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APPROVAL PACKAGE FOR:

APPLICATION NUMBER
19-787/S-007

Administrative Documents

RHPM Review of Final Printed Labeling

Date: June 7, 1996

Application: NDA 19-787/S-007
Norvasc (amlodipine besylate) Tablets

JUN 14 1996

Sponsor: Pfizer

Document Date: June 4, 1996

Receipt Date: June 6, 1996

NDA 19-787 provides for labeling revised under the **CLINICAL PHARMACOLOGY** and **WARNINGS** sections to include additional safety data regarding the use of Norvasc in patients with heart failure.

An approvable letter was issued on April 22, 1996. A meeting was held between the Agency and the sponsor on May 28, 1996 to discuss the sponsor's counterproposals to our labeling recommendations (see background package dated May 22, 1996 and minutes of the meeting).

The following labeling changes were agreed upon:

The last paragraph of the **CLINICAL PHARMACOLOGY: Pharmacokinetics and Metabolism** subsection was revised to read as follows:

DRAFT

The following paragraph was moved from the end of the **CLINICAL PHARMACOLOGY: Pharmacodynamics** subsection to follow the second paragraph of that subsection:

> In hypertensive patients with normal renal function, therapeutic doses of Norvasc resulted in a decrease in renal vascular resistance and an increase in glomerular filtration rate and effective renal plasma flow without change in filtration fraction or proteinuria.

The entire text of the **CLINICAL PHARMACOLOGY: Studies in Patients with Congestive Heart Failure** subsection was replaced with the following paragraph:

DraPt

Draft

The entire text of the **PRECAUTIONS: Use in Patients with Congestive Heart Failure** subsection was replaced with the following paragraph:

Draft

The final printed labeling is identical to that which was agreed upon at the May 28 meeting, with the following minor exception:

The reference to the AUC in the last paragraph of the **CLINICAL PHARMACOLOGY: Pharmacokinetics and Metabolism** subsection was changed from [redacted] to "approximately 40-60%."

I recommend that the application be approved.

/S/

David Roeder
Regulatory Health Project Manager

dr/6-7-96

cc: NDA 19-787
HFD-110
HFD-110/DRoeder/SBenton

RHPM Approval Overview

JUN 14 1996

Application: NDA 19-787/S-007
Norvasc (amlodipine besylate) Tablets

Sponsor: Pfizer

Supplement Date: April 25, 1995

Supplement Type: SE5

NDA 19-787 provides for labeling revised under the **CLINICAL PHARMACOLOGY** and **WARNINGS** sections to include additional safety data regarding the use of Norvasc in patients with heart failure.

An approvable letter was issued on April 22, 1996. A meeting was held between the Agency and the sponsor on May 28, 1996 to discuss the sponsor's counterproposals to our labeling recommendations (see background package dated May 22, 1996 and minutes of the meeting). The sponsor submitted final printed labeling on June 6, 1996 (letter date: June 4, 1996).

There are no unresolved issues. The supplemental application can be approved.

/S/

David Roeder
Regulatory Health Project Manager

dr/6-10-96

cc: NDA 19-787
HFD-110
HFD-110/DRoeder