

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

19-766/S041

Trade Name: Zocor Tablets

Generic Name: simvastatin

Sponsor: Merck & Co., Inc.

Approval Date: March 15, 2000

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-766/S041

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**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

19-766/S041

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-766/S-041

MAR 15 2000

Merck & Co., Inc.
Attention: Robert Silverman, M.D., Ph.D.
Senior Director, Regulatory Affairs
Sumneytown Pike, P. O. Box 4
BLA-20
West Point, PA 19486

Dear Dr. Silverman:

Please refer to your supplemental new drug application dated September 15, 1999, received September 16, 1999, submitted pursuant to section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Zocor (simvastatin) Tablets.

This "Changes Being Effectuated" supplemental new drug application provides for changes that encompass the deletion of a listed process parameter and a categorical exclusion from the requirement to prepare an environmental assessment.

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 Margaret Simoneau, R.Ph., Regulatory Management Officer, at (301) 827-6418.

Sincerely,

Stephen K. Moore 3/15/2000

Stephen K. Moore, Ph.D.
Chemistry Team Leader I for
Division of Metabolic and Endocrine Drug Products,
(HFD-510)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

cc:

Archival NDA 19-766

HFD-510/Div. Files

HFD-510/M. Simoneau

HFD-510/SMoore/Skelly

HFD-095/DDMS-IMT

HFD-820/DNDC Division Director

DISTRICT OFFICE

Drafted by: Mas/March 15, 2000

Initialed by:SKelly3.15.00/JRhee for Enid Galliers3.15.00

final:Mas3.15.00

filename: 19766.41

APPROVAL (AP)

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
19-898/S041

CHEMISTRY REVIEW(S)

MAR 14 2000

CHEMIST'S REVIEW		
1. ORGANIZATION CDER/HFD-510 Division of Metabolism and Endocrine Drug Products		2. NDA # 19-766 Original NDA approved: 23-DEC-1991
3. NAME AND ADDRESS OF APPLICANT Merck & Co., Inc. P.O. Box 4 West Point PA 19486 (Phone): 610-397-2944		4. SUPPLEMENT SCS-041 15-SEPT-99 (Rec'd 16-SEPT-99)
		5. Name of the Drug ZOCOR™
		6. Nonproprietary Name Simvastatin
7. SUPPLEMENT PROVIDES for changes that encompass the deletion of a listed process parameter and a categorical exclusion from the requirement to prepare an environmental assessment.		8. AMENDMENT --
9. PHARMACOLOGICAL CATEGORY HMG-CoA inhibitor used to treat hyper-lipidemia	10. HOW DISPENSED Oral	11. RELATED -N. A. -
12. DOSAGE FORM Tablet	13. POTENCY 80 mg	
14. CHEMICAL NAME AND STRUCTURE Butanoic acid, 2,2-dimethyl-, 1,2,3,7,8,8α-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)-ethyl]-1-naphthalenyl ester, [1S-[1α,3α,7β,8β(2S*,4S*),-8αβ]]; C ₂₅ H ₃₈ O ₅ , F.W. = 418.57, CAS 56180-94-0 (For the structure, see Chemistry Review #1, dated 16-MAR-1988 in Vol. 3.1 of NDA 19-766).		
15. COMMENTS See next page.		
16. CONCLUSIONS AND RECOMMENDATIONS Satisfactory CMC information has been provided for this CBE supplement to support the technical justification for changing a process parameter. The request for categorical exclusion from the requirements to prepare an Environmental Assessment is reasonable. Issue Approval letter.		
17. REVIEWER NAME (AND SIGNATURE) COMPLETED 14-MAR-2000 Sharon Kelly, PhD R/D INITIATED BY <i>Sharon Kelly</i>		DATE <i>March 14, 2000</i>
filename: 19766NDASup		
DISTRIBUTION: Original: sNDA 19-766 cc: HFD-510 Division File CSO Reviewer		

AP

1 *Stephen Moore*
3/14/2000

1 Page(s) Withheld

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

 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

19-766/S041

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-766/S-041

Merck & Co., Inc.
Sumneytown Pike, P.O. Box 4
BLA-20 West Point, PA 19486

SEP 27 1999

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

Dear Dr. Silverman:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: ZOCOR™ (simvastatin)

NDA Number: 19-766

Supplement Number: S-041

Date of Supplement: September 15, 1999

Date of Receipt: September 16, 1999

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on November 15, 1999, 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,

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

NDA 19-766/S-041

Page 2

cc:

Original NDA 19-766/S-041

HFD-510/Div. Files

HFD-510/CSO/P.Simoneau

filename: C:\WPFILES\19766.WPD

SUPPLEMENT ACKNOWLEDGEMENT

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

**These copies are
OFFICIAL FDA Copies
not desk copies.**

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

September 15, 1999

NDA NO. 19-766 REF NO. 041

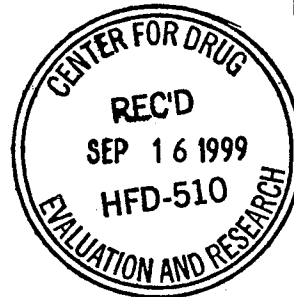
NDA SUP FOR SCS



MERCK

Research Laboratories

Solomon Sobel, MD, 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



Dear Dr. Sobel:

NDA 19-766: ZOCOR™ Tablets 80 mg (Simvastatin)

SPECIAL SUPPLEMENT - CHANGES BEING EFFECTED

Reference is made to the supplemental New Drug Application for ZOCOR™ Tablets 80 mg cited above.

Pursuant to Section 505(b) of the Food Drug and Cosmetic Act and in accordance with 21 CFR 314.70 (c), we submit a supplement to NDA 19-766. As indicated on the attached Form FDA 356h, this supplemental application provides for changes in the Chemistry Section of the approved New Drug Application for ZOCOR™. The supplemental application provides for changes that encompass the deletion of a listed process parameter. The supporting documentation includes a technical justification to clarify the phrasing of the current manufacturing process description, a detailed description, the annotated and clean copies of the manufacturing process description and a request for a categorical exclusion.

In accordance with the Food and Drug Administration Modernization Act of 1997, as indicated in the attached Form 3397, no user fee is required for this supplemental application.

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

Merck & Co., Inc. is requesting a categorical exclusion for the requirements to prepare an Environmental Assessments under 21 CFR 25.31(a). This supplement meets the requirements of a categorical exclusion under 21 CFR 25.31(a) because it will not increase the use of the active moiety. To the best of the firm's knowledge no extraordinary circumstances exist in regards to this action.


Solomon Sobel, MD, Director
NDA 19-766: ZOCOR™ Tablets 80 mg (Simvastatin)
Page 2

As required by Section 306(k)(1) of the Generic Enforcement Act [21 U.S.C. 335a(k)(1)], 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 that the Food and Drug Administration not 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, MD, PhD, (610/397-2944) or, in my absence, to Bonnie J. Goldmann, MD (610/397-2383).

Sincerely,



Robert E. Silverman, MD, PhD
Senior Director, Regulatory Affairs

Attachments

Federal Express

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

Q:\Michener\Tisa\Letters\NDA19-766

REVIEWS COMPLETED	
CSO ACTION:	
<input type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
CSO INITIALS	DATE

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-02
Expiration Date: 04-30-01

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

1. APPLICANT'S NAME AND ADDRESS

Merck & Co., Inc.
Sumneytown Pike, BLA-10
P. O. Box 4
West Point, PA 19486

2. TELEPHONE NUMBER (Include Area Code)

(610) 397-2383

5. USER FEE I.D. NUMBER

3. PRODUCT NAME

ZOCOR (Simvastatin)

4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?
IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW:

- ☐ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION
☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO (APPLICATION NO. CONTAINING THE DATA).

6. LICENSE NUMBER / NDA NUMBER

N019766

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92
(Self Explanatory)

☒ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
(See item 7, reverse side before checking box.)

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act
(See item 7, reverse side before checking box.)

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act
(See item 7, reverse side before checking box.)

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY.
(Self Explanatory)

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?

☐ YES ☐ NO

(See reverse side if answered YES)

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0297)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please DO NOT RETURN this form to this address.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE

Bonnie J. Goldmann

TITLE Bonnie J. Goldmann, M.D.
Vice President, Domestic Liaison
Regulatory Affairs

DATE

September 15, 1991