CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-945

APPROVAL LETTER(S)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-945

JUN 29 1999

Abbott Laboratories
Attention: Rebecca A. Welch
Associate Director, PPD Regulatory Director
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-6108

Dear Ms. Welch:

Please refer to your new drug application (NDA) dated November 21, 1997, received November 24, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Norvir (ritonavir capsules) soft gelatin.

Please also refer to the not approvable letter dated November 23, 1998, and to your resubmission dated March 1, 1999, received March 2, 1999, in response to the not approvable letter.

We acknowledge receipt of your submissions dated:

March 30, 1999
April 29, 1999
June 9, 1999
June 10, 1999
June 18, 1999
June 23, 1999
June 28, 1999 (2)

This new drug application provides for the use of Norvir (ritonavir capsules) soft gelatin 100 mg for the treatment of HIV-infection.

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 submitted draft labeling (package insert submitted June 28, 1999, patient package insert submitted June 28, 1999). The provided information in this resubmission adequately addresses the deficiencies listed in the November 23, 1998, not approvable letter. Accordingly, the application is approved effective on the date of this letter.

In addition, this application provides for changes in the CLINICAL PHARMACOLOGY, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and HOW SUPPLIED sections of the package insert.

The final printed labeling (FPL) must be identical to the draft label (text for the package insert and text for the patient package insert) submitted June 28, 1999. 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 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 20-945." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitments specified in your submission dated June 28, 1999. These commitments, along with any completion dates agreed upon, are listed below.

1.

2.

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."

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 note that you have not fulfilled the requirements of 21 CFR 314.55 (or 601.27), since pharmacokinetic, safety, and activity data in neonates and children under the age of two are needed. We are deferring submission of your pediatric studies until July 1, 2001.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). Please refer to the Pediatric Written Request dated April 8, 1999, from the Office of Drug Evaluation IV.

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-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 Sylvia D. Lynche, Pharm.D., at 301 827-2335.

Sincerely,

/S/

Heidi M. Jolson, M.D., M.P.H.

Director
Division of Antiviral Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Concurrence:
HFD-530/MTL/Murray- 5/
HFD-530/RRO/Struble- 5/
HFD-530/BPTL/Reynolds-eso 6/28/1999
HFD-530/CTL/Millers- 5/ 5/
HFD-530/CR/Lo-
HFD-530/SCSO/Decicco 5/
HFD-530/DDD/Birnkraut- 5/

cc:

Archival NDA 20-945
HFD-530/Div. Files
HFD-530/RPM/Lynche
HF-2/MedWatch (with labeling)
HFD-002/ORM (with labeling)
HFD-104/ADRA (with labeling)
HFD-40/DDMAC (with labeling)
HFD-613/OGD (with labeling)
HFD-95/DDMS (with labeling)
HFD-830/DNDC Division Director
DISTRICT OFFICE

APPROVAL (AP) (with Phase 4 Commitments)