



NDA 020216/S-067

**SUPPLEMENT APPROVAL**

Pfizer Inc.  
Attention: Ursula Campbell, Senior Director  
Worldwide Regulatory Strategy  
235 East 42<sup>nd</sup> Street  
New York, NY 10017

Dear Ms. Campbell:

Please refer to your Supplemental New Drug Application (sNDA) dated April 7, 2009, received April 8, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Premarin<sup>®</sup> (conjugated estrogens) Vaginal Cream.

We acknowledge receipt of your amendments dated September 24, 2009 and March 24, 2010.

This supplemental new drug application proposes:

- A revision to section **17.4 Instructions for Use of Applicator** in the **PATIENT COUNSELING INFORMATION** to include the addition of a graphic as a visual aid for applicator use.
- Adding visual aid graphics to the text under “How should I use PREMARIN Vaginal Cream?” in Patient Labeling.
- A minor revision of Table 3, which is entitled “Mean Change in Dyspareunia Severity Compared to Placebo MITT Population of Most Bothersome Symptom Score for Dyspareunia, LOCF.” The revision includes changing the p-value from <0.01 to <0.001 for the comparison of Premarin Vaginal Cream 2x/week with placebo 2x/week.
- Inclusion of a 30-gm packaging configuration.
- Updating the labeling to conform to the latest class labeling information for estrogen products for the treatment of menopausal symptoms.

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

**CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(1)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at

<http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling, with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As” at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

### **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

### **PROMOTIONAL MATERIALS**

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

### **REPORTING REQUIREMENTS**

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 George Lyght, R.Ph., Sr. Regulatory Health Project Manager, at (301) 796-0948.

Sincerely,

*{See appended electronic signature page}*

Scott Monroe, M.D.  
Director  
Division of Reproductive and Urologic Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

ENCLOSURE(S):  
Content of Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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SCOTT E MONROE  
04/22/2011