DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 18-200/S-026
NDA 18-201/S-040

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

Dear Mr. Kramer:

Please refer to your supplemental new drug applications dated February 5, 2003 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Midamor (amiloride HCl) 5 mg Tablets (NDA 18-200) and Moduretic (amiloride HCL/ hydrochlorothiazide) 5/50 mg Tablets (NDA 18-201).

These "Changes Being Effected" supplemental new drug applications provide for electronic final printed labeling revised as follows:

NDA 18-200 (Midamore)

Under the WARNINGS/ Hyperkalemia and PRECAUTIONS/ Drug Interactions subsections, the following has been added:

> "an angiotensin II receptor antagonist" to the list of agents that when administered concomitantly with amiloride hydrochloride may increase the risk of hyperkalemia

NDA 18-201 (Moduretic)

Under the WARNINGS/ Hyperkalemia and PRECAUTIONS/ Amiloride HCl subsections, the following has been added:

> "an angiotensin II receptor antagonist" to the list of agents that when administered concomitantly with amiloride hydrochloride may increase the risk of hyperkalemia

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the final printed labeling included in your submission dated February 5, 2003. Accordingly, these supplemental applications are 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:

Mr. Daryl Allis
Regulatory Health Project Manager
(301) 594-5309

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 this page is the manifestation of the electronic signature.

/s/

Doug Throckmorton

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