DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-549/S-010

Vijay Tammara, Ph.D.
Director, Global Strategic Regulatory Development
Merck & Co., Inc.
P.O. Box 1000, UG2CD-48
North Wales, PA 19454

Dear Dr. Tammara:

Please refer to your supplemental new drug application dated August 29, 2005, received August 30, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for EMEND™ (aprepitant) Capsules, 40 mg.

We acknowledge receipt of your submissions dated December 28, 2005, January 30, February 3, March 1, March 9, April 11, May 4, June 8, June 20, June 23, June 28, June 29, and June 30, 2006.

This supplemental new drug application provides for the use of Emend™ (aprepitant) Capsules for the prevention of post-operative nausea and vomiting (PONV) utilizing a new 40 mg strength.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling text for the Package Insert (PI) submitted June 23, 2006, Patient Package Insert submitted June 21, 2006, and the container and carton labels submitted January 30, 2006 with the inclusion of the following changes agreed to during our June 27, 2006 teleconference and your June 30, 2006 submission. In your June 30, 2006 submission, you agreed to make changes A, B, and C at your next printing of your carton, blister, and tri-fold labeling.

A. CARTON LABELING

- Change the color schemes used for the carton for each strength (40 mg, 80 mg, and 125 mg) in order to differentiate each strength.
- Relocate the net quantity so that it is not presented in close proximity to the product strength.
- Relocate the word “capsules” from directly under the text box containing the product strength to immediately following the established name.
- Increase the prominence of the word “capsules” so that it is the same size font as the active ingredient, aprepitant.

B. BLISTER LABELING

- Increase the font size of the strength of each blister label, and retain the current black/white color.
- For consistency, will change the physician sample package to read as follows: “Sample–Not for Sale”

C. TRI-FOLD LABEL

- Relocate the word “capsules” from directly under the text box containing the product strength to immediately following the established name.
- Increase the prominence of the word “capsules” so that it is the same size font as the active ingredient, aprepitant.
- Label each tri-fold section so that the strength contained in each blister is clearly delineated.

These revisions are terms of the NDA approval. Marketing the product before making the revisions, exactly as stated, in the product’s labeling may render the product misbranded and an unapproved new drug. Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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 supplement NDA 21-549/S-010**." Approval of this submission 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 are deferring submission of your pediatric studies for ages 0 to less than 17 years of age until December 31, 2009.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of these postmarketing studies shall be reported annually according to 21 CFR 314.81. These commitments are listed below.

1. Deferred pediatric study under PREA for the treatment of post-operative nausea and vomiting pediatric patients ages 0 to less than 17 years of age.

   Final Report Submission: December 31, 2009.

Submit final study reports to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated “**Required Pediatric Study Commitments**”.

In addition, we remind you of your postmarketing study commitment in your submission dated June 29, 2006. This commitment is listed below.

> Title: *An open label study to evaluate the effect of a single 40-mg dose of aprepitant on the activity of Cytochrome P-450 2C9 in healthy young adult subjects*.
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> |---|---|
> | Protocol Submission: | October 31, 2006 |
> | Study Start: | February 28, 2007 |
> | Final report Submission: | December 31, 2007 |

Please note that we recommend that you submit your proposed protocol for review and comment in order for us to craft a mutually agreed-upon study to fulfill this commitment.

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

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:

> Food and Drug Administration
> Center for Drug Evaluation and Research
> Division of Drug Marketing, Advertising, and Communications
> 5901-B Ammendale Road
> Beltsville, MD 20705-1266

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
> Food and Drug Administration
> WO 22, Room 4447
> 10903 New Hampshire Avenue
> Silver Spring, MD 20993-0002

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Betsy Scroggs, Regulatory Health Project Manager, at (301) 796-0991.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Deputy Director
Division of Gastroenterology Products
Office of Drug Evaluation III
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/

Joyce Korvick
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