DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 20690/S-037
NDA 21720/S-010
NDA 22568/S-007

SUPPLEMENT APPROVAL

Eisai Inc.
Attention: Carlos Langezaal, PhD
Director, Global Regulatory Affairs CFU
155 Tice Blvd
Woodcliff Lake, NJ 07677

Dear Dr. Langezaal:

Please refer to your Supplemental New Drug Application (sNDA) dated and received April 19, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Aricept (donepezil hydrochloride) 5mg and 10 mg Tablet, Aricept (donepezil hydrochloride) ODT, Aricept (donepezil hydrochloride) 23 mg Tablets.

We acknowledge receipt of your amendments dated September 4, 2013.

These "Prior Approval" supplemental new drug applications provide labeling as requested in the NDA 22568 Aricept 23 mg Tablets February 5, 2013 Fulfillment of Postmarketing Requirement & Supplement Request Agency letter.

In addition to minor editorial and formatting changes, these supplemental new drug applications provide the following revision to the Animal Toxicology section of labeling for Aricept products:

13.2 Animal Toxicology

In an acute dose neurotoxicity study in female rats, oral administration of donepezil and memantine in combination resulted in increased incidence, severity, and distribution of neurodegeneration compared with memantine alone. The no-effect levels of the combination were associated with clinically relevant plasma donepezil and memantine levels.

~~In a published study, female rats were given single doses of donepezil and memantine by intraperitoneal injection, each alone or in combination. When given in combination with memantine, donepezil increased the incidence and severity of memantine-induced neurodegeneration.~~

The relevance of this finding to humans is unknown.

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.

We note that your September 4, 2013, submissions include final printed labeling (FPL) for your package inserts. We have not reviewed these FPLs. You are responsible for assuring that the wording in this printed labeling is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

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 patient package insert), 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 includes 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 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).

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 Teresa Wheelous, Sr. Regulatory Project Manager, at (301)796-1161.

Sincerely,

{See appended electronic signature page}

Eric Bastings, MD
Acting Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE(S):
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/

ERIC P BASTINGS
09/06/2013