CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 19-766/S023

Trade Name: Zocor Tablets

Generic Name: simvastatin

Sponsor: Merck Research Laboratories

Approval Date: September 9, 1997

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APPLICATION NUMBER:
NDA 19-766/S019

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APPLICATION NUMBER:

NDA 19-766/S023

APPROVAL LETTER

NDA 19-766/S-023

Merck Research Laboratories
Attention: Robert E. Silverman, M.D., Ph.D.
P.O. Box 4, BLA-20
Sumneytown Pike
West Point, PA 19486

SEP 9 1997

Dear Dr. Silverman:

Please refer to your supplemental new drug application dated May 19,1997, received May 22, 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 November 22, 1997.

The supplemental application provides for deletion of the original GC methods for [redacted] with a new GC method and an alternative method (both formerly alternate methods), and deletion of the original [redacted] in the drug substance and replacement with a new GC method (formerly an alternate method).

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, please contact Ms. Margaret Simoneau, R.Ph., at (301)-827-6430.

Sincerely yours,

Stephen K. Moore 9/9/97

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/MSimoneau
HFD-510/WBerlin/SMoore
HFD-820/ONDC Division Director
HFD-92/DDM-DIAB
DISTRICT OFFICE

Drafted by: mas/September 3, 1997/n19766.s23
Initialed by: WB/9/3/&4/SM/9/3,4&9//EG9/9/97
final:MSimoneau 9/9/97

APPROVAL (AP)

FOI: Please redact the phrases [redacted] and [redacted] the above.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-766/S023

CHEMISTRY REVIEW(S)

ORIGINAL

Addendum to Chemistry Review of N 19-766/S-023

CHEMISTS REVIEW	1. ORGANIZATION	2. NDA NUMBER SEP 4 1997
	DMEDP II, HFD-510	19-766
3. NAME AND ADDRESS OF APPLICANT		4. SUPPLEMENT NUMBER, DATE
Merck Research Labs. Sumneytown Pike West Point, PA 19486		SCS-023 5-19-97
5. PROPRIETARY NAME	6. NAME OF THE DRUG	7. AMENDMENTS, REPORT, DATE
Zocor	Simvastatin	

8. SUPPLEMENT PROVIDES FOR

1. Deletion of the original GC methods for [redacted] and replacement with a new GC method and an alternate method (both previously alternate methods), and 2. deletion of the original GC method for [redacted] in the drug substance and replacemnt with a new GC method (formerly an alternate method).

9. PHARMACOLOGICAL CATEGORY	10. HOW DISPENSED	11. RELATED IND, NDA, DMF
antihypercholestremic	RX	
12. DOSAGE FORM	13. POTENCY	
tablets, oral	10,20,40 mg	

14. CHEMICAL NAME AND STRUCTURE

See Chemistry Review #1

15. COMMENTS

Based on discussions with the sponsor (telephone conversation 9/4/97 between Dr. S. Moore of the agency and Dr. R. Silverman of Merck), the wording in the "Supplement Provides For" section was clarified. The original method was roughly equivalent to the USP method for [redacted], and the proposed method differs only slightly more [redacted] and will not be validated.

16. CONCLUSION AND RECOMMENDATION

This addendum to the original chemistry reveiw of this SNDA is for the purpose of clarification of the "Supplement Provides For" statement. Since the proposed method for analysis [redacted] differs little from the USP method, no method validation will be performed. Issue an approval letter.

17. NAME	18. REVIEWERS SIGNATURE	19. DATE COMPLETED
WILLIAM K. BERLIN		9-4-97

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Stephen K. Moore
9/4/97

ORIGINAL

CHEMISTS REVIEW	1. ORGANIZATION	2. NDA NUMBER JUL 17 1997
	DMEDP II, HFD-510	19-766
3. NAME AND ADDRESS OF APPLICANT		4. SUPPLEMENT NUMBER, DATE
Merck Research Labs. Sumneytown Pike West Point, PA 19486		SCS-023 5-19-97
5. PROPRIETARY NAME	6. NAME OF THE DRUG	7. AMENDMENTS, REPORT, DATE
Zocor	Simvastatin	

8. SUPPLEMENT PROVIDES FOR

Deletion of the original GC methods for identification of the [redacted] in favor of two alternate GC methods.

9. PHARMACOLOGICAL CATEGORY	10. HOW DISPENSED	11. RELATED IND, NDA, DMF
antihypercholestremic	RX	
12. DOSAGE FORM	13. POTENCY	
tablets, oral	10,20,40 mg	

14. CHEMICAL NAME AND STRUCTURE

See Chemistry Review #1

15. COMMENTS

The sponsor has concluded that the original methods for analysis of the [redacted] two alternate methods, already described in the NDA, for acceptance (assay) purposes. Each of the methods is a GC assay. [redacted] the sponsor notes that the alternate method is capable of detecting and quantitating several potential impurities that the original method could not. The sponsor only cited an increase in the "efficiency of the chromatography allowing improvement in the determination [redacted] for the change in the [redacted] In both instances, the alternate methods involve the use [redacted] Further, the methods are similar to methods described in the USP for these materials, however, the [redacted] differ in both instances for both the current and the alternate methods.

16. CONCLUSION AND RECOMMENDATION

The alternate GC methods described for the analysis of the [redacted] are not fundamentally different from the current GC methods. The sponsor has noted that better results are obtained using the alternate methods, and therefore product quality should be improved. Issue an approval letter.

17. NAME	18. REVIEWERS SIGNATURE	19. DATE COMPLETED
WILLIAM K. BERLIN		7-17-97

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Stephen K. Moore
7/17/97

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APPLICATION NUMBER:

NDA 19-766/S023

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-766/S-023

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

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

Dear Dr. 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-023

Date of Supplement: May 19, 1997

Date of Receipt: May 22, 1997

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on July 21, 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,

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-023
HFD-510/Div. Files
HFD-510/CSO/M. Simoneau

filename: C:\WPFILES\19766ACK.WPD

SUPPLEMENT ACKNOWLEDGEMENT

NDA NO. 19766 REF. NO. 023

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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not desk copies.

May 19, 1997

MERCK
Research Laboratories

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

Supplemental New Drug Application: NDA 19-766

ZOCOR™ (Simvastatin)

Dear Dr. Sobel:

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

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

The attached supplemental application provides for the removal of the original GC method included for [redacted] and the original GC test method [redacted] simvastatin drug substance. The two alternate GC methods included for [redacted] alternate GC method [redacted] in simvastatin currently outlined in NDA 19-766 are superior to the original methods and therefore will no longer be used for testing.

Please find attached an electronically annotated and clean copy of the [redacted] section as well as the deletion of the original GC method for [redacted] in simvastatin. A brief summary of the supplement has also been included.

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

As required by Section 306(k)(1) of the Generic Drug 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 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, to Bonnie J. Goldmann, M.D. (610/397-2383).

Sincerely,

Robert E. Silverman
Senior Director
Regulatory Affairs

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

Attachments

Certified No. P 914 177 865

Desk Copy: Philadelphia District Office, FDA.
U. S. Custom House, Room 900
2nd and Chestnut Streets
Philadelphia, PA 19106-2973
Certified No. P 914 177 859

Q/young/766.doc

6-23-97

See Review 9-4-97