CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 19-766/S022

Trade Name: Zocor Tablets

Generic Name: simvastatin

Sponsor: Merck Research Laboratories

Approval Date: July 18, 1997
**APPLICATION NUMBER:**
NDA 19-766/S022

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APPLICATION NUMBER:
NDA 19-766/S022

APPROVAL LETTER
NDA 19-766/S-022

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 9, 1997, received May 12, 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 12, 1997.

The supplemental application provides for an alternate site for film-coating of the 10 mg strength tablet cores at your manufacturing division facility in Arecibo, Puerto Rico.

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, Consumer Safety Officer, at 301-443-3510.

Sincerely yours,

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

7-18-97
cc:
Original NDA 19-766
HFD-510/Div. Files
HFD-510/CSO/MSimoneau
HFD-510/ WBerlin/SMoore
HFD-820/ONDC Division Director
HFD-92/DDM-DIAB
DISTRICT OFFICE

Drafted by: JWeber/6/23/97/N19766.022


final: JWeber/7/18/97

APPROVAL (AP)
**CHEMISTS REVIEW**

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<td>2. NDA NUMBER</td>
<td>19-766</td>
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<td>Merck Research Labs.</td>
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<tr>
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<td>P.O. Box 4, BLA-20</td>
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<td></td>
<td>West Point, PA 19486</td>
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<td>4. SUPPLEMENT NUMBER, DATE</td>
<td>SCS-022</td>
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<tr>
<td></td>
<td>5-9-97</td>
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<td>5. PROPRIETARY NAME</td>
<td>Zocor Tablets</td>
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<td>6. NAME OF THE DRUG</td>
<td>Simvastatin</td>
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<td>7. AMENDMENTS, REPORT, DATE</td>
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<td>8. SUPPLEMENT PROVIDES FOR</td>
<td>An alternate site for film-coating of 10 mg-strength tablet cores at the Merck Manufacturing Division facility in Arecibo, Puerto Rico.</td>
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<td>9. PHARMACOLOGICAL CATEGORY</td>
<td>Antihypercholestermic</td>
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<td>10. HOW DISPENSED</td>
<td>RX</td>
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<td>11. RELATED IND, NDA, DMF</td>
<td></td>
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<td>Tablets</td>
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<td>13. POTENCY</td>
<td>10, 20, 40 mg</td>
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<td>14. CHEMICAL NAME AND STRUCTURE</td>
<td>See Chemistry Review #1</td>
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<td>15. COMMENTS</td>
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This supplement provides for a change in the site to film-coat 10-mg tablets of Zocor at Arecibo PR rather than Wilson NC. Essentially, this application is identical to N 19-766, S-019, submitted 11-26-96 for the 20-mg tablet site change for film coating, which was approved, subsequent to an acceptable Establishment Evaluation. The sponsor has provided adequate indication that the alternate facility will utilize the same equipment and procedures at the same scale for the process as is currently performed at the approved site of Wilson NC. The sponsor has also included comparative batch results, comparative multi-point dissolution data, and comparative stability data for tablets coated at both facilities, and the data are acceptable.

**16. CONCLUSION AND RECOMMENDATION**

The sponsor has provided adequate data to demonstrate equivalence of the tablets film-coated at both the current and proposed facilities. The Arecibo facility was inspected and found to be acceptable (see attached copy of the CDER Establishment Evaluation Report dated 11-June, 1997). Issue an approval letter.

| 17. NAME             | WILLIAM K. BERLIN          |
| 18. REVIEWERS SIGNATURE |                         |
| 19. DATE COMPLETED   | 6-11-97                   |

DISTRIBUTION: ORIGINAL JACKET CSO REVIEWER DIVISION FILE
CDER Establishment Evaluation Report for June 11, 1997

Application: NDA 19766/022
Stamp: 12-MAY-1997 Regulatory Due: 12-NOV-1997
Applicant: MERCK SUMNEYTOWN PIKE WEST POINT, PA 19486

Priority: 1S Org Code: 510
Brand Name: ZOCOR (SIMVASTATIN)
Established Name:
Generic Name: SIMVASTATIN
Dosage Form: TAB (TABLET)
Strength: 10, 20, 40 MG

FDA Contacts: M. SIMONEAU (HFD-510) 301-443-3510, Project Manager
W. BERLIN (HFD-510) 301-443-3520, Review Chemist
S. MOORE (HFD-510) 301-443-3510, Team Leader

Overall Recommendation:
ACCEPTABLE on 11-JUN-1997 by M. EGAS (HFD-322) 301-594-0095

Establishment: 2650235 DMF No: 9593
MERCK SHARP AND DOHME QUIMI RD 2 KM 60.3 BO SAB HOYO ARECIBO, PR 00688
Profile: TCM OAI Status: NONE
Last Milestone: OC RECOMMENDATIO 11-JUN-1997
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Responsibilities:
FINISHED DOSAGE MANUFACTURER
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 19-766/S022

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS
DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

NDA 19-766/S-022

MERCK RESEARCH LABORATORIES, INC.
Sumneytown Pike, P.O. Box 4, BLA-20
West Point, PA 19486

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

MAY 16 1997

Dear Dr. Silverman:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: ZOCOR (Simvastatin) Tablets
NDA Number: 19-766
Supplement Number: S-022
Date of Supplement: May 9, 1997
Date of Receipt: May 12, 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 11, 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,

[Signature]

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-022
  HFD-510/Div. Files
  HFD-510/CSO/M. Simoneau

filename: C:\WPFILES\19766ACK.WPD

SUPPLEMENT ACKNOWLEDGEMENT
May 9, 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, the supplemental application provides for changes in Item 3 of the approved New Drug Application for ZOCOR™.

The attached prior-approval supplement provides for the alternate film-coating of Tablets ZOCOR™10 mg at the Merck Manufacturing Division (MMD) facility in Arecibo, Puerto Rico.

The location of the Arecibo facility is:

Merck Manufacturing Division
Division of Merck and Co., Inc.
Road #2, Kilometer 60.3
Bo. Sabana Hoyos
Arecibo, PR 00688

The mailing address of the Arecibo facility is:

Merck Sharp & Dohme, Quimica de Puerto Rico
P.O. Box 6060
Barceloneta, PR 00617

Currently, the film-coated tablets are subsequently
Merck & Co., Inc. requests approval for film-coating the core tablets at MMD Arecibo, in addition to the currently approved Wilson facility.

This supplement contains CMC information similar to that which was provided previously in Supplement 019 (submitted on November 20, 1996 and approved on March 17, 1997) to support the use of MMD, Arecibo as an alternate site for the film-coating of Tablets ZOCOR™, 20 mg. The following chemistry documentation is provided:

- An Updated Film-Coating Manufacturing Process Description of the Arecibo facility.
- Accelerated stability data for tablets of Tablets ZOCOR™ 10 mg film-coated at the Arecibo facility (these samples will also be retained for long-term stability data to be provided in subsequent Annual Reports).
- Multi-point dissolution profiles for Tablets ZOCOR™ 10 mg film-coated at the Arecibo and Wilson facilities.
- Data comparison of batches film-coated at Wilson and Arecibo.

The Arecibo facility was inspected by the San Juan District Office from February 5 through February 21, 1997 as part of the Preapproval Inspection for the manufacture of Tablets and the film-coating of Tablets ZOCOR™, 20 mg. All observations issued as a result of this inspection were successfully resolved.

Please note that CMC information for

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)(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, to Bonnie J. Goldmann, M.D. (610/397-2383).

Sincerely,

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

attachments

Federal Express #1
Desk Copy: Philadelphia District Office, FDA
U. S. Customs House, Room 900
2nd & Chestnut Streets
Philadelphia, PA 19106-2973

Q/young766.doc