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
Center for Drug Evaluation and Research

Application Number:
NDA 19-766/S019

Contents

Reviews / Information Included in this NDA Review.

<table>
<thead>
<tr>
<th>Approval Letter</th>
<th>X</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approvable Letter</td>
<td></td>
</tr>
<tr>
<td>Labeling</td>
<td></td>
</tr>
<tr>
<td>Medical Review(s)</td>
<td></td>
</tr>
<tr>
<td>Chemistry Review(s)</td>
<td>X</td>
</tr>
<tr>
<td>Pharmacology Review(s)</td>
<td></td>
</tr>
<tr>
<td>Statistical Review(s)</td>
<td></td>
</tr>
<tr>
<td>Microbiology Review(s)</td>
<td></td>
</tr>
<tr>
<td>Clinical Pharmacology/Biopharmaceutics Review(s)</td>
<td></td>
</tr>
<tr>
<td>Administrative/Correspondence Document(s)</td>
<td>X</td>
</tr>
</tbody>
</table>
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 19-766/S023

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

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 with a new GC method and an alternative method (both formerly alternate methods), and deletion of the original \( \), 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,

[Signature]

Stephan 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
FOI: Please redact the phrases and the above.
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 19-766/S023

CHEMISTRY REVIEW(S)
Addendum to Chemistry Review of N 19-766/S-023

<table>
<thead>
<tr>
<th>CHEMISTS REVIEW</th>
<th>1. ORGANIZATION</th>
<th>2. NDA NUMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DMEDP II, HFD-510</td>
<td></td>
</tr>
</tbody>
</table>

3. NAME AND ADDRESS OF APPLICANT
Merck Research Labs.
Sumneytown Pike
West Point, PA 19486

4. SUPPLEMENT NUMBER, DATE
SCS-023
5-19-97

5. PROPRIETARY NAME
Zocor

6. NAME OF THE DRUG
Simvastatin

7. AMENDMENTS, REPORT, DATE

8. SUPPLEMENT PROVIDES FOR

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

9. PHARMACOLOGICAL CATEGORY
antihypercholesteremic

10. HOW DISPENSED
RX

11. RELATED IND, NDA, DMF

12. DOSAGE FORM
tablets, oral

13. POTENCY
10, 20, 40 mg

14. CHEMICAL NAME AND STRUCTURE

See Chemistry Review #1

15. COMMENTS
Based on discussions with the sponsor (telephone conversation 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 , and the proposed method differs only slightly more and will not be validated.

16. CONCLUSION AND RECOMMENDATION

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

17. NAME
WILLIAM K. BERLIN

18. REVIEWERS SIGNATURE

19. DATE COMPLETED
9-4-97

DISTRIBUTION: ORIGINAL JACKET CSO REVIEWER DIVISION FILE

Stephen Moore 9-4-97
Deletion of the original GC methods for identification of the
in favor of two alternate GC methods.

antihypercholesteremic
RX

10,20,40 mg

See Chemistry Review #1

The sponsor has concluded that the original methods for analysis of the
two alternate methods, already described in the NDA,
for acceptance (assay) purposes. Each of the methods is a GC assay. 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 for the change in the . In both instances, the
alternate methods involve the use . Further, the methods are
similar to methods described in the USP for these materials, however, the
differ in both instances for both the current and the alternate methods.
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 19-766/S023

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS
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
May 19, 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

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 simvastatin drug substance. The two alternate GC methods included for alternate GC method 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 section as well as the deletion of the original GC method for 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.
Solomon Sobel, M.D. - Director
NDA 19-766 ZOCOR™ (Simvastatin)
Page 2

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,

[Signature]
Robert E. Silverman
Senior Director
Regulatory Affairs

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