FOI

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JUL - 2 1997

TRANSMITTED VIA FACSIMILE

Ellen R. Westrick
Senior Director, Office of Medical/Legal
Merck & Co., Inc.
P.O. Box 4, WP37B-113
West Point, Pennsylvania 19486

Re: **NDA 20-560**
Fosamax (alendronate sodium tablets)
MACMIS ID #5575

Dear Ms. Westrick:

Reference is made to Merck & Co. Inc.'s (Merck) June 6, 1997, FDA form 2253 submission for Fosamax. This material consists of a brochure customized for Blue Cross Blue Shield for Georgia (#974652) titled "Are you one of 20 million American women with osteoporosis."

The Division of Drug Marketing, Advertising and Communications (DDMAC) has reviewed this material and has determined that it is misleading and in violation of the Federal Food, Drug, and Cosmetic Act and applicable regulations for the following reasons:

. The headline on page two, "Menopause is the single most important cause of osteoporosis" is false because although menopause is a factor contributing to the development of osteoporosis, menopause alone does not cause osteoporosis. Further, the headline is misleading because it overstates the population eligible for therapy with Fosamax by implying that all women develop osteoporosis at menopause. DDMAC has commented on this issue previously in our December 15, 1995, advisory letter and most recently in our April 14, 1997, advisory letter for Fosamax.

DDMAC requests that Merck immediately discontinue the dissemination and use of this brochure and other promotional materials that contain similar themes. DDMAC requests that Merck submit a written response to this letter no later than

July 18, 1997, including Merck's plan to comply with DDMAC's request.

If Merck has further comments or issues, please contact me at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-40, Rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857.

In all future correspondence related to this matter, please refer to MACMIS ID #5575 and the NDA number.

Sincerely,

Anne M. Reb, MS, NP
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications

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.

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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

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