DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-690/S-016

Eisai Inc.
Attention: Michele Ferlaino
Glenpointe Centre West
500 Frank W. Burr Blvd
Teaneck, NJ 07666

Dear Ms. Ferlaino:

Please refer to your supplemental new drug application dated February 27, 2001, received February 28, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Aricept ® (Donepezil) Tablets.

This "Changes Being Effected in 30 days" supplemental new drug application provides for the following changes to labeling:

1. The addition of neuroleptic malignant syndrome to the Adverse Reactions; Postintroduction Reports section of labeling.

2. Revisions of the Cardiovascular Conditions section under WARNINGS to read as follows:

   Because of their pharmacological action, cholinesterase inhibitors may have vagotonic effects on the sinoatrial and atrioventricular nodes. This effect may manifest as bradycardia or heart block in patients both with and without known underlying cardiac conduction abnormalities. Syncopal episodes have been reported in association with the use of Aricept.

We have completed the review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (package insert submitted February 27, 2001). Accordingly, the supplemental application is approved effective on the date of this letter.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under

21 CFR 314.80 and 314.81.

If you have any questions, call Melina Fanari, R.Ph., Regulatory Management Officer, at (301) 594-5526.

Sincerely,

{See appended electronic signature page}

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