DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-558/S-049
19-778/S-039

Merck & Company, Inc.
Attention: Mr. Kenneth Kramer
PO Box 1000, UG2CD-48
North Wales, PA 19454-1099

Dear Mr. Kramer:

Please refer to your supplemental new drug applications dated May 1, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prinivil® (lisinopril) 2.5, 5, 10, 20 and 40 mg Tablets (NDA 19-558) and Prinzide® (lisinopril/hctz) 20/12.5 and 20/25 Tablets (NDA 19-778).

These "Changes Being Effected" supplemental new drug applications provide for revisions to the **DESCRIPTION** (Prinivil, NDA 19-558), **PRECAUTIONS** and **HOW SUPPLIED** sections of the labeling.

These supplemental new drug applications provide for electronic draft labeling with the following revisions:

NDA 19-558

1. Under the **DESCRIPTION** section**:**
   The text referring to the 40 mg tablet was deleted.

2. Under the **PRECAUTIONS**, ***Drug Interactions*** the following text has been added describing nitritoid reactions occurring in patients:

   Gold: Nitritoid reactions (symptoms include facial flushing, nausea, vomiting and hypotension) have been reported rarely in patients on therapy with injectable gold (sodium aurothiomalate) and concomitant ACE inhibitor therapy including PRINIVIL.

3. Under the **HOW SUPPLIED** section the following revisions of product numbers and tablet descriptions were made due to change in manufacturing site:

   No. 8110 — Tablets PRINIVIL, 5 mg, are white, oval shaped compressed tablets with code MSD 19 on one side and scored on the other side. They are supplied as follows:
   NDC 0006-0019-54 unit of use bottles of 90.
   No. 8111 — Tablets PRINIVIL, 10 mg, are light yellow, oval shaped compressed tablets with code MSD 106 on one side and scored on the other side. They are supplied as follows:
   NDC 0006-0106-54 unit of use bottles of 90.
   No. 8112 — Tablets PRINIVIL, 20 mg, are peach, oval shaped compressed tablets with code MSD 207 on one side and scored on the other side. They are supplied as follows:
   NDC 0006-0207-54 unit of use bottles of 90.

NDA 19-778

1. Under the **PRECAUTIONS**, ***Drug Interactions*** the following text has been added describing nitritoid reactions occurring in patients:

   Gold: Nitritoid reactions (symptoms include facial flushing, nausea, vomiting and hypotension) have been reported rarely in patients on therapy with injectable gold (sodium aurothiomalate) and concomitant ACE inhibitor therapy including PRINIVIL.

2. Under the **HOW SUPPLIED** section the following revisions of product numbers and tablet descriptions were made due to change in manufacturing site:

   No. 8439 — Tablets PRINZIDE 10-12.5, are blue, hexagon-shaped tablets with code 145 on one side and plain on the other side. Each tablet contains 10 mg of lisinopril and 12.5 mg of hydrochlorothiazide. They are supplied as follows:
   NDC 0006-0145-58 unit of use bottles of 100.
   No. 8247 — Tablets PRINZIDE 20-12.5, are yellow, hexagon-shaped tablets with code MSD/140 on one side and scored on the other side. Each tablet contains 20 mg of lisinopril and 12.5 mg of hydrochlorothiazide. They are supplied as follows:
   NDC 0006-0140-58 unit of use bottles of 100.
   No. 3595 — Tablets PRINZIDE 20-25, are peach, round, fluted-edge tablets, coded MSD 142 on one side and PRINZIDE on the other. Each tablet contains 20 mg of lisinopril and 25 mg of hydrochlorothiazide. They are supplied as follows:
   NDC 0006-0142-31 unit of use bottles of 30
   NDC 0006-0142-58 unit of use bottles of 100.

We have completed our review of these applications, and they are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

We also note the corporate signature, **MERCK SHARP & DOHME LTD Cramlington, Northumberland, UK NE23 3JU** has been added to both labels.

The final printed labeling (FPL) must be identical to the submitted labeling dated May 1. 2006.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate these submissions "**FPL for approved supplement NDA 19-558/S-049 and NDA 19-778/S-039**." Approval of these submissions by FDA is not required before the labeling is used.

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
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please call:

Alisea Crowley, Pharm.D.
Senior Regulatory Project Manager
(301) 796-1144

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.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 this page is the manifestation of the electronic signature.

/s/

Norman Stockbridge

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