CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 18-200/S-024
NDA 18-201/S-037

Administrative Documents

RHPM Review of Draft Labeling
NDA's 18-200/S024 & 18-201/S037

Date of Submissions: June 28, 2001
Date of Review: July 16, 2001
Applicant Name: Merck & Co., Inc.
Product Names:
Midamor (amiloride hydrochloride) 5 mg Tablets (NDA 18-200)
Moduretic (amiloride HCl/hydrochlorothiazide) 5/50 mg Tablets (NDA 18-201)

Evaluation:

These supplements provide for draft labeling with the following revision to the **PRECAUTIONS**/*Geriatric Use* section of the labeling:

NDA 18-200 (Midamor)

Added sub-section:

> *Geriatric Use*
> Clinical studies of Midamor did not include sufficient numbers of subjects aged 65 and over to determine whether they responded 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.
> 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, and it may be useful to monitor renal function. (See CONTRAINDICATIONS, *Impaired Renal Function.*)

In addition, the following minor editorial changes were noted:

1. The molecular weight for this compound was changed from " [redacted] to "301.12."
2. The key for the Adverse Reactions table was revised.
3. The text "on one side and MIDAMOR on the other" was added to the **HOW SUPPLIED** section describing the code printed on the tablet.
4. The distribution section was revised by adding the company logo and text "**MERCK & CO., INC.,** West Point, PA 19486, USA."
5. The "Issued" date was revised.

NDA 18-201 (Moduretic)

Added sub-section:

> *Geriatric Use*
> Clinical studies of Moduretic did not include sufficient numbers of subjects aged 65 and over to determine whether they responded 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.
> 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, and it may be useful to monitor renal function. (See CONTRAINDICATIONS, *Impaired Renal Function.*)

In addition, the following minor editorial changes were noted:

1. The "Issued" date was revised.

These supplements were submitted electronically to the Electronic Document Room. The review was completed by comparing the proposed labeling, current labeling and the last approved final printed labeling in the archival jacket.

Recommendation:
An approvable letter should be issued for these supplements as set forth under 21 CFR 201.57 (f)(10)(ii)(A)(iii)(B) [Specific requirements on content and format of labeling for human prescription drugs; Precautions; Geriatric use].

/S/

Daryl Allis, RHPM

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

/s/

Daryl L. Allis
8/7/01 02:00:54 PM
CSO

RHPM Review of FPL
NDAs 18-200/S024 & 18-201/S037

Date of Submissions: June 28, 2001
Date of FPL: February 5, 2002
Date of Review: March 11, 2002
Applicant Name: Merck & Co., Inc.
Product Names:
Midamor (amiloride hydrochloride) 5 mg Tablets (NDA 18-200)
Moduretic (amiloride HCl/hydrochlorothiazide) 5/50 mg Tablets (NDA 18-201)

Evaluation:

These supplemental new drug applications provide for final printed labeling with the following revision to the **PRECAUTIONS**/*Geriatric Use* section of the labeling:

NDA 18-200/S-024 (Midamor)

Added sub-section:

Geriatric Use

Clinical studies of Midamor did not include sufficient numbers of subjects aged 65 and over to determine whether they responded 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.

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, and it may be useful to monitor renal function. (See CONTRAINDICATIONS, *Impaired Renal Function.*)

In addition, the "Issued" date and manufacturing code were revised.

NDA 18-201/S-037 (Moduretic)

Added sub-section:

Geriatric Use

Clinical studies of Moduretic did not include sufficient numbers of subjects aged 65 and over to determine whether they responded 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.

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, and it may be useful to monitor renal function. (See CONTRAINDICATIONS, *Impaired Renal Function.*)

In addition, the "Issued" date and the manufacturing code were revised.

These supplements were submitted electronically to the Electronic Document Room. The review was completed by comparing the proposed FPL with the last approved labeling/current package insert (February 2001). The FPL is identical to the changes included in the approvable letter dated August 7, 2001.

Recommendation:

An approval letter should be issued for these supplements as set forth under 21 CFR 201.57 (f)(10)(ii)(A)(iii)(B) [Specific requirements on content and format of labeling for human prescription drugs; Precautions; Geriatric use].

/S/

Daryl Allis, RHPM

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

/s/

Daryl L. Allis
3/20/02 10:51:57 AM
CSO