CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

20-560/S019

Trade Name: Fosamax Tablets

Generic Name: alendronate sodium

Sponsor: Merck Research Laboratories

Approval Date: May 28, 1999
## Reviews / Information Included in this NDA Review.

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<td>Clinical Pharmacology/Biopharmaceutics Review(s)</td>
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
20-560/S019

APPROVAL LETTER
Merck Research Laboratories
Attention: Michelle Kloss, Ph.D.
Director, Regulatory Affairs
Sunneytown Pike, P.O. Box 4
BLA-20
West Point, PA 19486

Dear Dr. Kloss:

Please refer to your supplemental new drug application dated February 2, 1999, received
February 4, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act
for Fosamax® (alendronate sodium) Tablets.

We note that this supplement was submitted as a 'Special Supplement - Changes Being Effecte'd'
under 21 CFR 314.70(c).

This supplemental new drug application provides for an additional site for the
packaging of Fosamax Unibisters (a previously approved blister package), and a categorical
exclusion from the requirement to prepare an environmental assessment for the tablets in these
blisters. Your submission stated March 1, 1999 as the implementation date for the change.

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, contact Randy Hedin, R.Ph., Senior Regulatory Management Officer,
at (301) 827-6392.

Sincerely,

Duu-Gong Wu, Ph.D.
Chemistry Team Leader II, DNDC II for the
Division of Metabolic and Endocrine Drug Products,
(HFD-510)
Office of New Drug Chemistry
Center for Drug Evaluation and Research

MAY 28 1999

5/8/99
cc:
Archival NDA 20-560
HFD-510/Div. Files
HFD-510/R.Hedën
HFD-510/Reviewers and Team Leaders
HFD-95/DDMS (with labeling)
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: RH/May 25, 1999
Initialed by: SMarkofsky/5.25/DWu/5.26/EGalliers/5.27.99
final: RH/5.28.99
filename: N20560AP.L13

APPROVAL (AP)
<table>
<thead>
<tr>
<th>CHEMIST'S REVIEW</th>
<th>1. ORGANIZATION</th>
<th>2. NDA NUMBER</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>DMEDP, HFD-510</td>
<td>20-560</td>
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<table>
<thead>
<tr>
<th>NAME AND ADDRESS OF APPLICANT</th>
<th>4. SUPPLEMENT NUMBER, DATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Merck &amp; Co., Inc.</td>
<td>SCM-019 02-Feb.-1999</td>
</tr>
<tr>
<td>Sumneytown Pike, BLA-20</td>
<td>User Fee Date: 8-2-99</td>
</tr>
<tr>
<td>P.O. Box 4</td>
<td></td>
</tr>
<tr>
<td>West Point, PA 19486</td>
<td></td>
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<thead>
<tr>
<th>5. NAME OF DRUG</th>
<th>6. NONPROPRIETARY NAME</th>
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<tbody>
<tr>
<td>Fosamax</td>
<td>Alendronate Sodium Tablets</td>
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<tr>
<th>7. SUPPLEMENT PROVIDES FOR:</th>
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<tbody>
<tr>
<td>1) An additional site for the</td>
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<tr>
<td>2) A Categorical Exclusion from the requirement to prepare an Environmental Assessment for the tablets in these blisters</td>
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<tr>
<th>9. PHARMACOLOGICAL CATEGORY</th>
<th>10. HOW DISPENSED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment and prevention of</td>
<td>Prescription</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td></td>
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<tr>
<th>12. DOSAGE FORM</th>
<th>13. POTENCY</th>
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<tbody>
<tr>
<td>Tablets (oral)</td>
<td>5, 10, &amp; 40 mg tablets</td>
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<tr>
<th>15. COMMENTS:</th>
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<tbody>
<tr>
<td>This Changes Being Effective supplement (CBE) provides for an additional packaging site for Merck's previously approved Uniblister cards (Supplement-010), for Fosamax (10mg) tablets, under the provisions of SUPAC-IR (Stand Alone Packaging Operations Site Changes).</td>
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<tr>
<th>16. CONCLUSION AND RECOMMENDATIONS</th>
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<tr>
<td>From a Chemistry point of view, the proposed supplement is acceptable. Issue an approval letter.</td>
</tr>
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</table>

<table>
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<tr>
<th>17. NAME</th>
<th>REVIEWER SIGNATURE</th>
<th>DATE COMPLETED</th>
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</thead>
<tbody>
<tr>
<td>Sheldon Markofsky, Ph.D.</td>
<td>[Signature]</td>
<td>4-13-99</td>
</tr>
</tbody>
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DISTRIBUTION: ORIGINAL JACKET/CSO/REVIEWER/DIVISION FILE

R/D initiated by: [Signature] 5/1/99

File name: n20560s.019
Page(s) Withheld

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

§ 552(b)(4) Draft Labeling

§ 552(b)(5) Deliberative Process
Application: NDA 20560/019
Stamp: 04-FEB-1999 Regulatory Due: 04-AUG-1999
Applicant: MERCK
SUMNEYTOWN PIKE BLA20
WEST POINT, PA 19486

Priority: 1P
Action Goal: 
Brand Name: FOSAMAX (ALENDRONATE SODIUM) 10+40MG TABS

Established Name:
Generic Name: ALENDRONATE SODIUM
Dosage Form: TAB (TABLET)
Strength: 10 MG

FDA Contacts:
D. HEDIN (HFD-510) 301-827-6392, Project Manager
S. MARKOFSKY (HFD-510) 301-827-6430, Review Chemist
D. WU (HFD-510) 301-827-6375, Team Leader

Overall Recommendation:
ACCEPTABLE on 22-FEB-1999 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment: 
DMF No: 
AADA No: 

Profile: TCM OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date 22-FEB-1999
Decision: ACCEPTABLE
Reason: BASED ON PROFILE
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
20-560/S019

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS
NDA 20-560/S-019

Merck Research Laboratories
Sumneytown Pike P.O. Box 4 BLA-20
West Point, PA 19486

Attention: Michelle W. Kloss, Ph.D.
Director, Regulatory Affairs

Dear Dr. Kloss:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Fosamax® (Alendronate Sodium Tablets)
NDA Number: 20-560
Supplement Number: S-019
Date of Supplement: February 2, 1999
Date of Receipt: February 4, 1999

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on April 5, 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,

[Signature]

Emid 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 20-560/S-019
HFD-510/Div. Files
HFD-510/CSO/R. Hedin

filename: C:\DATA\WPFILES\20560ACK.

SUPPLEMENT ACKNOWLEDGEMENT /CBE
February 2, 1999

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  
9201 Corporate Blvd.  
Rockville, Maryland 20850

NDA NO. 20-560  
NDA SUPPL FOR  
NDA 20-560: FOSAMAX™  
(Alendronate Sodium Tablets)

SPECIAL SUPPLEMENT – CHANGES BEING EFFECTED

Dear Dr. Sobel:

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 20-560.

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 FOSAMAX™.

The purpose of this supplement is to add __________________ as a packaging site for the FOSAMAX™ UNIBLISTERTM. This filing is being submitted in accordance with the provisions of SUPAC-IR involving Stand Alone Packaging Operations Site Changes as stipulated in correspondence from Roger L. Williams, M.D., (FDA) dated February 18, 1997. The following items are included in this submission:

- Address of the __________________ and the dates of the last GMP inspection conducted by FDA at that facility
- Letter of authorization from __________________ to refer to their DMF, including certification that the facility is in conformance with cGMPs
- Request for categorical exclusion from the requirements for preparing an environmental assessment
- Commitment to place on stability the ___ of FOSAMAX™ packaged in the UNIBLISTERTM at __________________

Packaging operations at __________________ are targeted to begin on March 1, 1999.

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.

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 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 Michelle W. Kloss, Ph.D. (610/397-2905) or, in my absence, to Larry P. Bell, M.D. (610/397-2310).

Sincerely,

[Signature]
Michelle W. Kloss, Ph.D.
Director
Regulatory Affairs

Attachments

Federal Express #1

Desk Copy
Mr. Randy Hedin, HFD-510, Room 14B-04 - Federal Express #1

Ms. Debra Pagano
Philadelphia District Office
Food & Drug Administration
U.S. Custom House Room 900
2nd and Chestnut Street
Philadelphia, Pennsylvania 19106-2973 - Federal Express #2
See Instructions on Reverse Side Before Completing This Form

1. APPLICANT'S NAME AND ADDRESS
Merck & Co., Inc.
Summit, New Jersey, BLA-10
P.O. Box 4
West Point, PA 19486

2. TELEPHONE NUMBER (Include Area Code)

(610) 397-2383

3. PRODUCT NAME
Fosamax™

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).

5. USER FEE I.D. NUMBER

6. LICENSE NUMBER / NDA NUMBER

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)
   □ 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
     COMMERCIALLy
     (Self Explanatory)
   □ WHOLE BLOOD OR BLOOD COMPONENT FOR
     TRANSFUSION
   □ AN APPLICATION FOR A BIOLOGICAL PRODUCT
     FOR FURTHER MANUFACTURING USE ONLY
   □ BOVINE BLOOD PRODUCT FOR TOPICAL
     APPLICATION LICENSED BEFORE 9/1/92
   □ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
     (See Item 7, reverse side before checking box.)
   □ A CRUDE ALLERGENIC EXTRACT PRODUCT
   □ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT
     LICENSED UNDER SECTION 351 OF THE PHS ACT

6. 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. Goldman, M.D.
Vice President, Domestic Liaison
Regulatory Affairs

DATE 2/2/99

FORM FDA 3397 (5/96)