CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION: NDA 20527/S004

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	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
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Medical Review(s)	X			
Chemistry Review(s)			X	
EA/FONSI			X	
Pharmacology Review(s)			X	
Statistical Review(s)			X	
Microbiology Review(s)			X	
Clinical Pharmacology Biopharmaceutics Review(s)			X	
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CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: NDA 20527/S004

Trade Name: Prempro/Premphase

Generic Name:(conjugated estrogens/medroxyprogesterone acetate tablets)/(conjugated estrogens/medroxyprogesterone acetate)

Sponsor: Wyeth-Ayerst Laboratories

Approval Date:July 31, 1997

INDICATION: Provides for revised labeling to combine the information from the separate PREMPRO and PREMPHASE direction circulars into single combined insert.

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number:NDA 20527/S004

APPROVAL LETTER

JUL 31 1997

NDA 20-527/S-004

Wyeth-Ayerst Laboratories
Attention: Joan E. Barton, Associate Director
Marketed Products
Drug Regulatory Affairs
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Ms. Barton:

We acknowledge your supplemental new drug application dated October 18, 1996, received October 21, 1996, 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)

The supplemental application provides for revised labeling to combine the information from the separate PREMPRO™ and PREMPHASE® direction circulars into a single combined insert.

We have completed the review of this supplemental application and it is approved effective on the date of this letter.

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, please contact Diane Moore, Consumer Safety Officer, at (301) 827-4260.

Sincerely,

/S/ 7/30/97

Lisa D. Rarick, M.D.
Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20527/S004

MEDICAL REVIEW(S)

FEB 27 1997

December 5, 1996

ORIGINAL

NDA 20-527/S-004

PREMPRO™ and PREMPHASE™
Conjugated Estrogens/Medroxyprogesterone Acetate
0.625 mg CE/2.5 mg MPA and 0.625 mg CE/5.0 mg MPA
Combination Tablets
Wyeth-Ayerst Laboratories
Philadelphia, PA

Type of Submission: Supplemental Application - Labeling Update
Date of Submission: October 18, 1996

SYNOPSIS

The proposed annotated combined labeling for PREMPRO and PREMPHASE was reviewed with reference to the labeling for PREMPRO and PREMPHASE (combination tablets, NDA 20-527) approved on June 13, 1996. The sponsor's October 18, 1996 supplemental application proposes to combine the information from the separate PREMPRO and PREMPHASE labeling into a single combined insert.

FINDINGS:

Clinical Pharmacology: Satisfactory combined text. The correction to the total number of patients from 279 to 277 in the table summarizing the incidence of endometrial hyperplasia after one year of treatment with the combined regimens (page 4 of the draft labeling) is appropriate.

RECOMMENDATION:

Since the proposed revised draft physician and patient labeling for the present NDA 20-527/S-004 is identical to that provided for NDA 20-527 for PREMPRO and appropriately updates the clinical pharmacology section of the PREMPHASE labeling, this supplemental application is recommended for approval.

Please convey the Recommendation as appropriate to the sponsor.

/S/

Theresa H. van der Vlugt, M.D., M.P.H.
Medical Officer

Concur: /S/ 2/27/97

cc: NDA 20-527
HFD-580/T.van der Vlugt
HFD-580/H. Jolson
HFD-580/Diane Moore

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20527/S004

CORRESPONDENCE

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-527/S-004

OCT 29 1996

Wyeth-Ayerst Laboratories
P. O. Box 8299
Philadelphia, PA 19101-8299

Attention: Joan E. Barton, Associate Director
Marketed Produts
Drug Regulatory Affairs

Dear Ms. Barton:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Prempro/Premphase Tablets

NDA Number: 20-527

Supplement Number: S-004

Date of Supplement: October 18, 1996

Date of Receipt: October 21, 1996

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on December 20, 1996 in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Office of Drug Evaluation II
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

/S/

Lana Pauls
Chief, Project Management Staff
Division of Reproductive and Urologic
Drug Products, HFD-580
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Original NDA 20-527/S-004
HFD-580/Div. Files
HFD-580/CSO/Moore

SUPPLEMENT ACKNOWLEDGEMENT

WYETH-AYERST RESEARCH

P.O. BOX 8299, PHILADELPHIA, PA 19101-8299 • (610) 902-3710
FAX: (610)964-5973

Division of American Home Products Corporation

U.S. REGULATORY AFFAIRS

NDA No. 20-527
PREMPRO™/PREMPHASE® Tablets

NDA No. 20-527 REF. NO. S-004
NDA SUPPL FOR Labeling

October 18, 1996

REVIEWS COMPLETED
ACTION: ☑ LETTER ☐ N.A.I. ☐ MEMO
CSO INITIALS
DATE 1/31/97

REC'D
OCT 21 1996
HFD-580

Lisa Rarick, M.D., Director
Division of Reproductive
and Urologic Drug Products
Room 17B-20
Food and Drug Administration (HFD-580)
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. Rarick:

Reference is made to our approved New Drug Application No. 20-527 for PREMPRO, conjugated estrogens/medroxyprogesterone acetate tablets and PREMPHASE, conjugated estrogens/medroxyprogesterone acetate tablets.

The purpose of this supplemental application is to provide revised labeling to combine the information from the separate PREMPRO and PREMPHASE direction circulars into a single combined insert. The only change in the text is to correct the total number of women from 279 to 277 in the table (page 4 of the draft) for the PREMPHASE arm of the study demonstrating the incidence of endometrial hyperplasia. In support of this supplemental application provided herewith are four copies of draft labeling.

We trust that you will find this information satisfactory and will approve this labeling at your earliest convenience. Should you have any questions, please call the undersigned at (610) 902-3772 or Mr. Robert Quinty at (610) 902-3789.

Sincerely,

WYETH-AYERST LABORATORIES

Joan Barton /ODV

Joan E. Barton, Associate Director
Marketed Products
Drug Regulatory Affairs

:JEB:crms\J2194

LTH-138C