DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Ellen R. Westrick
Executive Director, Office of Medical/Legal
Merck & Co., Inc.
UG3BC-10
P.O. Box 1000
North Wales, PA 19454-1099

RE: NDA# 20-560
Fosamax (alendronate sodium tablets)
MACMIS ID # 9727

Dear Ms. Westrick:

As part of its routine monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware of the Fosamax web site www.FOSAMAX.com (6-20-01) disseminated by Merck & Co., Inc. (Merck) which promotes this drug product in violation of the Federal Food, Drug, and Cosmetic Act (the Act) and its implementing regulations. Specifically, we object because the web site overstates the benefits of Fosamax while minimizing the risks associated with the drug.

Overstatement of Benefit

In the patient information section of the Fosamax web site, each web page has the same side bar on the left side of the page. The side bar consists of links to other web pages within the Fosamax web site. One link is titled "Preserving Your Independent Lifestyle." Use of this phrase in the context of product-specific promotional materials misleadingly implies an outcome of Fosamax treatment that has not been demonstrated by substantial evidence. Therefore, this claim is misleading because it overstates the potential benefit of Fosamax. Previous correspondence, dated October 4, 2000, addressed this concept in our response to your request for comment.

The information provided regarding the use of Fosamax in conjunction with Estrogen/Hormone Replacement Therapy (ERT/HRT) which appears in the patient information portion of the web site is misleading because it does not include facts material in light of representations made. For example, you provide information that "In clinical studies, the combination of FOSAMAX and ERT/HRT increased bone density more than either FOSAMAX or HRT alone." This presentation is misleading without the additional contextual information from the approved product labeling (PI) that no significant effect was seen for total body bone mineral density (BMD) or that the long-term effects of combined Fosamax and HRT on fracture occurrence and fracture healing have not been studied.

Inadequate Communication of Risk Information

The "Product Highlights" section of the healthcare professional portion of the web site is further divided into headings entitled "Efficacy," "Proven Tolerability," and "Indications." Presenting risk information under the heading "Proven Tolerability" minimizes the serious adverse effects associated with Fosamax therapy. According to the PI, these effects include cases of severe esophageal adverse reactions requiring hospitalization. Previous correspondence, dated December 20, 2000, and January 18, 2001, addressed this concept in our response to your request for comment.

The warning that patients should discontinue Fosamax and seek medical attention if they develop signs or symptoms signaling a possible esophageal reaction is incomplete because it does not include new or worsening heartburn. Therefore, the presentation is misleading because it is inconsistent with the PI in regard to this important warning. Previous correspondence, dated December 20, 2000, addressed this concept in our response to your request for comment.

The reference to inclusion of "Up to 54% of patients with a history of GI disorders at baseline" in the postmenopausal osteoporosis treatment studies is misleading. It does not convey the material information that patients who had a history of major upper GI tract disease were excluded from the studies. Previous correspondence, dated October 23, 2000, addressed this concept in our response to your request for comment.

DDMAC requests that Merck immediately discontinue the violative portions of the web site and all other promotional materials that contain the same or similar violative claims or representations. DDMAC requests that Merck submit a written response to this letter no later than July 5, 2001, including your plan to comply with DDMAC's request. Your written response should include a list of all materials that you have discontinued and the date that they were discontinued.

If you have any questions or comments, please contact me by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds you that only written communications are considered official. In all future correspondence regarding this particular matter, please refer to MACMIS ID #9727 in addition to the NDA number.

Sincerely,

{See appended electronic signature page}

Margaret M. Kober, R. Ph.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

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

/s/

Margaret Kober
6/20/01 01:18:09 PM

FOSAMAX®
(alendronate sodium tablets)

What's News Click here

Once Weekly! Click Here!

Proven to Help Build Bone.

Welcome to www.fosamax.com

(How Did You Hear About www.fosamax.com?)

(Free Information Concerning Osteoporosis)

(Rate Our Site)

FOSAMAX is a registered trademark of Merck & Co., Inc.

MERCK

20106757(1)-01/01-FOS

FOSAMAX®
(alendronate sodium tablets)

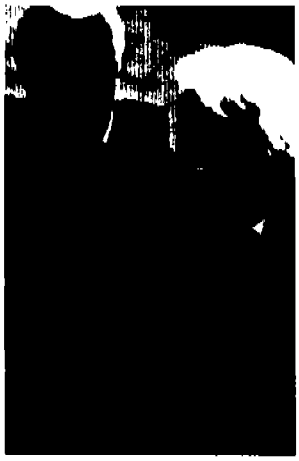
Products
Site Services
Site Guide
Home

Proven to Help Build Bone.

[redacted]is?
[redacted]
[redacted]Test?
[redacted]MAX Right For You?
What You Should Know About FOSAMAX
[redacted]Independent
[redacted]nity
[redacted]tion About

[redacted] This Link to a Friend

Is FOSAMAX Right For You?



FOSAMAX is for the treatment or prevention of osteoporosis (thinning of bone) in postmenopausal women. It reduces the chance of fractures, including those of the spine and hip.

FOSAMAX can be used in combination with Estrogen/Hormone Replacement Therapy (ERT/HRT). In clinical studies, the combination of FOSAMAX and ERT/HRT increased bone density more than either FOSAMAX or HRT alone. In these studies, the side-effects profile of combined treatment was consistent with those of the individual treatments.

FOSAMAX is a treatment to increase bone mass in men with osteoporosis.

FOSAMAX is for the treatment of osteoporosis in certain men and women receiving corticosteroid medications in a 7.5 mg or higher prednisone equivalent dose who have low bone mass.

FOSAMAX is for the treatment of Paget's disease of bone in certain men and women. Click here to find out about The Paget's Patient Support Program.

Important Information About FOSAMAX

FOSAMAX should not be used if you have certain disorders of the esophagus (the tube that connects your mouth with your stomach, or are unable to stand or sit upright for at least 30 minutes, have severe kidney disease, low blood calcium, are allergic to FOSAMAX, or are pregnant or nursing. Use with caution if you have certain stomach or digestive problems.

Side effects in clinical studies usually have been mild and generally have not caused patients to stop taking

Product Highlights

Prescribing Information

Patient Tools

Order Selected Reprints

OTHER RESOURCES:

Selected Media Features

Bone Mineral Density Tools

Medline Search

Related Links And Resources

Product Highlights

- Efficacy
- Proven Tolerability
- Indications

Scanning electron microscope image © David W. Dempster, Ph.D., 1999

Product Highlights • Prescribing Information • Patient Tools • Order Selected Reprints
Selected Media Features • Bone Mineral Density Tools
Medline Search • Related Links And Resources

Home • Site Services • Site Guide • Site References • Privacy Policy • Products • Merck

MERCK

20106760(4)-04/01-FOS

FOSAMAX®
(alendronate sodium tablets)

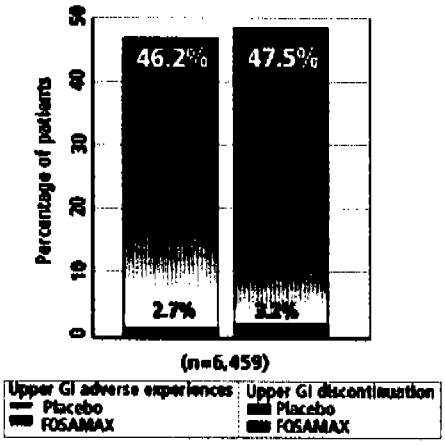
Accept nothing less...

Proven Tolerability Profile

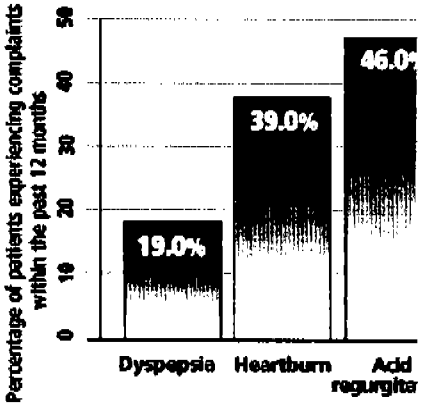
Postmenopausal Osteoporosis Treatment Studies With FOSAMAX Included:

- Up to 54% of patients with a history of GI disorders at baseline
- Up to 89% of patients who used NSAIDs or aspirin at some time during the studies

Incidence of Upper GI Complaints and Discontinuations in the FIT Study (Mean Age 69 Years)[5]



Age-Adjusted Prevalence Rates of GI Complaints In U.S. Caucasian Wo (45–74 Years)[6,†]



†Applying age-adjusted prevalence rates of GI complaints among Caucasian women 45–74 years 1990 U.S. Census Bureau Data (based on epidemiologic data from Caucasian women residing in County, Minnesota, who self-reported experiencing any of these reflux symptoms at any time in th months); adapted from: Locke GR III et al. Prevalence and clinical spectrum of gastroesophageal population-based study in Olmsted County, Minnesota. *Gastroenterology*. 1997;112:1448–1456.

Like other bisphosphonates, FOSAMAX may cause local irritation of the upper gastrointestinal mucosa.

- Esophageal adverse experiences, such as esophagitis, esophageal ulcers, and esophageal erosions, occasionally with bleeding and rarely followed by esophageal stricture, have been reported in patients receiving treatment with FOSAMAX. In some cases these have been severe and required hospitalization. Physicians should therefore be alert to any signs or symptoms signaling a possible esophageal reaction and patients should be instructed to discontinue FOSAMAX and seek medical attention if they develop dysphagia, odynophagia, or retrosternal pain.
- Because of possible irritant effects of FOSAMAX on the upper gastrointestinal mucosa and a potential for worsening of the underlying disease, caution should be used when FOSAMAX is given to patients with active upper gastrointestinal problems (such as dysphagia, esophageal diseases, gastritis, duodenitis, or ulcers).
- FOSAMAX may be administered to patients taking NSAIDs. However, since NSAID use is associated with gastrointestinal irritation, caution should be used during concomitant use with FOSAMAX.
- Abdominal pain was the most commonly reported drug-related adverse