**DEPARTMENT OF HEALTH & HUMAN SERVICES** Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-560/S-047 & S-048
NDA 21-575/S-010 & S-011
NDA 21-762/S-002 & S-003

Merck & Co., Inc.
Attention: Michele Flicker, M.D., Ph.D.
Senior Director, Regulatory Affairs
P.O. Box 2000, Mail Drop: RY 33-204
Rahway, NJ 07065

Dear Dr. Flicker:

Please refer to the following supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fosamax (alendronate sodium) Tablets (NDA 20-560), Fosamax (alendronate sodium) Oral Solution (NDA 21-575) and Fosamax Plus D (alendronate sodium 70 mg/2800 I.U. Vitamin D) Tablets (NDA 21-575):

| NDA No. | Supplement No. | Submitted Date | Receipt Date |
|---|---|---|---|
| 20-560 | S-047 | October 25, 2005 | October 26, 2005 |
| 21-575 | S-010 | October 25, 2005 | October 26, 2005 |
| 21-762 | S-002 | October 25, 2005 | October 26, 2005 |
| 20-560 | S-048 | March 23, 2006 | March 24, 2006 |
| 21-575 | S-011 | March 23, 2006 | March 24, 2006 |
| 21-762 | S-003 | March 23, 2006 | March 24, 2006 |

We also refer to your submissions dated May 1, and November 17, 2006 to NDAs 20-560, 21-575, and 21-762.

These supplemental new drug applications provide for the following:

| NDA No. | |
|---|---|
| 20-560/S-047<br>21575/S-010<br>21-762/S-002 | A revised patient package insert (PPI) where important risk language is highlighted at the beginning of the insert, redundancy is eliminate, and information on osteoporosis and vitamin D is moved to the end of the insert. |
| 20-560/S-048<br>21575/S-011<br>21-762/S-003 | Revisions to the post-marketing adverse experiences section of the package insert (PI) to include asthenia, dizziness, joint swelling, peripheral edema and vertigo, and the patient package insert has been updated to include the following adverse events, dizziness, joint swelling and swelling of the hands and legs. |

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

We note that final printed labeling (FPL) was submitted for the PI on March 23, 2006.

The final printed labeling (FPL) for the PPI must be identical to the text for the submitted draft labeling dated November 17, 2006.

Please submit an electronic version of the FPL according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format - NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate these submissions "FPL for approved supplements NDA 20-560/S-047, NDA 21-575/S-010. and NDA 21-762/S-003." Approval of these submissions by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have fulfilled the pediatric study requirement for this application.

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) 796-1224.

Sincerely,

*{See appended electronic signature page}*

Mary H. Parks, M.D.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
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/

---

Theresa Kehoe
12/28/2006 10:17:15 AM
Theresa Kehoe for Mary Parks