



NDA 20-896

April 30, 1998

Hoffman-La Roche Inc.
340 Kingsland Street
Nutley, NJ 07110-1199

Attention: Cynthia Dinella, Pharm. D.
Group Director, Regulatory Affairs

Dear Dr. Dinella:

Please refer to your new drug application dated October 28, 1997, received October 30, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Xeloda (capecitabine) tablets, 150 mg and 500 mg.

We acknowledge receipt of the following amendments:

1997 November 11 and 13
December 23

1998 January 9, 27 (2), 28, and 29
February 4, 9, 12, 13, 20, 24 (2), 25, 27 (2),
March 2, 4, 5, 9, 10, 11, 12, 13, 16, 17, 18, 26, and 27
April 2, 9, 15 (2), 16 (2), 21, 23, and 27.

The User Fee goal date for this application is April 30, 1998.

This new drug application provides for the treatment of patients with metastatic breast cancer resistant to both paclitaxel and an anthracycline-containing chemotherapy regimen or resistant to paclitaxel and for whom further anthracycline therapy may be contraindicated, e.g., patients who have received cumulative doses of 400 mg/m² of doxorubicin or doxorubicin equivalents. Resistance is defined as progressive disease while on treatment, with or without an initial response, or relapse within 6 months of an anthracycline-containing adjuvant regimen.

We have completed the review of this application, including the submitted draft labeling, according to the regulations for accelerated approval and have concluded that adequate information has been presented to approve Xeloda (capecitabine) tablets, 150 mg and 500 mg. for use as recommended in the enclosed marked-up draft labeling. Accordingly, the application is approved under 21 CFR 314.520. Approval is effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed revised draft labeling. Marketing the product with FPL that is not identical to this draft labeling 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

Should additional information relating to the safety and effectiveness of the drug become available, revision of that labeling may be required.

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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. In addition, we request under 21 CFR 314.81(b)(2)(vii) that you include in your annual report to this application, a status summary of each commitment. 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".

Further, we acknowledge your April 9 and 14, 1998 commitments to address the following

chemistry, manufacturing and controls concerns with due diligence:

1. Three batches of each dosage strength Xeloda (capecitabine) Tablets manufactured using the improved manufacturing process will be placed on stability, and the data will be included in the annual report.
2. Within one year, R(b)(4)CC-----ined from commercially manufactured lots of capecitabine will be reviewed and compared to the current specifications to determine how these specifications can be tightened. Revised specifications will be developed and submitted in a pre-approval supplement.

We also remind you that, under 21 CFR 314.550, after the initial 120 day period following this approval, you must submit all promotional materials, including promotional labeling as well as advertisements, at least 30 days prior to the intended time of initial dissemination of the labeling or initial publication of the advertisement.

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.

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, please contact Maureen Pelosi, Project Manager, at (301) 594-5768.

Sincerely yours,

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

ENCLOSURE