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APPROVAL PACKAGE FOR:

APPLICATION NUMBER

20-386/S-019 and 029

Approval Letter(s)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-386/S-019 & 029

Merck and Co., Inc.
Attention: Jeffrey R. Tucker, M.D.
Sumneytown Pike
P.O. Box 4, BLA-20
West Point, PA 19486

Dear Dr. Tucker:

Please refer to your supplemental new drug applications dated August 25, 1999 (NDA 20-386/S-019) and December 21, 2001 (NDA 20-386/S-029), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cozaar (losartan potassium) 25, 50, and 100 mg Tablets.

We acknowledge receipt of your submissions dated February 27, 2004, (to NDA 20-386/S-019) and October 29, 2002, July 3 and October 28, 2003, and February 27, 2004 (to NDA 20-386/S-029). Your submissions of February 27, 2004 constituted a complete response to our April 11, 2000 and May 20, 2003 approvable letters for NDA 20-386/S-019 and our October 21, 2002 approvable letter for NDA 20-386/S-029.

Electronic Final Printed Labeling (FPL) was submitted on February 27, 2004, received March 1, 2004, revised as follows:

NDA 20-386/S-029

This supplemental new drug application provides for pediatric-related changes to the **CLINICAL PHARMACOLOGY, PRECAUTIONS, ADVERSE REACTIONS,** and **DOSAGE AND ADMINISTRATION** sections of the labeling. In addition, there are other, minor revisions to the **DESCRIPTION** and **CLINICAL PHARMACOLOGY** sections of the labeling.

NDA 20-386/S-019

1. Information regarding interactions of losartan with rifampin, fluconazole, and erythromycin has been added under **CLINICAL PHARMACOLOGY,** *Drug Interactions* and **PRECAUTIONS,** *Drug Interactions.*
2. Under **PRECAUTIONS,** the sub-heading "*Use in the elderly*" has been changed to "*Geriatric Use.*"

We have completed our review of these supplemental new drug applications, 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 electronic final printed labeling (package

inserts included in your submissions of February 27, 2004). Accordingly, these supplemental applications are 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. Edward Fromm
Regulatory Health Project Manager
(301) 594-5332

Sincerely,

/S/

{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

Enclosed Labeling Text

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

/s/

Doug Throckmorton
3/11/04 10:06:05 AM

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APPROVAL PACKAGE FOR:

APPLICATION NUMBER

20-386/S-019 and 029

Approvable Letter (S)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-386/S-029

AE Letter + Marked-up Draft Labeling

Merck & Co., Inc.
Attention: Michael C. Elia, Ph.D., DABT
Sumneytown Pike
P.O. Box 4, BLA-20
West Point, PA 19486

Dear Dr. Elia:

Please refer to your supplemental new drug application dated December 21, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cozaar (losartan potassium) Tablets, 25, 50 and 100 mg.

We acknowledge receipt of your submissions dated March 13 and 26, June 28, July 19 and October 2, 2002.

This supplemental new drug application proposes pediatric-related changes to the **CLINICAL PHARMACOLOGY, PRECAUTIONS**, and **DOSAGE AND ADMINISTRATION** sections of the labeling.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to submit final printed labeling (FPL) for the drug. The FPL should be identical in content to the enclosed draft labeling (text for the package insert).

In addition, all previous revisions as reflected in the most recently approved labeling 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.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL, ten of which individually mounted on heavy weight paper or similar material.

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

Within 10 days after the date of this letter, you are required to amend the 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 any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major

amendment nor will the review clock be reactivated until all deficiencies have been addressed.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with these changes prior to approval of this supplemental application.

If you have any questions, please contact:

Mr. Edward Fromm
Regulatory Health Project Manager
(301) 594-5332

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

Enclosure: Marked-up Draft Labeling

11 pages redacted from this section of the approval package consisted of draft labeling