



NDA 20-387/S-041

Merck & Co., Inc.
Attention: Kenneth A. Kramer, RPh
Sumneytown Pike
P.O. Box 4, BLA-20
West Point, PA 19486

Dear Mr. Kramer:

Please refer to your supplemental new drug application dated February 9, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hyzaar (losartan potassium/hydrochlorothiazide) 50-12.5, 100-12.5, and 100-25 mg Tablets.

We acknowledge receipt of your submission dated August 16, 2006.

This "Changes Being Effected" supplemental new drug application provides for electronic final printed labeling revised as follows:

1. Under the "**DESCRIPTION**" section, the second to last sentence was changed from:

HYZAAR 100-12.5 may also contain carnauba wax.

to:

HYZAAR 50-12.5, HYZAAR 100-12.5, and HYZAAR 100-25 may also contain carnauba wax.

2. Under the "**PRECAUTIONS/Drug Interactions/Losartan Potassium**" subsection, the following subheading and text were added:

Lithium: As with other drugs which affect the excretion of sodium, lithium excretion may be reduced. Therefore, serum lithium levels should be monitored carefully if lithium salts are to be co-administered with angiotensin II receptor antagonists.

3. Under the "**ADVERSE REACTIONS/Post-Marketing Experience**" subsection, the following subheading and text were added:

Skin: Erythroderma has been reported with losartan.

In addition, the following minor editorial changes were also noted:

1. Under the "**DESCRIPTION**" section, a comma was deleted from the first sentence so that it now reads:

HYZAAR* 50-12.5 (losartan potassium-hydrochlorothiazide), HYZAAR* 100-12.5 (losartan potassium-hydrochlorothiazide) and HYZAAR* 100-25 (losartan potassium-

hydrochlorothiazide) combine an angiotensin II receptor (type AT₁) antagonist and a diuretic, hydrochlorothiazide.

2. Under the “**CLINICAL PHARMACOLOGY**/*Mechanism of Action*” subsection, a comma was deleted from the third sentence so that it now reads:

Losartan and its principal active metabolite block the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT₁ receptor found in many tissues (e.g., vascular smooth muscle, adrenal gland).

3. The issue date at the end of the package insert has been updated so that it now reads:

Issued December 2005

We have completed our review of this supplemental new drug application, as amended. It is approved, effective on the date of this letter, for use as recommended in the electronic labeling submitted on August 16, 2006.

If you issue a letter communicating important information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
WO 22, Room 4447
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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:

Quynh Nguyen, Pharm.D.
Regulatory Health Project Manager
(301) 796-0510

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal 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/

Norman Stockbridge
8/29/2006 11:25:00 AM