CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 19-766/S025

Trade Name: Zocor Tablets

Generic Name: Simvastatin

Sponsor: Merck & Company, Inc.

Approval Date: December 2, 1997

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 19-766/S025

CONTENTS

Reviews / Information Included in this NDA Review.	
Approval Letter	X
Approvable Letter	
Labeling	
Medical Review(s)	
Chemistry Review(s)	X
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/ Biopharmaceutics Review(s)	
Administrative/Correspondence Document(s)	X

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APPLICATION NUMBER:

NDA 19-766/S025

APPROVAL LETTER

NDA 19-766/S-025

DEC - 2 1997

Merck Research Laboratoris
Attention: Robert E. Silverman, M.D., Ph.D.
Sumneytown Pike
West Point, PA 19486

Dear Dr. Silverman:

Please refer to your supplemental new drug application dated July 25, 1997, received July 29, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zocor (simvastatin) tablets.

The User Fee goal date for this application is January 29, 1998.

The supplemental application provides for the addition of a test method and specification for a _____ in simvastatin drug substance.

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

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

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 contact Margaret Simoneau, R.Ph., Regulatory Management Officer, at (301) 827-6430.

Sincerely yours,

Stephen K. Moore 12-2-97

Stephen K. Moore, Ph.D.
Chemistry Team Leader I, DNDC II
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:

Original NDA 19-766
HFD-510/Div. Files
HFD-510/CSO/M. Simoneau
HFD-510/E.Barbehenn/B.Berlin/S.Moore
HFD-820/ONDC Division Director
HFD-92/DDM-DIAB
DISTRICT OFFICE

Drafted by: Mas/November 18, 1997/19766.025 Aug 12.2.97
Initialed by:E.Barbehenn 11/18/97/B.Berlin 11/24/97/S.Moore 11/24/97/E.Galliers11/26/97
final: Mas 12/1/97

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-766/S025

CHEMISTRY REVIEW(S)

ORIGINAL

CHEMISTS REVIEW	1. ORGANIZATION	2. NDA NUMBER OCT 23 1997
	DMEDP II, HFD-510	19-766
3. NAME AND ADDRESS OF APPLICANT		4. SUPPLEMENT NUMBER, DATE
Merck Research Labs. P.O. Box 4, BLA-20 West Point, PA 19486		SCS-025 7-25-97
5. PROPRIETARY NAME	6. NAME OF THE DRUG	7. AMENDMENTS, REPORT, DATE
Zocor Tablets	Simvastatin	
8. SUPPLEMENT PROVIDES FOR		
The addition of a test and specification for the [redacted] in the simvastatin drug substance.		
9. PHARMACOLOGICAL CATEGORY	10. HOW DISPENSED	11. RELATED IND, NDA, DMF
Antihypercholestremic	RX	
12. DOSAGE FORM	13. POTENCY	
Tablets	10, 20, 40 mg	
14. CHEMICAL NAME AND STRUCTURE		
See Chemistry Review #1		

15. COMMENTS

The sponsor intends to add a test and specification for the [redacted] for the drug substance simvastatin (structures provided p. 4), with a limit of [redacted] by peak area on the HPLC chromatogram. The sponsor claims that the impurity has probably always been present, but advances in analytical techniques have made it possible to accuately detect and quantify this impurity. The impurity occurs due to the [redacted]. Therefore, the sponsor has also provided a test and specification for [redacted] in the [redacted] controll sheet for this substance. Batch analysis has provided evidence that [redacted] has been present at a level of about [redacted] of lovastatin for the past 4 years, consistently. A limit of [redacted] has been set for [redacted] The HPLC method to determine [redacted] in the drug substance is identical to that for Assay of the drug substance, except that the detection is done at [redacted] nm and the [redacted] is well separated from simvastatin by this method. Lastly, data from bulk drug substance lots produced during 1992-1997 were provided, and the largest amount of the impurity recorded has been [redacted] %.

16. CONCLUSION AND RECOMMENDATION

The sponsor has provided adequate justification for the proposed test and specification for [redacted] in the bulk drug substance. The method of anlaysis for this impurity is essentially identical to that approved for assay of the drug substance, however, this method will be validated by FDA labs. Issue an approval letter.

17. NAME	18. REVIEWERS SIGNATURE	19. DATE COMPLETED
WILLIAM K. BERLIN		10-23-97

DISTRIBUTION: ORIGINAL JACKET CSO REVIEWER DIVISION FILE

Stephen K. Moore
10/23/97

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-766/S025

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-766/S-025

AUG 13 1997

MERCK RESEARCH LABORATORIES, INC.
Sumneytown Pike
West Point, PA 19486

Attention: Robert E. Silverman, M.D., Ph.D., Senior Director, Regulatory Affairs

Dear Dr. R. E. Silverman:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: ZOCOR (Simvastatin) Oral Tablets

NDA Number: 19-766

Supplement Number: S-025

Date of Supplement: July 25, 1997

Date of Receipt: July 29, 1997

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on September 27, 1997, in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Attention: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

/Mark F. Johnson FOR

Enid Galliers
Chief, Project Management Staff
Division of Metabolic and Endocrine
Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Original NDA 19-766/S-025
HFD-510/Div. Files
HFD-510/CSO/M. Simoneau

filename:

SUPPLEMENT ACKNOWLEDGEMENT

NDA NO. 19766 REF. NO. 025

NDA SUPPL FOR SCS

ORIGINAL

NDA SUPPLEMENT

Robert E. Silverman, M.D., Ph.D.
Senior Director
Regulatory Affairs

Merck & Co., Inc.
P.O. Box 4
West Point PA 19486
Fax 610 397 2516
Tel 610 397 2944
215 652 5000

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MERCK
Research Laboratories

July 25, 1997

Solomon Sobel, M.D. - Director
Division of Metabolism and Endocrine
Drug Products HFD-510, Room 14B-04
Office of Drug Evaluation II (CDER)
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
JUL 29 1997
HFD-510

Dear Dr. Sobel:

SPECIAL SUPPLEMENT - CHANGES BEING EFFECTED

NDA 19-766: ZOCOR™ (Simvastatin)

Pursuant to Section 505(b) of the Food Drug and Cosmetic Act and in accordance with 21 CFR 314.70(c), we submit, for your approval, a supplement to NDA 19-766.

As indicated on the attached Form FDA 356h, the supplemental application provides for changes in Item 3 of the approved New Drug Application for ZOCOR™.

The attached supplemental application provides for the addition of a test method and specification for a [redacted] in simvastatin drug substance. [redacted] is not a new [redacted] in simvastatin; however, it has only currently been observed due to recent studies using the advanced technology of mass spectroscopy.

Pursuant to 21 CFR 314.70(a), a complete field copy of the supplement has been submitted to the FDA Philadelphia District Office.

As required by Section 306(k)(l) of the Generic Drug Enforcement Act [21 U.S.C. 335a (k)(l)], we hereby certify that, in connection with this application, Merck & Co., Inc. did not and will not use in any capacity the services of any person debarred under subsections 306 (a) or (b) of the Act.

We consider the filing of this Supplemental New Drug Application to be a confidential matter, and request the Food and Drug Administration not to make its content, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Questions concerning this supplemental application should be directed to Robert E. Silverman, M.D., Ph.D. (610/397-2944) or, in my absence, Bonnie J. Goldmann, M.D. (610/397-2383).

REVIEWS COMPLETED

CSO ACTION:
☑ LETTER ☐ N.A.I. ☐ MEMO
mas 12-2-97 AP letter
CSO INITIALS DATE

Sincerely yours,

Robert E. Silverman, M.D., Ph.D.
Senior Director
Regulatory Affairs

Attachments

Certified No. P. 963 213 144

Desk Copy: Philadelphia District Office, FDA
U.S. Custom House, Room 900
2nd & Chestnut Streets
Philadelphia, PA 19106-2973

q:\saxon\murakami\19-766\spsubch3.doc

noted - level of very low amount.
EKB
9/25/97