DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-685/S-050, 053, 056

Merck Research Laboratories
Attention: Michelle Kloss, Ph.D.
P.O. Box 4, BLA-20
West Point, PA 19486-0004

Dear Dr. Kloss:

We acknowledge the receipt of your April 2, 2002 submission containing final printed labeling for the package insert and the June 5, 2002 submission containing final printed labeling for the patient package insert in response to our supplement 050 and 053 approval letter dated January 25, 2002, approving your supplemental new drug applications for Crixivan™ (indinavir sulfate) 100 mg, 200 mg, 333 mg, and 400 mg capsules. Please also refer to your supplemental-056 new drug application dated January 9, 2002, received January 10, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Crixivan™ (indinavir sulfate) 100 mg, 200 mg, 333 mg, and 400 mg capsules.

We acknowledge receipt of your submissions dated April 2, 2002.

This S-056 "Changes Being Effected in 30 days" supplemental new drug application provides for revisions to the INDICATIONS and USAGE, PRECAUTIONS, and HOW SUPPLIED sections of the label.

The following changes are noted in the final printed labeling for the package insert:

1. On page 5, under INDICATIONS AND USAGE, a hyphen was added to AIDS-defining.

2. On page 13, under PRECAUTIONS, Fat Redistribution, facial wasting, was added as an adverse event, and “protease inhibitors” was changed to “antiretroviral therapy”.

3. On page 13, under PRECAUTIONS, Information for patients, “protease inhibitors” was changed to “antiretroviral therapy”.

4. On page 14, under PRECAUTIONS, Information for patients, Calcium Channel Blockers, the following paragraph was added:

   Calcium channel blockers are metabolized by CYP 3A4 which is inhibited by indinavir. Coadministration of CRIXIVAN with calcium channel blockers may result in increased plasma concentrations of the calcium channel blockers which could increase or prolong their therapeutic and adverse effects.

5. On page 18, under PRECAUTIONS, Information for patients, Hypersensitivity, vasculitis was added as an adverse event.

6. On page 19, under HOW SUPPLIED, unit-of-use had hyphens added to it.

The following changes are noted in the in the final printed labeling for the patient package insert:

1. On page 5, the following information was added:

   TALK TO YOUR DOCTOR ABOUT ANY MEDICATIONS YOU ARE TAKING.

   Calcium Channel Blockers: Tell your doctor if you are taking calcium channel blockers (e.g., amlodipine, felodipine).

2. On page 4, under the section, **What are the possible side effects of CRIXIVAN?, "**protease inhibitors" was changed to "antiretroviral therapy", and "legs and arms" was changed to "legs, arms and face".

We have completed the review of this supplemental 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 submitted final printed labeling (package insert submitted April 2, 2002 and patient package insert submitted June 5, 2002). Accordingly, the supplemental application is approved effective on the date of this letter.

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 Virginia Yoerg, Regulatory Project Manager, at (301) 827-2335.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
Director
Division of Antiviral Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Jeffrey Murray
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