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**APPROVAL PACKAGE FOR:**

**APPLICATION NUMBER  
20-896/S-010/S-011**

**Approval Letter**



NDA 20-896/S-010, S-011

SEP - 7 2001

Hoffman-LaRoche Inc  
340 Kingsland Street  
Nutley, NJ 07110-1199

Attention: Murad Husain  
Program Director

Dear Mr. Husain:

Please refer to your supplemental new drug application dated March 7, 2001, received March 8, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Xeloda (capecitabine) Tablets.

We acknowledge receipt of your submissions dated March 28, April 18, May 14 and 25, June 7, 11, 21, and 28, and August 30, 2001.

This supplemental new drug application provides for the use of Xeloda (capecitabine) Tablets in combination with Taxotere (docetaxel) for the treatment of patients with locally advanced or metastatic breast cancer after failure of prior anthracycline containing chemotherapy.

Additionally, we acknowledge receipt of your July 27, 2001 warfarin labeling supplement #011.

We have completed the review of these supplemental applications, 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, these supplemental applications are 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).

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 supplement NDA 20-896/S-010 and S-011." Approval of this submission by FDA is not required before the labeling is used.

This NDA was approved under the regulations for accelerated approval of new drugs for serious or life-threatening illnesses, specifically, 21 CFR 314.510. Approval of this supplement fulfills your commitments made under 21 CFR 314.510.

We remind you of your September 5, 2001 E-mail post-marketing study commitments listed below:

1. A Phase 2, three-arm Randomized Study of Standard Dose Intermittent Oral Capecitabine (Q3W) versus "Low" Dose Intermittent Oral Capecitabine versus Alternate Dose and Schedule Intermittent Oral Capecitabine (Q4W) in Patients with Locally Advanced or Metastatic Breast Cancer.

Protocol Submission: December 2001 – January 2002

Study Start: March 2002

Final Report Submission: December 2003

2. Pharmacokinetic study of the combination of Xeloda plus docetaxel to determine if long term coadministration of capecitabine and docetaxel alters the pharmacokinetics of capecitabine, capecitabine's metabolites, docetaxel, or a combination of these moieties. The performance of the analytical methods and the reporting of the analytical methods for these data should be consistent with FDA's guidance: Bioanalytical Method Validation which is available at <http://www.fda.gov/cder/guicance/index.htm>.

Protocol Submission: December 2001

Study Start: March 2002

Final Report Submission: December 2003

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these post-marketing study commitments must be prominently labeled "Postmarketing Study Protocol", "Post-marketing Study Final Report", or "Post-marketing Study Correspondence."

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

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2  
FDA  
5600 Fishers Lane  
Rockville, MD 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 Maureen Pelosi, Project Manager, at (301) 594-5778.

Sincerely,

*{See appended electronic signature page}*

Richard Pazdur, M.D.  
Director  
Division of Oncology Drug Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

Enclosure