CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

20-560/S036

Trade Name: Fosamax Tablets

Generic Name: alendronate sodium

Sponsor: Merck & Co., Inc.

Approval Date: August 5, 2002

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-560/S036

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	X
Approvable Letter	
Labeling	X
Summary Review	
Officer/Employee List	
Office Director Memo	
Cross Discipline Team Leader Review	
Medical Review(s)	
Chemistry Review(s)	X
Environmental Assessment	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/Biopharmaceutics Review(s)	
Risk Assessment and Risk Mitigation Review(s)	
Proprietary Name Review(s)	
Administrative/Correspondence Document(s)	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-560/S036

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-560/S-036

Merck & Co., Inc.
Attention: Michele Flicker, M.D., Ph.D.
Director, Regulatory Affairs
P.O. Box 2000
Mail Drop: Ry 33-720
Rahway, NJ 07065

Dear Dr. Flicker:

Please refer to your supplemental new drug application dated February 15, 2002, received February 19, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fosamax (alendronate sodium) Tablets.

We acknowledge receipt of your submission dated March 8, 2002.

This supplemental application, submitted as a "Supplement - Changes Being Effected" supplement, proposes alternative ("push-through" design) packaging to the currently approved 35 and 70 mg once weekly tablet 4-count trade bifold packaging ("peel-push" design). The "push-through" design blister is identical to the design of the approved 1-count sample package approved with supplements -021 and -022.

We have completed the review of this supplemental application 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 submitted final printed labeling (text for the 35, and 70 mg strength 4-count trade bifold blister packages submitted February 15, 2002). Accordingly, the supplemental application is approved effective on the date of this letter.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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

Sincerely,

{See appended electronic signature page}

Sheldon Markofsky, Ph.D.
Acting Chemistry Team Leader II, DNDC II for the
Division of Metabolic and Endocrine Drug Products
Office of New Drug Chemistry
Center for Drug Evaluation and Research

Enclosure

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Sheldon Markofsky
8/5/02 02:11:31 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-560/S036

LABELING

WEEK 1

Peel back strip

WEEK 2

Peel back strip

WEEK 3

Peel back strip

WEEK 4

Peel back strip

Important information:
Please read the enclosed Patient Information leaflet before taking *Once Weekly* FOSAMAX® (Alendronate Sodium Tablets). Keep this and all drugs out of the reach of children. Store at room temperature, 15–30°C (59–86°F).

ONCE WEEKLY FOSAMAX® (alendronate sodium tablets)

3 0006-0077-44 9

Apply Prescription Label Here

9508400

Once Weekly FOSAMAX® (Alendronate Sodium Tablets) 35 mg – No. 3813

For the prevention of osteoporosis in postmenopausal women

ONCE · WEEKLY FOSAMAX® 35 mg
(Alendronate Sodium Tablets)

Osteoporosis is a disease that causes bones to become thin, weak, and easy to break.

That's why it is important you take *Once Weekly* FOSAMAX to help protect your bones.

MERCK & CO., INC.
Whitehouse Station, NJ 08889, USA

Each tablet contains 45.68 mg alendronate sodium (35 mg free acid equivalent).

4 Tablets
No. 3813

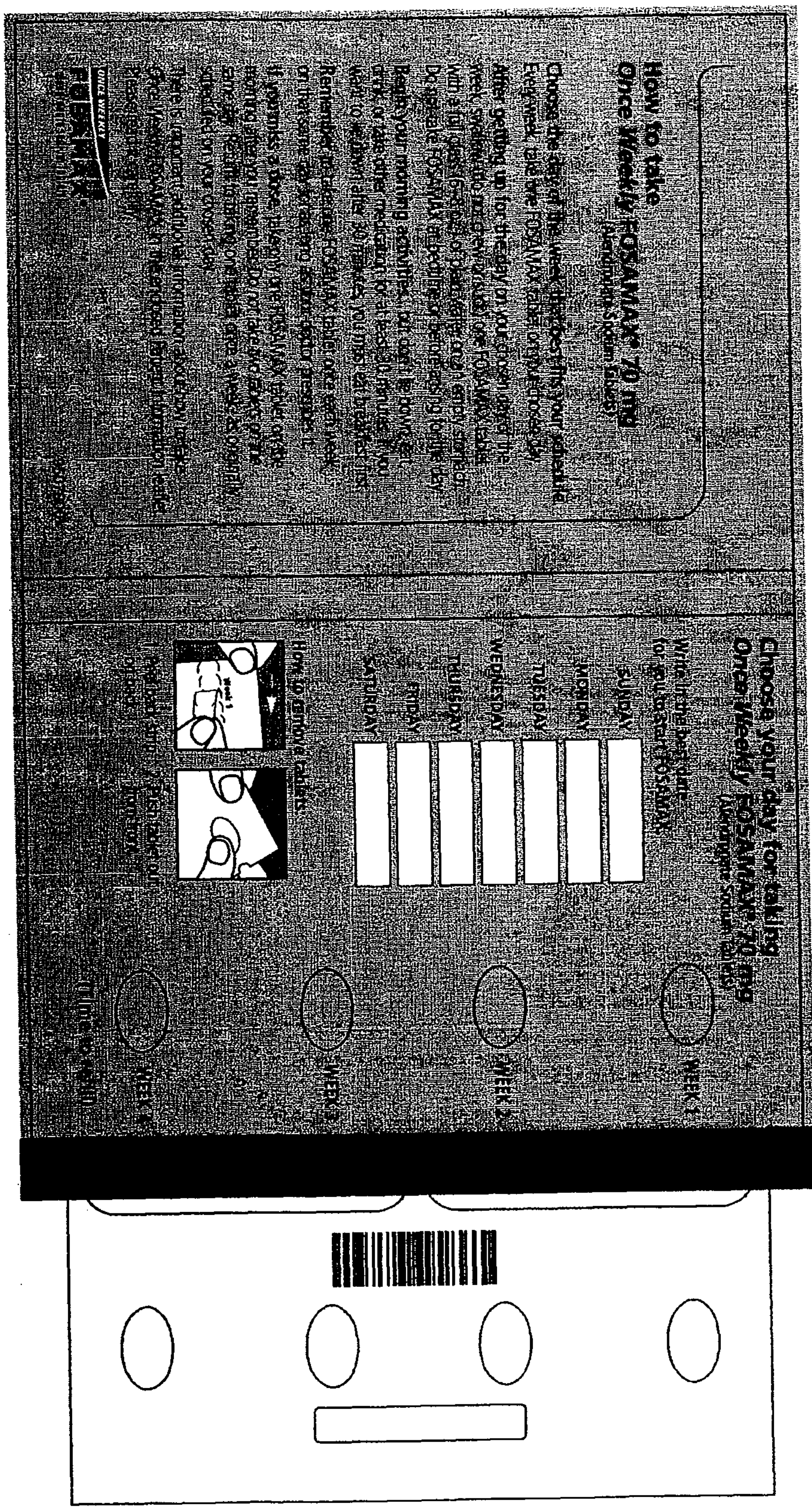
Rx only

USUAL ADULT DOSAGE:
ONE 35 mg TABLET
ONCE WEEKLY

See accompanying circular for complete dosage information.

How to take Once Weekly FOSAMAX 35 mg
Choose your day for taking Once Weekly FOSAMAX 35 mg
SUNDAY
MONDAY
TUESDAY
WEDNESDAY
THURSDAY
FRIDAY
SATURDAY
WEEK 1
WEEK 2
WEEK 3
WEEK 4

ONCE WEEKLY
FOSAMAX®
70 mg
Once Weekly FOSAMAX (Alendronate Sodium Tablets) 70 mg –No. 3814
Important information:
Please read the enclosed Patient Information leaflet before taking Once Weekly FOSAMAX® (Alendronate Sodium Tablets). Keep this and all drugs out of the reach of children. Store at room temperature, 15–30°C (59–86°F).
FOSAMAX®
(alendronate sodium tablets)
3 0006-0031-44 1
Apply Prescription Label Here
WEEK 1
Peel back strip
WEEK 2
Peel back strip
WEEK 3
Peel back strip
WEEK 4
Peel back strip
9508000


How to take
Once Weekly FOSAMAX® 70 mg
(Alendronate Sodium Tablets)
Choose the day of the week that best fits your schedule.
Every week, take one FOSAMAX tablet on your chosen day.
Choose your day for taking
Once Weekly FOSAMAX® 70 mg
(Alendronate Sodium Tablets)
Write in the best date
for you to start FOSAMAX.
SUNDAY
MONDAY
TUESDAY
WEDNESDAY
THURSDAY
FRIDAY
SATURDAY
How to remove tablets:
WEEK 1
WEEK 2
WEEK 3
WEEK 4
Time to refill
ONCE WEEKLY
FOSAMAX

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-560/S036

CHEMISTRY REVIEW(S)

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. P.O. Box 2000 Rahway, NJ 07065	SCP-036, (CBE-30) 2/15/02 User Fee date: 8/16/02 (6 months)

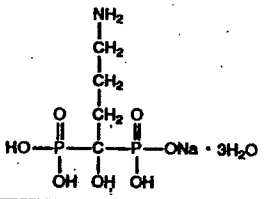
5. NAME OF THE DRUG	6. NONPROPRIETARY NAME	8. AMENDMENTS/REPORT, DATE
Fosamax™	Alendronate sodium tablets	3/8/02

7. SUPPLEMENT PROVIDES FOR:
The addition of an alternative "push-through" bifold packaging to the currently approved 4-count trade "peel-push" bifold packaging for the 35 and 70 mg tablets.

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 mg, 10 mg, 35 mg, 40 mg, and 70 mg	

14. CHEMICAL NAME AND STRUCTURE

(4-amino-1-hydroxybutylidene) bisphosphonic acid monosodium salt trihydrate, $C_4H_{12}NNaO_7P_2.3H_2O$



15. COMMENTS

This supplement is submitted, in electronic format, to HFD-510 as a CBE-30. The sponsor is requesting the addition of an alternative 4-count bifold packaging [child-resistant package ("push through") blister] to the currently approved 4-count trade bifold packaging [child-resistant ("peel push") blister package] for the 35 and 70 mg tablets. The amendment dated 3/8/02 provides samples of the currently approved and the proposed packaging materials.

16. CONCLUSION AND RECOMMENDATION

From a chemistry standpoint, adequate information has been provided. Issue an approval letter.

17. NAME	REVIEWER SIGNATURE	DATE COMPLETED
Elsbeth G. Chikhale, Ph.D.		7/18/02

DISTRIBUTION: ORIGINAL JACKET CSO REVIEWER DIVISION FILE

Init. by:
CC: HFD-510, NDA 20-560/S-036
HFD-510/S Markofsky /R Hedin /EG Chikhale/Division file/NDA 20-560

4 Page(s) Withheld

1 § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 20-560
5036

Environmental Assesment:

The sponsor is requesting a categorical exclusion from the requirements to prepare an Environmental Assessment under 21 CFR §25.31(a) because the change will not increase the use of the active moiety. This categorical exclusion is **acceptable**.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Elsbeth Chikhale
7/18/02 01:50:24 PM
CHEMIST

Sheldon Markofsky
7/18/02 02:26:01 PM
CHEMIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-560/S036 `

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Division of Metabolic and Endocrine Drug Products

PROJECT MANAGER LABELING REVIEW

Application Number: 20-560/S-036

Name of Drug: Fosamax (alendronate sodium) 35, and 70 mg Tablets

Sponsor: Merck Research Laboratories

Material Reviewed

Submission Dates:

- February 15, 2002, containing text for the 35, and 70 mg strength 4-count trade bifold blister package.

Background and Summary Description:

This Changes-Being-Effected (CBE) supplemental new drug application was submitted on April 9, 2001, and proposes an alternative to the currently approved 35 and 70 mg Once Weekly Tablet 4-count trade bifold packaging. The "peel-push" design will be replaced with a "push-through" blister identical to that approved for the 1-count sample package approved with supplements -021 and -022.

Review

- The submitted final printed labeling (FPL) for the text for the 35, and 70 mg strength 4-count trade bifold blister package (Identifier Number 9508400 (35 mg) and 9508000 (75 mg), Issued No Date) was compared to the currently approved FPL for the text for the 35, and 70 mg strength 4-count trade bifold blister package (Identifier Number 9362000 (35 mg), Revised No Date, Approved with S-021 on May 17, 2000, Acknowledged and Retained April 17, 2001 and Identifier Number 9361900 (70 mg), Revised No Date, Approved with S-022 on May 17, 2000, Acknowledged and Retained April 17, 2001).

The following changes have been made:

The "How to remove tablets:" section is changed from:

1. [redacted]
2. [redacted]

To:

1. Tear away tab along perforations or use scissors.
2. Turn card over, peel backing off at corner notch. Push tablet through foil.

These revisions are acceptable.

Conclusions

The label is acceptable, and an approval letter should be issued.

Reviewed by: Randy Hedin, R.Ph., Senior Regulatory Management Officer

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Randy Hedin
8/5/02 01:22:58 PM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-560/S-036

CBE-30 SUPPLEMENT

Merck & Co., Inc.
Attention: Michele R. Flicker, M.D., Ph.D., FACP
Director, Regulatory Affairs
P.O. Box 2000
Mail Drop: Ry 33-720
Rahway, NJ 07065-0900

Dear Dr. Flicker:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Fosamax (alendronate sodium) Tablets

NDA Number: 20-560

Supplement Number: S-036

Date of Supplement: February 15, 2002

Date of Receipt: February 19, 2002

This supplemental application, submitted as a "Supplement - Changes Being Effected in 30 days" supplement, proposes an alternative to the currently approved 35 and 70 mg Once Weekly Tablet 4-count trade bifold packaging. The "peel-push" design will be replaced with a "push-through" blister identical to that approved for the 1-count sample package approved with supplements -021 and -022.

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on April 20, 2002, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be August 19, 2002.

Please cite the application number listed above at the top of the first page of any communications concerning this application. All communications concerning this supplemental application should be addressed as follows:

U.S. Postal/Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Attention: Division Document Room, 14B-19
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, call me at (301) 827-6392.

Sincerely,

{See appended electronic signature page}

Randy Hedin, R.Ph.
Senior Regulatory Management Officer
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Randy Hedin
3/18/02 10:27:58 AM