CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 19834/S009

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

DF

Food and Drug Administration
Rockville MD 20857

NDA 19-834/S-009

JAN 13 1998

Astra Merck
Attention: Daniel J. Cushing, Ph.D.
725 Chesterbrook Blvd.
Wayne, PA 19087-5677

Dear Dr. Cushing:

Please refer to your September 19, 1996 supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Plendil (felodipine) Tablets, 2.5, 5 and 10 mg.

We acknowledge receipt of your submissions dated May 20 and June 20, 1997.

The supplemental application, as amended, provides for final printed labeling revised as follows under **CLINICAL PHARMACOLOGY, Pharmacokinetics and Metabolism** and **DOSAGE AND ADMINISTRATION** to update the information on the effect of food on the pharmacokinetics of Plendil:

Under **CLINICAL PHARMACOLOGY: Pharmacokinetics and Metabolism**, the last paragraph was revised as follows:

> The bioavailability of Plendil is influenced by the presence of food. When administered either with a high fat or carbohydrate diet, C-max is increased by approximately 60%. AUC is unchanged. When Plendil was administered after a light meal (orange juice, toast and cereal), however, there is no effect on felodipine's pharmacokinetics. The bioavailability of felodipine was increased approximately two-fold when taken with grapefruit juice. Orange juice does not appear to modify the kinetics of Plendil. A similar finding has been seen with other dihydropyridine calcium antagonists, but to a lesser extent than that seen with felodipine.

Under **DOSAGE AND ADMINISTRATION,** the following was added as the first sentence of the second paragraph:

> Plendil should regularly be taken either without food or with a light meal (see **CLINICAL PHARMACOLOGY, Pharmacokinetics and Metabolism**).

We have completed the review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the final printed labeling included with your June 20, 1997 submission. Accordingly, the supplemental application is approved effective on the date of this letter.

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:

Mr. David Roeder
Regulatory Health Project Manager
(301) 594-5313

Sincerely yours,

Raymond J. Lipicky, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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APPLICATION NUMBER: NDA 19834/S009

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APPROVABLE LETTER

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MAY 13 1997

Astra Merck
Attention: Daniel J. Cushing, Ph.D.
725 Chesterbrook Blvd.
Wayne, PA 19087-5677

Dear Dr. Cushing:

Please refer to your September 19, 1996 supplemental new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Plendil (felodipine) Tablets, 2.5, 5 and 10 mg.

The supplemental application provides for draft labeling revised under **CLINICAL PHARMACOLOGY, Pharmacokinetics and Metabolism** and **DOSAGE AND ADMINISTRATION** to update the information on the effect of food on pharmacokinetics of Plendil.

We have completed the review of this supplemental application as submitted with draft labeling and it is approvable. Before this supplement may be approved, however, it will be necessary for you to submit final printed labeling (FPL). The labeling should be identical in content to the enclosed marked-up draft. In addition, all previous revisions as reflected in the most recently approved package insert must be included. To facilitate review of your submission, please provide a highlighted or marked-up copy that shows the changes that are being made.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the FPL may be required.

Please submit sixteen copies of the printed labeling ten of which are individually mounted on heavy weight paper or similar material.

Within 10 days after the date of this letter, you are required to amend this supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of such action, FDA may take action to withdraw this supplemental application.

These changes may not be implemented until you have been notified in writing that this supplemental application is approved.

Should you have any questions, please contact:

Mr. David Roeder
Regulatory Health Project Manager
Telephone: (301) 594-5313

Sincerely yours,

/S/ 5/13/97

Raymond J. Lipicky, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

cc:
Original NDA
HFD-92
HFD-110
HFD-40/DDMAC (with labeling)
DISTRICT OFFICE
HFD-110/DRoeder
sb/4/22/97;5/8/97
R/D: EFadiran/4/23/97
AParekh/4/29/97
AKarkowsky/4/30/97
GBuehler for NMorgenstern/5/7/97

Approval Date: 7/26/91

APPROVABLE

5-13-97