



NDA 19-778/S-032

Merck Research Laboratories
Attention: Michael C. Elia, Ph.D.
Director, Regulatory Affairs
Sumneytown Pike
P.O. Box 4, BLA-20
West Point, PA 19486

Dear Dr. Elia:

Please refer to your supplemental new drug application dated August 3, 2000, submitted pursuant to section 505(b)(2) 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 February 4, 2002 that constitutes a complete response to our May 26, 2001 action letter.

This supplemental new drug application provide for electronic final printed labeling (FPL) revised as follows:

1. A new subsection entitled *Geriatric Use* has been added to the **PRECAUTIONS** section as follows:

Geriatric Use

Clinical studies of PRINZIDE did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. In a multiple dose pharmacokinetic study in elderly versus young hypertensive patients using the lisinopril/hydrochlorothiazide combination, area under the plasma concentration time curve (AUC) increased approximately 120% for lisinopril and approximately 80% for hydrochlorothiazide in older patients.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection. Evaluation of the hypertensive patient should always include assessment of renal function. (See DOSAGE AND ADMINISTRATION.)

2. Under **DOSAGE AND ADMINISTRATION**, the subsection *Use in the Elderly* has been deleted.

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 submitted February 4, 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, please call:

Alisea Sermon, Pharm.D.
Regulatory Project Manager
(301) 594-5334

Sincerely,

{See appended electronic signature page}

Douglas C. Throckmorton M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
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/s/

Doug Throckmorton
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