

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION: NDA 19-778/S-028

CONTENTS

	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
Tentative Approval Letter				X
Approvable Letter	X			
Final Printed Labeling	X			
Medical Review(s)			X	
Chemistry Review(s)	X			
EA/FONSI			X	
Pharmacology Review(s)			X	
Statistical Review(s)			X	
Microbiology Review(s)			X	
Clinical Pharmacology Biopharmaceutics Review(s)			X	
Bioequivalence Review(s)			X	
Administrative Document(s)	X			
Correspondence			X	

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: NDA 19-778/S-028

Trade Name: Prinzide 20-12.5 and 20-25 mg Tablets

Generic Name:(lisinopril/hydrochlorthiazide)

Sponsor: Merck Research Laboratories

Approval Date: October 28, 1998

Indication: Provides for final printed labeling revisions.

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 19-778/S-028

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

NDA 19-778/S-028

OCT 28 1998

Merck Research Laboratories
Attention: Jeffery R. White, M.D.
Sumneytown Pike, P.O. Box 4
BLA-20
West Point, PA 19486

Dear Dr. White:

Please refer to your supplemental new drug application dated October 20, 1997, received October 23, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prinzide (lisinopril/hydrochlorothiazide) 20-12.5 and 20-25 mg Tablets.

We acknowledge receipt of your submission dated September 22, 1998 that constituted a full response to our January 7, 1998 action letter.

This supplemental new drug application provides for final printed labeling revised as follows:

DOSAGE AND ADMINISTRATION:

The first sentence has been revised to read "Lisinopril is an effective treatment of hypertension in once-daily doses of 10-80 mg, while hydrochlorothiazide is effective in doses of 12.5-50 mg."

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 final printed labeling included in your September 22, 1998 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:

Ms. Kathleen Bongiovanni
Regulatory Health Project Manager
(301) 594-5334

Sincerely yours,

R 2 10/28/98

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

cc:

Archival NDA 19-778

HFD-110/Div. Files

HF-2/MedWatch (with labeling)

HFD-002/ORM (with labeling)

HFD-101/ADRA (with labeling)

HFD-40/DDMAC (with labeling)

HFD-613/OGD (with labeling)

HFD-95/DDMS (with labeling)

HFD-810/DNDC Division Director

DISTRICT OFFICE

HFD-110/K.Bongiovanni

sb/10/5/98;10/22/98

Initialed by: J Short/10/5/98

K Srinivasachar/10/5/98

J Koerner/10/7/98

C Resnick/10/7/98

S Chen/10/13/98

N Morgenstern/10/21/98

filename: 19778s028ap.doc

APPROVAL (AP)

KBS
10 28 98

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 19-778/S-028

APPROVABLE LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-221/S-024

19-778/S-028

~~20-387/S-006~~

JAN 7 1998

Merck Research Laboratories
Attention: Larry P. Bell, M.D.
Sumneytown Pike
West Point, PA 19486

Dear Dr. Bell:

Please refer to your October 20, 1997 supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vasertic (enalapril maleate/hydrochlorothiazide) Tablets (NDA 19-221), Prinzide (lisinopril/hydrochlorothiazide) Tablets (NDA 19-778), and Hyzaar (losartan potassium/hydrochlorothiazide) Tablets (NDA 20-387).

The supplemental applications provide for draft labeling revised as follows:

DOSAGE AND ADMINISTRATION:

The second sentence has been revised to read "The usual dosage range of enalapril is 10 to 40 mg per day administered in a single or two divided doses; hydrochlorothiazide is effective in doses of 12.5 to 50 mg daily." The following sentence has been added: "Patients usually do not require doses of hydrochlorothiazide in excess of 50 mg daily when combined with other antihypertensive agents."

We have completed the review of these applications as submitted with draft labeling, and they are approvable. Before these applications may be approved, however, it will be necessary for you to submit final printed labeling revised as follows:

Please delete the sentence, "Patients usually do not require doses of hydrochlorothiazide in excess of 50 mg when combined with other antihypertensive agents."

Please submit 20 copies of the printed labels and other labeling, ten of which are individually mounted on heavy weight paper or similar material.

If additional information relating to the safety or effectiveness of these drugs becomes available, revision of the labeling may be required.

Within 10 days after the date of this letter, you are required to amend these applications, 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 these applications.

If you have any questions, please contact:

Ms. Kathleen Bongiovanni
Regulatory Health Project Manager
Telephone: (301) 594-5334

Sincerely yours,

RJL

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

cc:

Original NDA

HFD-110

HFD-92/DDM-DIAB

DISTRICT OFFICE

HFD-40/DDMAC (with labeling)

HFD-110/KBongiovanni

sb/12/24/97;1/6/98

R/D: RMittal/12/24/97

JShort/12/24/97

SZimmerman/12/29/97

RWolters/12/29/97

JKoerner/12/29/97

AProakis/1/5/98

CResnick/1/5/98

KKnudsen/1/5/98

CGanley/12/29/97

SChen/12/29/97

NMorgenstern/1/6/98

K Bongiovanni 1-6-98

Approval Date: 19-221 - 10/31/86

19-778 - 2/16/89

20-387 - 4/28/95

APPROVABLE (AE)