DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-527/S-017

Wyeth Pharmaceuticals
Attention: Jennifer D. Norman
Associate Director
Worldwide Regulatory Affairs
P.O. Box 8299
Philadelphia, PA 19101

APPROVAL LETTER

Dear Ms. Norman:

Please refer to your supplemental new drug application dated June 15, 2000, received June 15, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for PREMPRO™ (conjugated estrogens /medroxyprogesterone acetate tablets) and PREMPHASE® (conjugated estrogens/medroxyprogesterone acetate tablets).

We acknowledge receipt of your submissions dated April 23 and 30, September 27, 2001; July 31, August 2, September 11, 2002; February 10 and 28, March 4, 5, 6 and 12, 2003. Your September 11, 2002 submission constituted a complete response to our approvable letter of April 13, 2001.

This supplemental new drug application provides for the use of PREMPRO™ (0.45 mg conjugated estrogen/ 1.5 mg medroxyprogesterone acetate) in a continuous combined regimen for:

1. Treatment of moderate to severe vasomotor symptoms associated with the menopause.

2. Treatment of moderate to severe symptoms of vulvar and vaginal atrophy associated with the menopause. When prescribing solely for the treatment of symptoms of vulvar and vaginal atrophy, topical vaginal products should be considered.

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.

We remind you of our agreements that were made in our March 5, 2003, teleconference and in your submission dated March 6, 2003. These agreements are listed below.

1. You have agreed to an interim release and stability specification for CE dissolution at the 5 hour timepoint. This interim acceptance criterion is(b)(4) .
2. You have committed to the identification of additional/improved in-process controls at the(b)(4) (b)(4) of conjugated estrogens tablet manufacture. Once these improvements h identified, three revalidation batches will be manufactured and subjected to room temperature and accelerated stability studies. You anticipate that the results from these studies will be reported in the fourth quarter of 2003.
3. (b)(4)
4. You have committed to a Dissolution Surveillance Program for the dissolution of conjugated estrogens in the 0.45 mg/1.5 mg Premarin®/MPA drug product. In this commitment, every packaged lot will be tested for CE dissolution at six-month intervals. This surveillance program will be performed through expiration of the product.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert, immediate container and carton labels). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit the FPL electronically 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, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-527/S-017." Approval of this submission by FDA is not required before the labeling is used.

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, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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 Kassandra Sherrod, R.Ph., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Daniel Shames, M.D.
Director
Division of Reproductive and Urologic Drug 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/

Margaret Kober
3/12/03 05:55:25 PM
signed for Daniel Shames