NDA 11-961/S-017

Hoffmann-La Roche Inc.
Attention: Anthony Corrado
Drug Regulatory Affairs
340 Kingsland Street
Nutley, New Jersey 07110-1199

Dear Mr. Corrado:

Please refer to your supplemental New Drug Application submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Marplan (isocarboxazid) 10 mg tablets.

We additionally refer to an Agency approvable letter dated November 7, 1997, and we also acknowledge receipt of your resubmission dated February 18, 1998, providing for a full response to our approvable letter, as well as your submissions dated July 17, and August 6, 1998.

The supplemental application provides for safety and efficacy data from three adequate and well controlled studies in support of a claim for the effectiveness of Marplan as a second line treatment of depression.

We additionally note that Hoffmann-La Roche intends to transfer this NDA to Oxford Pharmaceutical Services, Inc. upon resolution of the DESI issues, and that your February 18, 1998, submission was a response written by Hoffmann-LaRoche in conjunction with Oxford Pharmaceutical Services.

We have completed the review of this supplemental application, as amended, and it is approved. This action approves this application on the basis of effectiveness of the drug as well as safety. This action also approves those supplemental applications that were permitted under provisions of 21 CFR 314.70 and that have not been superseded.

Accompanying this letter (ATTACHMENT) is the labeling, including the revisions agreed to, that should be used for marketing this drug product. These revisions are terms of the DESI approval. Marketing the product before making the agreed upon revisions in the product's labeling may render the product misbranded and an unapproved new drug.

We additionally note the following agreements to the above DESI supplement:

Phase 4 Agreements

We remind you of your Phase 4 commitment specified in your submission dated February 18, and August 6(b)(4)(CC)----------t, along with any completion dates agreed upon, are listed below.

We note Oxford's agreement, upon obtaining ownership of the Marplan NDA, to conduct a Phase 4 open label safety study in(b)(4)(CC)----------(b)(4)(CC)----------lowin----------

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We also note your commitment, once Oxford obtains ownership of the Marplan NDA, to complete this study and submit the results within 24 months from remarketing Marplan.

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 commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.82(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 these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

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 11-961/S-017." Approval of this submission by FDA is not required before the labeling is used.

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 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

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, contact Paul David, R.Ph., Regulatory Project Manager, at (301) 594-5530.

Sincerely yours,

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

ATTACHMENT