DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204736/S004
NDA 20973/S034

SUPPLEMENT APPROVAL

Eisai, Inc.
Attention: Amanda Goodwin
Associate Director, Global Regulatory Affairs
155 Tice Blvd.
Woodcliff Lake, NJ 07677

Dear Goodwin:

Please refer to your Supplemental New Drug Applications (sNDAs) dated October 3, 2014, received October 6, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Aciphex Sprinkle (rabeprazole sodium) Delayed-Release Capsules, 5mg & 10 mg
Aciphex (rabeprazole sodium) Delayed-Release Tablets, 20 mg

These "Changes Being Effected" supplemental new drug applications provide for revisions in Sections 8.1 and 13.2; regarding the potential effects of a proton pump inhibitor on developing bone. The pregnancy category has also been changed from a B to a C.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text and with the minor editorial revisions listed below:

1. In the Highlights Section of the package insert, the RECENT MAJOR CHANGES has been removed, as they are no longer applicable since more than one year has passed since their approval.

2. In Section 8.1 under the *Risk Summary*, the following statement has been revised:

   Because of ~~that study~~ these findings, ACIPHEX should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus

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, except with the revisions listed, the enclosed labeling (text for the package insert and 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 via 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 with the revisions listed and indicated above 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).

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in 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 address above or by fax to 301-847-8444.

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 Stacy Barley, Regulatory Project Manager, at (301) 796-2137.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Deputy Director for Safety
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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

/s/

JOYCE A KORVICK
10/15/2014