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APPLICATION NUMBER:

206439Orig1s000

PHARMACOLOGY REVIEW(S)

MEMORANDUM

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration

Division of Neurology Products (HFD-120)
Center for Drug Evaluation and Research

Date: November 23, 2014

From: Lois M. Freed, Ph.D.
Supervisory Pharmacologist

Subject: NDA 206-439 (Namzaric; memantine HCl ER and donepezil HCl; Forest Laboratories, Inc.)

NDA 206-439 is a 505(b)(2) application, submitted on February 26, 2014, to support marketing approval for Namzaric for treatment of moderate to severe Alzheimer's disease. Namzaric is a combination product, containing memantine HCl (MEM) ER and donepezil HCl (DPZ). Doses recommended by the sponsor are 28 mg MEM and 10 mg DPZ (14 mg MEM and 10 mg DPZ for patients with severe renal impairment). Clinical development of the combination was conducted under IND 109,763.

In support of this application, the sponsor cross-referenced two previously approved NDAs for MEM (NDA 21-487 for Namenda; NDA 22-525 for Namenda XR) and stated a reliance on FDA's previous findings of safety and effectiveness for Aricept (DPZ; NDA 20-690). In addition, the following nonclinical study reports were provided:

- Two pharmacology studies of the combination in rodent (MEM-PH-10; MEM-PH-14)
- acute dose study of the combination in female rat (MEM-TX-29)
- 28-day neurotoxicity study of the combination in rat (MEM-TX-27)
- TK/MTD study of the combination in rat (MEM-TX-30)

These studies were reviewed by Dr. Hawver (*cf. Pharmacology/Toxicology NDA Review and Evaluation, NDA 206-439, David B. Hawver, Ph.D., 10/25/2014*). Dr. Hawver notes that the studies MEM-TX-27 and MEM-TX-29 have previously been submitted and reviewed; therefore, his review focused on the pharmacology and TK/MTD studies. Based on his review, Dr. Hawver has concluded that the NDA is approvable, from a pharmacology/toxicology standpoint.

I concur with Dr. Hawver's recommendation on the approvability of the application and his conclusion that the pharmacology data provided do not support the sponsor's claims regarding any synergistic effects of MEM and DPZ on brain acetylcholine levels or on cognitive function (sponsor's labeling, Section 12.2). Additional comments on labeling will be provided separately.

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

/s/

LOIS M FREED
11/23/2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

PHARMACOLOGY/TOXICOLOGY NDA REVIEW AND EVALUATION

Application number:	206-439
Supporting document/s:	1
Applicant's letter date:	February 26, 2014
CDER stamp date:	February 26, 2014
Product:	Memantine HCl ER and Donepezil HCl
Indication:	Moderate to severe dementia of the Alzheimer's type
Applicant:	Forest Laboratories, Inc.
Review Division:	Neurology Products
Reviewer:	David B. Hawver, Ph.D.
Supervisor:	Lois M. Freed, Ph.D.
Acting Division Director:	Billy Dunn, M.D.
Project Manager:	Teresa Wheelous

Disclaimer

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