



NDA 18-482/S-043

Pfizer Inc.
Attention: Ms. Rita A. Wittich
Director, Regulatory Affairs
235 East 42nd Street
New York, NY 10017

Dear Ms. Wittich:

Please refer to your supplemental new drug application dated November 3, 1998 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Procardia (nifedipine) Capsules.

We acknowledge receipt of your submissions dated January 20 and December 29, 2000. Your submission of December 29, 2000 constituted a complete response to our May 18, 1999 action letter.

This supplemental new drug application provides for copies of final printed labeling revised by the addition of the following:

PRECAUTIONS

Geriatric Use: Although small pharmacokinetic studies have identified an increase half-life and increased C_{max} and AUC (see **CLINICAL PHARMACOLOGY: Pharmacokinetics and Metabolism**), clinical studies of nifedipine did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in response 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.

CLINICAL PHARMACOLOGY

Pharmacokinetics and Metabolism

In healthy subjects, the elimination half-life of a BID sustained release nifedipine formulation [that was neither Procardia Capsules nor Procardia XL (nifedipine) Extended Release Tablets] was longer in elderly subjects (6.7 h) compared to young subjects (3.8 h) following oral administration. A decreased clearance was also observed in the elderly (348 ml/min) following intravenous administration.

Co-administration of nifedipine with grapefruit juice resulted in approximately a 2-fold increase in nifedipine AUC and C_{max} with no change in half-life. The increased plasma concentrations are most likely due to inhibition of CYP 3A4 related first-pass metabolism.

PRECAUTIONS

Other Interactions

Grapefruit Juice: Co-administration of nifedipine with grapefruit juice resulted in approximately a 2-fold increase in nifedipine AUC and C_{max} with no change in half-life. The increased plasma concentrations are most likely due to inhibition of CYP 3A4 related first-pass metabolism. Co-administration of nifedipine with grapefruit juice is to be avoided.

DOSAGE AND ADMINISTRATION

Co-administration of nifedipine with grapefruit juice is to be avoided (**see CLINICAL PHARMACOLOGY AND PRECAUTIONS: Other Interactions**).

In addition you modified the **How Supplied** section to reflect the current NDC codes.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted copies final printed labeling (package insert included in your December 29, 2000 submission). Accordingly, the supplemental application is 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:

Ms. Colleen LoCicero, RPh
Regulatory Health Project Manager
Telephone number: (301) 594-5332.

Sincerely,

{See appended electronic signature page}

Raymond J. Lipicky, 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/

Raymond Lipicky
2/22/02 10:06:59 AM