CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 20-823

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

APR 21 2000

NDA 20-823

Novartis Pharmaceuticals Corporation
Attention: Robert W. Kowalski, Pharm.D.
59 Route 10
East Hanover, NJ 07936-1080

Dear Dr. Kowalski:

Please refer to your new drug application (NDA) dated April 7, 1997, received April 7, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Exelon (rivastigmine tartrate) capsules 1.5 mg, 3 mg, 4.5 mg, and 6 mg.

We also acknowledge receipt of your submissions dated:

October 21, 1999	March 2, 2000	April 4, 2000
February 10, 2000	March 10, 2000	April 12, 2000
February 22, 2000	April 3, 2000	April 20, 2000

Your submission of October 21, 1999 constituted a complete response to our May 12, 1999 action letter.

This new drug application provides for the following Indication.

> "Exelon is indicated for the treatment of mild to moderate dementia of the Ahzheimer's type."

We have completed the review of this application, as amended, 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 agreed upon enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 20-823." Approval of this submission by FDA is not required before the labeling is used.

Phase 4

We remind you of your Phase 4 commitment specified in your submission dated April 20, 2000. This commitment, along with any completion dates agreed upon, are listed below.

> "Novartis agrees, post-approval, to conduct additional analyses of existing data to compare the incidence of nausea, vomiting, and weight loss associated with the dosing regimen recommended in the final labeling to that resulting from a regimen utilizing smaller dosing increments (i.e., about 1 mg/day in divided doses) in the therapeutic range of 6 to 12 mg/day. We will provide this analysis within 6 months of approval of the application, i.e., on or before October 21, 2000.
>
> If the existing data are not adequate to support meaningful comparison of the adverse event incidence associated with these differing regimens, we agree to meet and discuss with the Division the design of a clinical study, if needed, to further address this issue."

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitment, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.81(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to this Phase 4 commitment must be clearly designated "Phase 4 Commitment."

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We are waiving the pediatric study requirement for this action on this application.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Neuropharmacological Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 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 Robbin Nighswander, R.Ph., Regulatory Management Officer, at (301) 594-2850.

Sincerely,

/S/

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure (Draft Package Insert)

APPEARS THIS WAY
ON ORIGINAL