CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 19787/S021

APPROVAL LETTER

FEB 1 2000

NDA 19-787/S-021

Pfizer Inc.
Attention: Jean Lyons, MS
235 East 42nd Street
New York, NY 10017-5755

Dear Ms. Lyons:

Please refer to your supplemental new drug application (NDA) dated August 4, 1999, received August 5, 1999, submitted under section 505 (b) of the Federal Food, Drug, and Cosmetic Act for Norvasc (amlodipine besylate) Tablets, 2.5 mg, 5.0 mg and 10.0 mg.

The supplemental application provides for a packaging modification to the closure lining system from a

We have completed the review of this supplemental application and it is approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

Sincerely yours,

/S/ 2-1-00

Kasturi Srinivasachar, Ph.D.
Chemistry Team Leader, DNDC I
Division of Cardio-Renal Drug Products (HFD-110)
Office of New Drug Chemistry
Center for Drug Evaluation and Research

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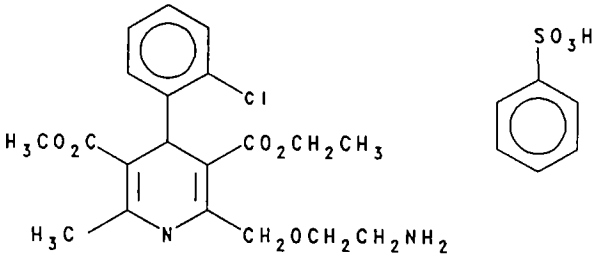
APPLICATION NUMBER: NDA 19787/S021

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW	1. ORGANIZATION HFD - 110	2. NDA Number 19-787
3. Name and Address of Applicant (City & State) Pfizer, Inc. 235 East 42nd Street New York, NY 10017-5755		4. Supplement(s) Number(s) SCP-021 Date(s) 08-04-99
5. Drug Name NORVASC	6. Nonproprietary Name Amlodipine Besylate	8. Amendments & Other (reports, etc) - Dates
7. Supplement Provides For: SPECIAL SUPPLEMENT - CBE a packaging modification to the closure lining system from for Norvasc Tablets.		
9. Pharmacological Category Antihypertensive and Antianginal	10. How Dispensed /x/ RX /__/ OTC	11. Related IND(s)/ NDA(s)/DMF(s)
12. Dosage Form(s) Tablet	13. Potency(ies) 2.5, 5, and 10 mg	
14. Chemical Name and Structure 3-Ethyl-5-methyl-2-(2-aminoethoxymethl)-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5-pyridinedicarboxylate benzenesulfonic acid 		15. Records/Reports Current /x/ Yes /__/ No Reviewed /x/ Yes /__/ No
16. Comments: Satisfactory,		
17. Conclusions and Recommendations: Satisfactory and recommended for approval.		
18. REVIEWER		
Name Ramsharan D. Mittal	Signature /S/	Date Completed 01/31/00
19. Distribution: /__/ Original Jacket /__/ Reviewer /__/ Division File /__/ CSO		

/S/
1-31-00

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CORRESPONDENCE

ORIGINAL

Pfizer Pharmaceuticals Group
Pfizer Inc
235 East 42nd Street
New York, NY 10017-5755
Tel 212 573 5999 Fax 212 573 1563
Email lyonsj@pfizer.com

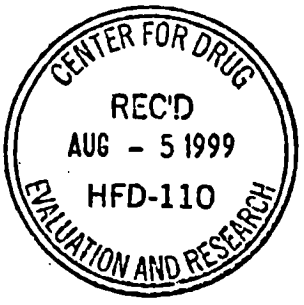
Pfizer Pharmaceuticals Group

Jean Lyons, MS
Director
Regulatory Affairs

NDA NO. 19-787 REF. NO. 021
NDA SUPPL FOR SCP

August 4, 1999

Raymond Lipicky, M.D., Director
Division of Cardio Renal Products (HFD-110)
Center for Drug Evaluation and Research
Office of Drug Evaluation I
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857



Re: Norvasc (amlodipine besylate) Tablets
NDA 19-787
SPECIAL SUPPLEMENT-CHANGES BEING EFFECTED

Dear Dr. Lipicky,

This submission is to notify you of a planned packaging change for Norvasc (amlodipine besylate) Tablets.

At the present time, Norvasc Tablets are packaged in bottles with continuous threaded closures. Specifically, this proposed packaging modification is to the closure lining system and involves a change from

Please note that Pfizer requested guidance from the Agency regarding the appropriate filing strategy and required data to support the requested change and received a response on September 9, 1998 (Appendix I). The response confirmed submission as a "Special Supplement - Changes Being Effected" and identified the necessary technical information to support this modification.

ORIGINAL

Included in the September 9th correspondence was the requirement that product release testing on at least one batch packaged with the proposed heat seal be performed in order to establish that the sealing process does not adversely affect the drug product.

Pfizer performed studies on the heat sealing method to determine the potential exposure of the product to heat and the results demonstrate there is no significant exposure. Therefore, the heat sealing process does not adversely affect the product (Appendix II). This information was reviewed during a teleconference on April 6, 1999 with Eric Sheinin, Ph.D. and Susan Lange M.P.H. who confirmed that based upon this data, product release testing on one batch packaged with the proposed heat seal method is not required.

An additional technical requirement outlined in the September 9th letter requested the results of USP Water Vapor Permeation Testing on the proposed container closure system with and without the innerseal. The resulting data (Appendix VIII) in the 30 cc bottle with the innerseal in place demonstrates compliance with the classification of a "tight container". In addition, the data also confirms compliance with the classification of a "well-closed" container, without the innerseal in place. Data has been generated that demonstrates Norvasc maintains the approved moisture specification limits throughout the use of the product with the innerseal removed (Appendix III). This information was also addressed in the April 6, 1999 teleconference.

Pursuant to 21 CFR 314.70(c)(1), we hereby propose this supplement be executed as a "Special Supplement - Changes Being Effected". Implementation of the change is proposed to occur within 30 days of the date of this letter with the commitment to place product from the first production batch, with the packaging modification, on stability based on the approved protocol.

Should you have any questions, please contact me.

Sincerely,

Jean Lyons
Enclosures
Desk Copy: David Roeder David (Fax cover letter only)