

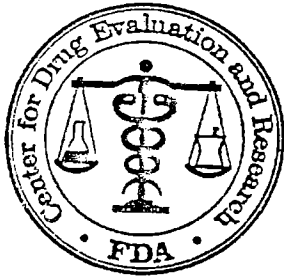
CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 19-787/S30

Medical Review(s)



DIVISION OF CARDIO-RENAL DRUG PRODUCTS

Clinical Review

NDA: 19-787 (amlodipine)
Sponsor: Pfizer Pharmaceuticals
Submission: SE5-030 (14 September 2001): response to a pediatric Written Request of 2 November 1999.

Review date: 6 November 2001

Reviewer: N. Stockbridge, M.D., Ph.D., HFD-110

Summary: The sponsor submitted results of two studies, parallel dose ranging and population pharmacokinetics. Exclusivity was granted. Labeling suggestions are made.

Distribution: NDA 19-787

HFD-110/Project Manager

Table of contents

1 Background	2
2 Labeling	3
3 Clinical studies	5
3.1 Protocol A0531018 (PATH-I): Pediatric use of amlodipine in the treatment of hypertension; a randomized, double-blind, placebo-controlled, parallel group dose-ranging study to evaluate the efficacy and safety of amlodipine in the treatment of hypertension in children	5
3.1.1 Study dates	5
3.1.2 Source materials reviewed	5
3.1.3 Protocol	5
3.1.4 Results	5
3.1.4.1 Conduct	5
3.1.4.2 Effectiveness	6
3.1.4.3 Safety	7
3.2 Protocol A0531023 (PATH-II): Pediatric use of amlodipine in the treatment of hypertension; a population pharmacokinetic trial	8
3.2.1 Study dates	8
3.2.2 Source materials reviewed	8
3.2.3 Protocol	8
3.2.4 Results	8
3.2.4.1 Conduct	8
3.2.4.2 Pharmacokinetics and pharmacodynamics	8
3.2.4.3 Safety	8
3.3 Other published data	9
4 Summary and recommendations	10

List of Tables

Table 1. Demographics in phase II (PATH-I)	6
Table 2. Change in systolic pressure (PATH-I)	6

List of Figures

Figure 1. Systolic and diastolic pressures by week (PATH-I)	7
---	---

1 Background

This supplement was received 17 September 2001. The user-fee goal date (10-month) is 17 July 2002.

The sponsor presents the results of two studies, a placebo withdrawal from two doses and a population pharmacokinetic study. In addition, the sponsor provides summaries of reports of clinical experience with amlodipine in children.

The studies used the commercially available tablet formulation for amlodipine. There are no chemistry issues.

The sponsor has provided a financial disclosure statement, denying inappropriate financial arrangements as defined under 21 CFR 54.2(a), (b), or (f).

**Appears This Way
On Original**

2 Labeling

The sponsor proposes inclusion of a description of the study results in the label for Norvasc (amlodipine besylate).

Under Pharmacokinetics, there is a new section, as follows:

[Redacted text block]

This section should be rewritten as follows:

[Redacted text block]

Following the section on effects in hypertension, the sponsor proposes to add the following:

[Redacted text block]

This section should be rewritten as follows:

[Redacted text block]

The sponsor proposes a specific new indication in hypertensive children. This change should be denied, since the only distinguishing characteristic of the new indication is the age group.

The sponsor proposes new language for Pediatric Use:

These data are not "unavailable"; they do not exist:

The sponsor proposes a new section of DOSAGE AND ADMINISTRATION:

Children

**Appears This Way
On Original**