20857

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, call Dorothy Demczar, Pharm.D., Regulatory Project Manager, at (301) 796-2263.

Sincerely,

{See appended electronic signature page}

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

Enclosures
Content of Labeling
Modified REMS

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20789	SUPPL-26	EISAI INC	ZONEGRAN 100 MG CAPSULES
NDA-20789	SUPPL-24	EISAI INC	ZONEGRAN 100 MG CAPSULES

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
04/19/2010