CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER
21-224

Approval Letter

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-224

6/22/01

Janssen Research Foundation
Attention: Charles LaPree
Assitant Director, Regulatory Affairs
1125 Trenton-Harbourton Road
P.O. Box 200
Titusville, NJ 08560-0200

Dear Mr. LaPree:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Reminyl® (galantamine hydrobromide) Oral Solution.

We acknowledge receipt of your submission dated June 6, 2001. Your submission of April 27, 2001 constituted a complete response to our December 1, 2000 action letter.

This new drug application provides for the use of Reminyl® (galantamine hydrobromide) Oral Solution for the treatment of mild to moderate dementia of the Alzheimer'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, text for the patient package insert) and submitted draft labeling (immediate container and carton labels submitted June 6, 2001). 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 the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no 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 21-224." Approval of this submission by FDA is not required before the labeling is used.

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

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 submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

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

Enclosure

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER
21-224

Approvable Letter

12/1/00

NDA 21-224

Janssen Research Foundation
Attention: Charles LaPree
Assitant Director, Regulatory Affairs
1125 Trenton-Harbourton Road
P.O. Box 200
Titusville, NJ 08560-0200

Dear Mr. LaPree:

Please refer to your new drug application (NDA) dated January 31, 2000, received February 3, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Reminyl® (galantamine hydrobromide) 4 mg/mL Oral Solution.

We also acknowledge receipt of the following submissions:

August 17, 2000
October 16, 2000

We have completed the review of this application, as amended, and it is approvable. However, since this application relies primarily on data submitted to your companion application for the tablet formulation of Reminyl (NDA 21-169), before it may be approved, it will be necessary that the Reminyl Tablet application be approved, either concurrent with/or before this application. Additionally, it will be necessary for you to submit final printed labeling (FPL) for Reminyl Oral Solution.

We also note that the Reminyl Tablet application received an approvable action letter from the Agency on July 29, 2000, and the Agency is currently reviewing the major amendment dated August 31, 2000 submitted to this application.

Package Insert

With regard to your package insert, a combination package insert for both the tablet and oral solution is recommended. We ask that, once agreement has been reached regarding text for the tablet package insert, a combination insert be prepared and submitted in response to this letter. The combined package insert would initially be reviewed under this application and, after approval, could be submitted as a "Changes Being Effected" supplemental application to the tablet NDA.

With regard to the Instructions for Use for the oral solution, agreement on language will be reached during the resubmission review period. However, it should be included at the end of the package insert, in addition to accompanying the drug product. Furthermore, a paragraph in

labeling under the PRECAUTIONS, Information for Patients and Caregivers section should be included stating the following:

> The caregiver should be instructed in the correct procedure for administering Reminyl Oral Solution. In addition, they should be informed of the existence of an Instruction Sheet (included with the product) describing how the solution is to be administered. They should be urged to read this sheet prior to administering Reminyl Oral Solution. Caregivers should direct questions about the administration of the solution to either their physician or pharmacist.

In addition, as requested in the approvable letter for the Reminyl Tablet application, the name galantamine hydrobromide should be established (package insert and carton and container labeling) as the official USAN name.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

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

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

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

Sincerely,

/S/

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