CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

18-998/S-062

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER(S)

NDA 18-998/S-062

Trade Name: Vasotec

Generic Name(s): (enalaprilat)

Sponsor: Merck and Company, Inc.

Agent:

Approval Date: April 3, 2002

Indication: The treatment of hypertension.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 18-998/S-062

Approval Letter(s)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 18-998/S-062

Merck and Company, Inc.
Attention: Virginia Snyder
P.O. Box 4, BLA-20
Sumneytown Pike
West Point PA 19486

Dear Ms. Snyder:

Please refer to your supplemental new drug application dated November 30, 2001, received December 3, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vasotec (enalapril maleate) Tablets, 2.5 mg, 5 mg, 10 mg and 20 mg.

We acknowledge receipt of your submission dated April 2, 2002.

This supplemental new drug application provides for updated specifications for Vasotec tablets incorporating the deletion of initially approved methods for Assay, Identity, and Related Substances (R02), Dissolution (R04) and Dose Uniformity (R06).

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.

If you have any questions, call Sandra L. Birdsong, Regulatory Project Manager, at (301) 594-5312.

Sincerely,

{See appended electronic signature page}

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

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/s/

Kasturi Srinivasachar
4/3/02 06:39:53 PM

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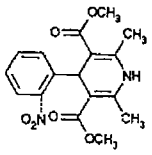
APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 18-998/S-062

Chemistry Review(s)

CHEMIST'S REVIEW	1. ORGANIZATION HFD-110	2. NDA Number 18-998
3. Name and Address of Applicant (City & State) Merck & Co., Inc.		4. Supplement(s) Number(s) Date(s) S-062 11/30/01 (CDER Date: 12/3//01)
5. Drug Name Vasotec	6. Nonproprietary Name enalapril maleate	8. Amendments: None S/A 4/2/02 (Rec. 4/3/02)
7. Supplement Provides for the deletion of previously approved analytical methods for Assay, Identity, and Related Substances (R02), Dissolution (R04) and Dose Uniformity (R06) for Vasotec .		
9. Pharmacological Category antihypertensive	10. How Dispensed [X] Rx [ ] OTC	11. Related NDA(s):
12. Dosage Form(s) Oral Tablets	Potency(ies) 2.5, 5, 10 & 20mg	
14.Chemical Name and Structure:  $C_{17}H_{18}N_2O_6$ 346.34 3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-, dimethyl ester. Dimethyl 1,4-dihydro-2,6-dimethyl-4-(*o*-nitrophenyl)-3,5-pyridinedicarboxylate {*21829-25-4*}.		15. Records/Reports Current

16. Comments: This is a PA supplement. The firm proposes to delete the HPLC method used for the assay since the current regulatory method has been found to have a low bias of about —— as evidenced by convincing comparative testing data that supports the change. In addition, it is proposed to delete the other related testing categories that also use this methodology (e.g., content uniformity and dissolution). In this regard, it is also noted that degradants are also tested using this method but are not included in the categorical deletion provided in the cover letter; this is considered to be an oversite and not a deficiency issue since there is reference to the evaluation of the related substances in the method description as given on page 3 of Reference #1 that deals with the deleted methods.

File:S-062(11-30-01)NDA 18998 (PM is S. Birdsong)

17. Conclusions and Recommendations: Send approval letter.

Name	Signature	Date Completed
Stuart Zimmerman		4/3/02

3 Page(s) Withheld

X § 552(b)(4) Trade Secret / Confidential

___ § 552(b)(5) Deliberative Process

___ § 552(b)(4) Draft Labeling

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/s/

Stuart Zimmerman
4/3/02 06:19:05 PM
CHEMIST

Kasturi Srinivasachar
4/3/02 06:25:39 PM
CHEMIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 18-998/S-062

Administrative/Correspondence

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-998/S-062

Merck & Co., Inc.
Attention: Ms. Virginia G. Snyder
Sumneytown Pike
P.O. Box 4, BLA-20
West Point, PA 19486

Dear Ms. Snyder:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: VASOTEC (enalapril maleate) Tablets

NDA Number: 18-998

Supplement number: S-062

Date of supplement: November 30, 2001

Date of receipt: December 3, 2001

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on February 1, 2002 in accordance with 21 CFR 314.101(a).

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service:
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products, HFD-110
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products, HFD-110
Attention: Division Document Room
1451 Rockville Pike
Rockville, Maryland 20852

If you have any questions, please call:

Ms. Sandra Birdsong
Regulatory Project Manager
(301) 594-5334

Sincerely yours,

Natalia A. Morgenstern
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Zelda McDonald
12/10/01 04:00:26 PM
For Natalia Morgenstern