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APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 19-787/S30

Approval Letter(s)



NDA 19-787/S-030

Pfizer Inc.
Attention: Mr. Robert Clark
235 East 42nd Street
New York, NY 10017

Dear Mr. Clark:

Please refer to your supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Norvasc (amlodipine besylate) 2.5, 5 and 10 mg Tablets.

We acknowledge receipt of your submissions dated October 23, 2002, March 21 and October 3, 2003. The submission dated October 3, 2003 constituted a complete response to our July 17, 2002 action letter.

This supplemental new drug application provides for electronic final printed labeling revised as follows:

1. The **CLINICAL PHARMACOLOGY, Pharmacokinetics and Metabolism, Pediatric Patients** subsection reads as follows:

Pediatric Patients: Sixty-two hypertensive patients aged greater than 6 years received doses of NORVASC between 1.25 mg and 20 mg. Weight-adjusted clearance and volume of distribution were similar to values in adults.

2. Under **CLINICAL PHARMACOLOGY, Effects in Hypertension,**

a) The first paragraph was placed under the heading "*Adult Patients*".

b) The **Adolescents and Pediatric Patients Ages 6 to 17 years** subsection was retitled and changed as follows:

Pediatric Patients: Two-hundred sixty-eight hypertensive patients aged 6 to 17 years were randomized first to NORVASC 2.5 or 5 mg once daily for 4 weeks and then randomized again to the same dose or to placebo for another 4 weeks. Patients receiving 5 mg at the end of 8 weeks had lower blood pressure than those secondarily randomized to placebo. The magnitude of the treatment effect is difficult to interpret, but it is probably less than 5 mmHg systolic on the 5 mg dose. Adverse events were similar to those seen in adults.

3. The following statement proposed under **INDICATIONS AND USAGE, Hypertension** was deleted:

T(b)(4)-----

4. The **PRECAUTIONS, Pediatric Use** reads as follows:

The effect of Norvasc on blood pressure in patients less than 6 years of age is not known.

5. The **DOSAGE AND ADMINISTRATION, Children** reads as follows:

The effective antihypertensive oral dose in pediatric patients ages 6-17 years is 2.5 mg to 5 mg once daily. Doses in excess of 5 mg daily have not been studied in pediatric patients. See **CLINICAL PHARMACOLOGY**.

We have completed our review of this supplemental new drug application. It is approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on October 3, 2003.

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. Denise M. Hinton, Regulatory Health Project Manager, at (301) 594-5333.

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

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/s/

Doug Throckmorton
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