DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22568/S-08
NDA 21720/S-12
NDA 20690/S-39

SUPPLEMENT APPROVAL

Eisai Inc.
Attention: Ira Do, PharmD
Associate Director, Global Regulatory Affairs
155 Tice Blvd.
Woodcliff Lake, NJ 07677

Dear Dr. Do:

Please refer to your Supplemental New Drug Applications (sNDA) dated February 10, 2015, received February 10, 2015, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

NDA & SUPPLEMENT NUMBER:
NDA 22568/S-08
NDA 21720/S-12
NDA 20690/S-39

PRODUCT NAME:
Aricept (donepezil HCl) 23 mg Tablet
Aricept ODT (donepezil HCl) 5mg & 10 mg Tablet
Aricept (donepezil HCl) 5 mg & 10 mg film coated Tablet

We acknowledge receipt of your amendments, dated July 01, 2015.

These Changes-Being-Effected supplemental New Drug Applications propose the following labeling changes: to add the adverse reaction terms "rhabdomyolysis," "QT_c prolongation and torsade de pointes," and "Stevens Johnson syndrome, and toxic epidermal necrolysis" to the Postmarketing Experience section (Section 6.2) of the United States (U.S.) Prescribing Information.

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. The agreed-upon labeling text provides not only for the inclusion of a modified version of the additions that you have proposed to Section 6.2, but also for additional

revisions to the following sections of the labeling text: Highlights of Prescribing Information, Section 2 (Dosage and Administration), Section 5 (Warnings and Precautions), Section 6 (Adverse Reactions), Section 7 (Drug Interactions), Section 8 (Use in Specific Populations), Section 12 (Clinical Pharmacology), Section 13 (Nonclinical Toxicology), Section 14 (Clinical Studies), and Section 17 (Patient Counseling Information).

We note that your July 1, 2015 submission includes a clean version of the agreed labeling (FPL) for your package insert and patient package insert. We have not reviewed this version of labeling. 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.

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 text for the 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 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 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}

Alice Hughes, MD
Deputy Director for Safety
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling (PI & PPI)

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
07/20/2015