



NDA 19-643/S-077

Merck & Co., Inc.
Attention: Kenneth A. Kramer
Manager, Regulatory Affairs
Sumneytown Pike, P.O. Box 4, BLA-20
West Point, PA 19486

Dear Mr. Kramer:

Please refer to your supplemental new drug application dated December 15, 2004, received December 16, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mevacor (lovastatin) Tablets.

We acknowledge receipt of your submission dated June 7, 2005.

This "Changes Being Effected" supplemental new drug application provides for changes to the **WARNINGS, PRECAUTIONS** and **DOSAGE AND ADMINISTRATION** sections of the package insert to add information on the drug interactions with telithromycin and danazol.

To the **WARNINGS, Myopathy/Rhabdomyolysis** subsection, the following changes were made to the cited subsection:

- Potent inhibitors of CYP3A4, telithromycin was added to the list.
- A third paragraph, under the first bullet, was added to read:
"Danazol, particularly with higher doses of lovastatin (see below: PRECAUTIONS, Drug Interactions, Other drug interactions)."
- To the paragraph that begins with "Consequently," the following changes and renumbering were made:
 1. Under number 1, telithromycin was added to the list of potent CYP3A4 inhibitors.
 2. A new number 3 was added to read:
"The dose of lovastatin should not exceed 20 mg daily in patients receiving concomitant medication with danazol. The benefits of the use of lovastatin in patients receiving danazol should be carefully weighed against the risk of this combination."

To the **PRECAUTIONS, Drug Interactions**, subsection, the following changes were made:

- *CYP3A4 Interactions*, telithromycin was added to the list of potent inhibitors of CYP3A4.
- *Other drug interactions*, the following new sentence was added to the list to read:
"Danazol: The risk of myopathy/rhabdomyolysis is increased by concomitant administration of danazol particularly with higher doses of lovastatin (see WARNINGS, Myopathy/Rhabdomyolysis)."

To the **DOSAGE AND ADMINISTRATION** section,

- *Dosage in Patients taking Cyclosporine* subsection title has been changed to *Dosage in Patients taking Cyclosporine or Danazol*. The paragraph was changed to read:
“In patients taking cyclosporine or danazol concomitantly with lovastatin (see WARNINGS, *Myopathy/Rhabdomyolysis*), therapy should begin with 10 mg of MEVACOR and should not exceed 20 mg/day.”

We completed our review of this supplemental new drug application. It is approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on June 7, 2005.

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.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

If you issue a letter communicating important information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
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.

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If you have any questions, call Margaret Simoneau, M.S., R.Ph., Regulatory Project Manager, at (301) 827-6411.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug 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
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/s/

Mary Parks
6/13/05 03:39:19 PM
for Dr. Orloff