

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

20-560/S020

Trade Name: Fosamax

Generic Name: (alendronate sodium)

Sponsor: Merck Research Laboratories

Approval Date: October 19, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-560/S020

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**CENTER FOR DRUG EVALUATION AND
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APPLICATION NUMBER:

20-560/S020

APPROVAL LETTER

NDA 20-560/S-016 & S-020

OCT 19 1999

Merck Research Laboratories
Attention: Michele Flicker, Ph.D.
Director, Regulatory Affairs
P.O. Box 4, BLA-20
West Point, PA 19486-0004

Dear Dr. Flicker:

Please refer to your supplemental new drug application dated October 30, 1998, received November 2, 1998 (Supplement 016) and your supplemental new drug application dated April 26, 1999, received April 27, 1999 (Supplement 020), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fosamax (alendronate sodium) 10 and 40 mg Tablets.

We acknowledge receipt of your submission dated June 22, 1999 (Supplement 016). Your submission of April 22, 1999, constituted a complete response to our March 2, 1999, action letter for Supplement 016. We also acknowledge receipt of your submissions dated June 22, 1999 (Supplement-016), and May 26, June 8, and August 17, 1999 (Supplement-020). Further, we refer to the October 6, 1999, telephone conversation between you and Mr. Randy Hedin of our Division in which you agreed to the change listed below concerning bullet three on page two of the physicians' sample blister package.

Supplement 016 proposes the following changes: A new physicians' sample blister package for the 10 mg strength of Fosamax Tablets, associated labeling for the new blister package, and two new packaging sites for these physicians samples. The submission also requests a categorical exclusion from the requirement to prepare an environmental assessment for the tablets in these blister packages. Supplement 020 provides for a wax polish and a shape change.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text with the minor revision listed below. Accordingly, these supplemental applications are approved effective on the date of this letter.

The third bullet on page two of the carton in supplement 016 should be changed from, to "FOSAMAX increased the amount of spinal bone in more than 9 out of 10 patients with osteoporosis."

NDA 20-560/S-016 & S-020

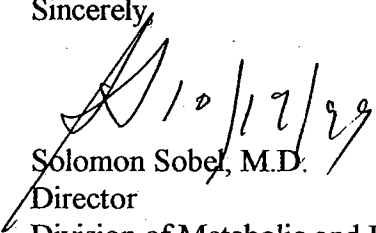
Page 2

The new labeling for the physicians' sample blister package must be identical, and include the minor revision indicated, to the submitted draft blister package submitted on April 22, 1999. This revision is a term of the approval.

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,


Solomon Sobel, M.D.

Director

Division of Metabolic and Endocrine Drug Products

Office of Drug Evaluation II

Center for Drug Evaluation and Research

RH 10/19/99

cc:

Archival NDA 20569/

HFD-510/Div. Files

HFD-510/R.Hedin

HFD-510/Reviewers and Team Leaders

HFD-095/DDMS-IMT

HFD-820/DNDC Division Director

DISTRICT OFFICE

Drafted by: RH/October 7, 1999

Initialed by: EChikhale/10.14/SMarkofsky/DWu/10.15/RShore for HAhn/EGalliers/10.18.99

final: RH 10.19.99

filename: N20560AP.L16

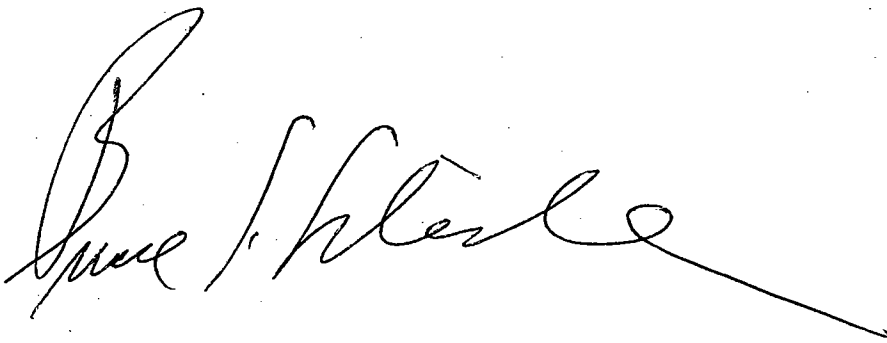
APPROVAL (AP)

October 13, 1999

sNDA 20560-020

MEMO TO THE FILE:

I have reviewed the labeling changes proposed by the sponsor in NDA 20560-020. These changes relate to the shape change and wax coating for Fosamax™ 10 mg tablets. The changes in the label and blister package are acceptable. It should be noted that these comments apply only to the changes proposed herein. Extensive labeling changes for Fosamax™ are currently pending, based on other supplemental NDA submissions.

A handwritten signature in black ink, appearing to read "Bruce Schneider", with a long horizontal line extending to the right.

**BRUCE S. SCHNEIDER, MD
MEDICAL OFFICER, DMEDP, HFD-510**

CC Drs. Sobel, Troendle, Mr. Hedin, HFD-510 file

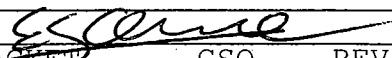
**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

20-560/S020

CHEMISTRY REVIEW(S)

SEP - 9 1999

CHEMIST'S REVIEW	1. ORGANIZATION	2. NDA NUMBER
	DMEDP, HFD-510	20-560
3. NAME AND ADDRESS OF APPLICANT		4. SUPPLEMENT NUMBER, DATE
Merck & Co., Inc. Sumneytown Pike P.O. Box 4 BLA-20 West Point, PA 19486		SCS-020, 04/26/99 User Fee date: 08/27/99 (4 months) 10/27/99 (6 months)
5. NAME OF THE DRUG	6. NONPROPRIETARY NAME	8. AMENDMENTS/REPORT, DATE
Fosamax™ tablets	Alendronate sodium	
7. SUPPLEMENT PROVIDES FOR:		5/26/99
An image change of Fosamax™ 10 mg tablets, including a shape change and addition of wax polish.		8/17/99
9. PHARMACOLOGICAL CATEGORY	10. HOW DISPENSED	11. RELATED IND/NDA/DMF
Treatment and prevention of osteoporosis. Treatment of Paget's disease of bone.	R _x	
12. DOSAGE FORM	13. POTENCY	
Tablet	5, 10, 40 mg	
14. CHEMICAL NAME AND STRUCTURE.		
(4-amino-1-hydroxybutylidene) bisphosphonic acid monosodium salt trihydrate, C ₄ H ₁₂ NNaO ₇ P ₂ .3H ₂ O See chemistry review #1.		
15. COMMENTS		
<p>This supplement is submitted to HFD-510 as a PA. The sponsor is requesting an image change for the 10 mg tablet, from the current round, non coated tablet to an oval, wax coated tablet. The changes were made for marketing purpose only. The first amendment (5/26/99) clarifies that the sponsor wants to use the same packaging packaging facilities as currently approved for the round tablets. It also contains minor corrections in the process description. The second amendment (8/17/99) provides for a response to our request for information: including acceptance/identity tests and criteria for carnauba wax NF and batch records for the stability lot, E980720, of the new image tablets. Other supporting information provided includes manufacturing and controls for the new tablet and revised labeling. Due to a change in tablet shape and the addition of wax coating that may affect the dissolution profiles, a biopharm consult was requested. The review is still pending. The Division of Clinical Pharmacology and Biopharmaceutics finds the change acceptable (see attached review).</p>		
16. CONCLUSION AND RECOMMENDATION		
From a chemistry standpoint, adequate information has been provided. Issue an approval letter. Request a final printed label (FPL).		
17. NAME	REVIEWER SIGNATURE	DATE COMPLETED
Elsbeth G. Chikhale, Ph.D.		9/9/99
DISTRIBUTION: ORIGINAL JACKET CSO REVIEWER DIVISION FILE		

Init. by: *Sanjiv* 9/9/99 (Chem review was completed on 8/27 waiting for biopharm review.)
 CC: HFD-510, NDA 20-560/S-020
 HFD-510/ DG Wu / R Hedin / EG Chikhale/Division file/NDA 20-560

4 Page(s) Withheld

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

 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

**CENTER FOR DRUG EVALUATION AND
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APPLICATION NUMBER:
20-560/S020

**CLINICAL PHARMACOLOGY AND
BIOPHARMACEUTICS REVIEW(S)**

SEP - 7 1999

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW

NDA 20-560/S-020

SUBMISSION DATE: 4/26/99

Fosamax™

Alendronate Sodium Tablets

Merck & Co., Inc.

REVIEWER: Hae-Young Ahn, Ph.D.

West Point, PA

SUBMISSION TYPE: Supplement for Shape Change

SUBMISSION: The sponsor has submitted a supplemental NDA to propose an image change for Fosamax™ 10 mg tablets from the currently marketed round tablet to an oval tablet, polished with wax. No changes to the currently approved formulation or method of manufacture was proposed, except for the addition of the wax. The process specifications for hardness and thickness will change to accommodate the manufacturing requirements of the new shape.

The sponsor compared dissolution profiles to the proposed tablets to those of the currently marketed tablets using the approved dissolution method and showed that two profiles were superimposable. (Note: The approved dissolution method is USA Method 2 with a paddle speed of 50 rpm in 900 mL water. The specification is Q = 1 at 15 minutes.)

Comparative Batch Analysis Data

Lot # Image	E980720* Oval/Wax	2022087* Round	2022088* Round	2022089* Round
Appearance	Conforms	Conforms	Conforms	Conforms
Dose Uniformity(%)	/			
Dissolution (%)	/			
Assay (%)	99.8	98.5	100.5	101.1
Identity	Conforms	Conforms	Conforms	Conforms

*Manufactured at the MMD facility at Arecibo, Puerto Rico.

Comparative Dissolution Profiles

Lot # Image	E980720** Oval/Wax	2022087** ^b Round	2022088** ^b Round	2022089** ^b Round
Time (min)				
10				
15				
20				
30				
40	not tested			

* Manufactured at the MMD facility at Arecibo, Puerto Rico.

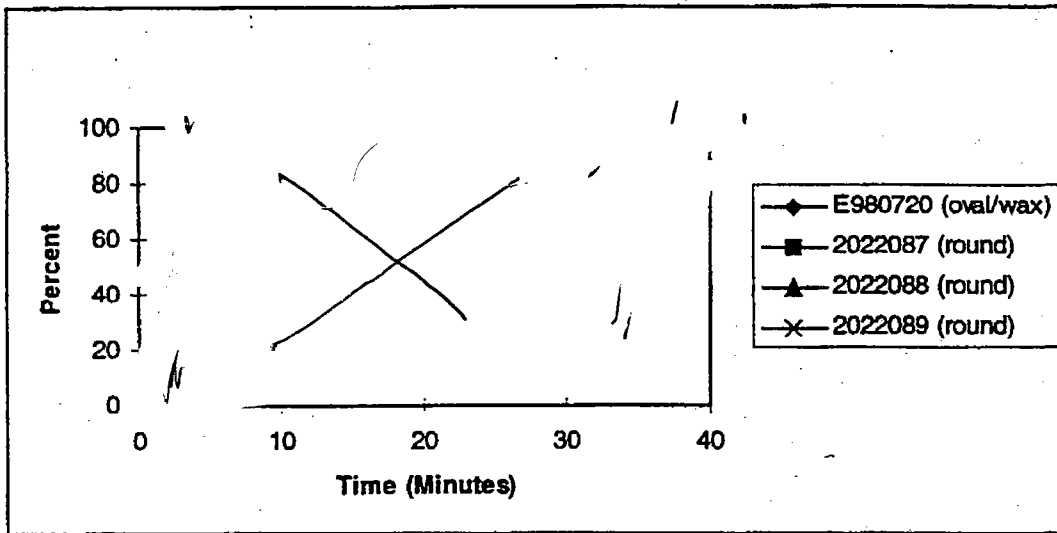
^a Data were generated for 12 tablets.

^b Data were generated for 6 tablets at 10, 20, 30, and 40 minutes, and 40 tablets at 15 minutes.

Specification: Conforms to USP; Q = 80% in 15 minutes

Profiles are shown in Figure 3.

Figure 3: Comparative Dissolution Profiles for FOSAMAX 10 mg
New Image vs. Current Image



The Agency's SUPAC IR guidance for industry does not cover a shape change. However, a shape change involves minor equipment and process changes. Head of equipment will be different and it can be considered as a level 1 change that does not require any additional dissolutions beyond application/compendial dissolution requirements. Process change such as mixing times and operating speeds, if any, can be considered as a level 1 change and it does not require anything beyond application/compendial dissolution requirements.


RECOMMENDATION:

The Office of Clinical Pharmacology and Biopharmaceutics/Division of Pharmaceutical Evaluation II has reviewed the supplemental NDA 20-560 submitted on 4/26/99 and finds the proposed change acceptable.

Please convey the Recommendation to the sponsor as appropriate.

Hae-Young Ahn, Ph.D.
Division of Pharmaceutical Evaluation II
Office of Clinical Pharmacology and Biopharmaceutics

RD/FT initialed by J. Hunt, Deputy Director

 9/7/99

CC: NDA 20-560, HFD-510 (Hedin, Wu), HFD-870 (M. Chen, Ahn), CDR (Murphy)

CODE:AP

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

20-560/S020

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

These copies are
OFFICIAL FDA Copies
not desk copies.

ORIGINAL

SUPPL NEW CORRESP

SES - 020 - SNC

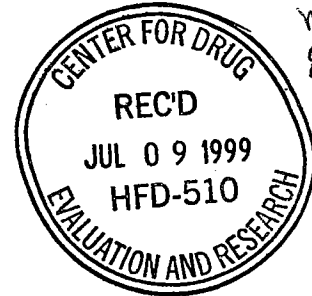
Mr. Randy Hedin, Senior Regulatory Manager
Division of Metabolism and Endocrine Drug Products
HFD-510, Room 14B-04
Office of Drug Evaluation II (CDER)
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857



Handwritten signature/initials

Handwritten note: No R/S... 7/21/99

NDA 20-560/S-020: FOSAMAX™
(Alendronate Sodium Tablets)



Handwritten note: noted EGC 7-20-99

Response to Request for Information

Dear Mr. Hedin:

Reference is made to the Supplemental New Drug Application cited above, submitted on April 26, 1999, which provides for an image change for FOSAMAX™ 10 mg tablets that involves a shape change and addition of wax polish, and to an amendment submitted on May 26, 1999 which clarified the packaging facilities for the new 10 mg image and corrected minor errors in the process description. Further reference is made to a July 8, 1999 telephone conversation between Mr. Randy Hedin (FDA) and Dr. Michele Flicker (MRL, a Division of Merck & Co., Inc.) in which Mr. Hedin requested that MRL provide a complete desk copy of the above referenced supplemental application.

With the attachment to this submission, we are providing an additional desk copy of the above referenced supplemental application (attachment A) and amendment (attachment B).

Questions concerning this submission should be addressed to Michele R. Flicker, MD, PhD (610/397-3193) or, in my absence, Larry P. Bell, MD (610/397-2310).

Sincerely,

Jenna L Goodrow
Michele R. Flicker, MD, PhD
Director, Regulatory Affairs

REVIEWS COMPLETED
CSO ACTION: <input checked="" type="checkbox"/> LETTER <input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
<i>Handwritten initials</i> <i>12/1/99</i>
CSO INITIALS DATE

q/carnal/mk0217/responses/s020res

Attachments

Federal Express #1

Desk copy (Letter Only): Dr. Solomon Sobel, HFD-510, Room 14B-04
Federal Express #1

ORIGINAL

Merck & Co., Inc.
West Point, PA 19486

NDA SUPP AMEND

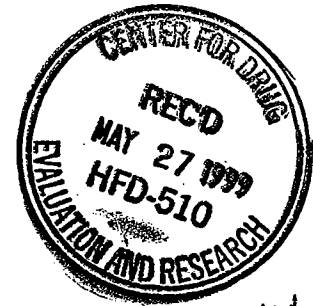
505-020
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May 26, 1999



Solomon Sobel, MD, Director
Division of Metabolism and Endocrine Drug Products
HFD-510, Room 14B-04
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857



*Noted
EJG*

**NDA 20-560/S-020: FOSAMAX™
(Alendronate Sodium Tablets)**

AMENDMENT TO PENDING SUPPLEMENTAL APPLICATION

Dear Dr. Sobel:

Reference is made to the Supplemental New Drug Application cited above, submitted on April 26, 1999, which provides for an image change for FOSAMAX™ 10 mg tablets that involves a shape change and addition of wax polish. With this submission, Merck Research Laboratories (MRL, a Division of Merck & Co., Inc.) is providing an amendment to the above referenced supplemental application for the following purposes:

- Clarify the identity of ~~the~~ packaging facilities for the new 10 mg image
- Correct minor errors in the process description

Specifically, Merck & Co., Inc. wishes to retain the ~~the~~ packaging facilities of ~~the~~ and ~~the~~, for the new image. The process description has been corrected regarding the amount of carnauba wax for the entire ~~the~~ batch size and the amount of tablets per pan load for the wax polishing step.

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

REVIEWS COMPLETED	
CSO ACTION:	
<input checked="" type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
<i>m</i>	<i>10-19-99</i>
CSO INITIALS	DATE

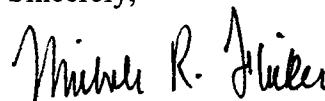
Solomon Sobel, MD, Director
NDA 20-560/S-020: FOSAMAX™ (Alendronate Sodium Tablets)
Page 2

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 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 submission should be addressed to Michele R. Flicker, MD, PhD (610/397-3193) or, in my absence, Larry P. Bell, MD (610/397-2310).

Sincerely,



Michele R. Flicker, MD, PhD
Director, Regulatory Affairs

q/carnal/mk0217/s020amnd

Attachments

Federal Express #1

Desk copies:

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

Dr. Shelly Markofsky, 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 Streets
Philadelphia, PA 19106-2973
Federal Express #2

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

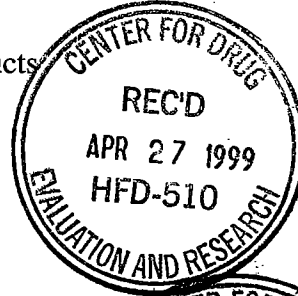
NDA NO. 20560 REF. NO. 102020
NDA SUPPL FOR SOS

Merck & Co., Inc.
P.O. Box 4, BLA-20
West Point PA 19486-0004
Tel 610 397 2905
Fax 610 397 2516

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Solomon Sobel, M.D., Director
Division of Metabolism & Endocrine Drug Products
HFD-510, Room 14B-04
Office of Drug Evaluation II (CDER)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857



NDA 20-560: FOSAMAX
(Alendronate Sodium Tablets)

Supplemental New Drug Application



Dear Dr. Sobel:

Reference is made to the NDA cited above. Further reference is made to a September 9, 1998 submission which provided a proposal regarding the submission of a supplemental application providing for an image change for FOSAMAX™ 10 mg tablets that involves a shape change and addition of wax polish. Further reference is made to a September 23, 1998 telephone conversation between Dr. Shelly Markofsky (FDA) and Dr. Michelle Kloss (MRL, a Division of Merck & Co., Inc)) during which the Agency's review of this proposal was discussed; during this conversation, Dr Markofsky indicated that the Agency agreed with MRL's proposal regarding the submission of a supplemental application providing for this image change.

Pursuant to Section 505(b) of the Food Drug and Cosmetic Act and in accordance with 21 CFR 314.70 (b), we submit a supplement to NDA 20-560. As indicated on the attached Form FDA 356h, this supplemental application provides for changes in the Labeling and Chemistry Sections of the approved New Drug Application for FOSAMAX™. As noted above, this supplemental application provides for the change of the FOSAMAX™ 10 mg image from the currently marketed round tablet to an oval tablet, polished with wax.

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.

Attached, for the Agency's review and approval, are the following:

- CMC documentation for the new image tablet
- Draft labeling which incorporates revisions provided for in this application
- Patent information.

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

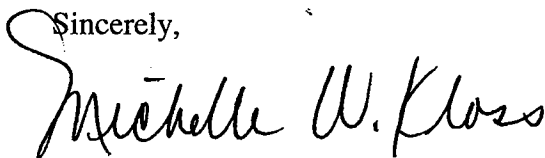
Merck is requesting a categorical exclusion from the requirements to prepare an Environmental Assessment under 21 CFR 25.31(a) for this supplemental application.

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

Sincerely,



Michelle W. Kloss, Ph.D.

Director

Regulatory Affairs

Q:\carnal\mk0217\10image.doc

Attachments

Federal Express #1

Desk copy:

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

Dr. Shelly Markofsky, 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

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



Food and Drug Administration
Rockville MD 20857

NDA 20-560/S-020

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

MAY 17 1999

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-020
Date of Supplement: April 26, 1999
Date of Receipt: April 27, 1999

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on June 26, 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 20-560/S-020

Page 2

cc:

Original NDA 20-560/S-020

HFD-510/Div. Files

HFD-510/CSO/D. Hedin

filename:

SUPPLEMENT ACKNOWLEDGEMENT

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

Form Approved: OMB No. 0910-0297
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	3. PRODUCT NAME FOSAMAXTM 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: <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION. <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO _____ (APPLICATION NO. CONTAINING THE DATA).
2. TELEPHONE NUMBER (Include Area Code) (610) 397-2383	6. LICENSE NUMBER / NDA NUMBER

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

<input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)	<input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE (See item 7, reverse side before checking box.)
<input type="checkbox"/> 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.)	<input type="checkbox"/> 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.)
<input type="checkbox"/> 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

<input type="checkbox"/> WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION	<input type="checkbox"/> A CRUDE ALLERGENIC EXTRACT PRODUCT
<input type="checkbox"/> AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY	<input type="checkbox"/> AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT
<input type="checkbox"/> 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)

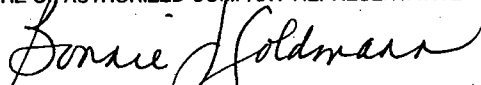
A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

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 	TITLE Bonnie J. Goldmann, M.D. Vice President, Domestic Liaison Regulatory Affairs	DATE 4/26/99
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