

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

20-216/S033

Trade Name: PREMARIN Vaginal Cream, 0.625 mg/g

Generic Name: (conjugated estrogens)

Sponsor: Wyeth-Ayerst Laboratories.

Approval Date: June 14, 1993

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APPLICATION NUMBER:

20-216/S033

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APPROVAL LETTER

20-216/S033

JUN 14 1993

Wyeth-Ayerst Laboratories
Attention: Joseph L. Morrison, Ph.D.
Division of American Home Products Corporation
P.O. Box 8299
Philadelphia, PA 19101-1245

Dear Dr. Morrison:

Reference is made to your supplemental new drug application dated July 31, 1992, submitted pursuant to section 505(b) of the Federal Food, Drug and Cosmetic Act for Premarin (conjugated estrogens) Vaginal Cream.

The supplement (S-033) provides for the use of benzyl alcohol as a preservative in place of the currently used preservative, _____

b(4)

We have completed the review of your supplemental application (S-033) and it is approved, effective on the date of this letter.

In addition, we have the following recommendations, although not required for approval:

1. The implementation _____ is suggested. These controls are deemed especially important for reprocessing operations. b(4)
2. A re-evaluation of the need for the _____ of active ingredients is suggested. b(4)

Although the use of _____ as a alternate supplier of _____ tubes and an alternate _____ cap was included in your _____

b(4)

b(4)

Comments concerning _____ will be conveyed under a separate cover letter for _____. The approval of supplement S-033 does not impact the status of _____

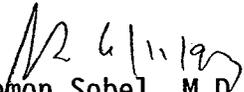
b(4)

b(4)

We remind you that you must comply with the requirements set forth under 21 CFR 314.80 and 314.81 for approved NDAs.

If you have any questions, please contact Ms. Sharon Olmstead at 301-443-3510.

Sincerely yours,


Solomon Sobel, M.D.
Director
Division of Metabolism and
Endocrine Drug Products (HFD-510)
Center for Drug Evaluation and Research

cc: NDA Arch
HFD-510
HFC-130/JAllen
HFD-80
HFD-510/SMoore
HFD-511/SOlmstead/5/27/93/ft/lp/6/9/93/N20216AP.S33
Concurrences: Moore 6/2/Chiu 6/3/93

SUPPLEMENT APPROVAL (S-033)

SO
6/9/93

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APPLICATION NUMBER:

20-216/S033

CHEMISTRY REVIEW(S)

ORIGINAL

NDA 20-216/S-033, S-034

APR 21 1993

*CSO: please issue
letters accordingly to
the recommendations
in the Addendum written
by Dr. S. Moore
of Chiu
4/21/93*

NAME AND ADDRESS OF APPLICANT:

Wyeth-Ayerst Laboratories
Attention: Mr. Joseph L. Morrison
P. O. Box 8299
Philadelphia, PA 19101-1245

PURPOSE OF AMENDMENT/SUPPLEMENT

Provides:

S/033: For the use of benzyl alcohol as a preservative in
place of _____ b(4)

For the _____ b(4)
_____ b(4)

DATE(S) OF SUBMISSION(S)

July 31, 1992

PHARMACOLOGICAL CATEGORY

Treatment of atrophic vaginitis and kraurosis vulvae

TRADE NAME

Premarin

NONPROPRIETARY NAME

Conjugated estrogens

DOSAGE FORM

Cream

POTENCY

0.625 mg/g

RX OR OTC

Rx

SAMPLES

N/A

RELATED IND/NDA/DMF

STERILIZATION

N/A

LABELING

N/A

BIOEQUIVALENCY STATUS

N/A

ESTABLISHMENT INSPECTION

N/A

4 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

Chemistry Review
20-216/5033

4) _____, found out of specifications, can be attributed to analytical mistakes _____ and therefore are not significant.

5) Issue a deficiency letter.

RECALLS

Reviewer

Date Completed

N/A

A. Croitoru

January 25, 1993

ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:

N/A

ORDER OF REVIEW:

The application submission(s) covered by this review was taken in the date order of receipt Yes X
No _____

A. Croitoru
20217CHS.WYA #7 f#7
January 25, 1993

CONFIRMED
Gibbs
1/24/93

5 Page(s) Withheld

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 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

*Addendum to Chemistry
Review
20-216/5033*

**CENTER FOR DRUG EVALUATION AND
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APPLICATION NUMBER:

20-216/S033

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: January 25, 1993

FROM: A. Croitoru

TO: Y. Y. Chiu, Ph.D

SUBJECT: NDA 20-216

Please note that Premarin Vaginal Cream is formulated with a ~~_____~~ overage (page 3), which the firm states is required for ~~_____~~ b(4)

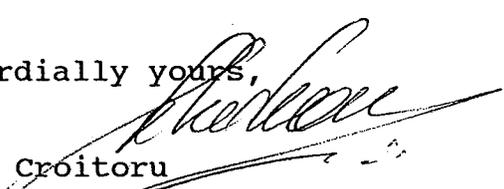
Therefore I may conclude that depending on the age of the cream and/or the accuracy of the testing, the % of active may range in between ~~_____~~ b(4)

This overage raises certain concerns:

- 1) The cream when dispensed may have a ~~_____~~ than expected. It is known that with the use of ~~_____~~ there is a risk of endometrial cancer, that depends on both the duration of the treatment and on estrogen dose. b(4)
- 2) Since ~~_____~~ indicated to be ~~_____~~ b(4) whow can the physician expect to know if the patient is getting ~~_____~~ or ~~_____~~ of the prescribed dose and how can he control it. b(4)

Will appreciate your comments.

Cordially yours,


A. Croitoru

2 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

*Attachments to
Memorandum*

Food and Drug Administration
Rockville MD 20857

Date 8-25-92

NDA No. 20--216

Wyeth-Ayerst Laboratories
P.O. Box 8299
Philadelphia, PA 19101-1245

Attention: Joseph L. Morrison, Ph.D.

Dear Sir/Madam:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Premarin, conjugated Estrogens, Vaginal Cream.

NDA Number: 20-216

Supplement Number: S-033

Date of Supplement: July 31, 1992

Date of Receipt: August 5, 1992

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Attention: Document Control Room 14B-03
5600 Fishers Lane, HFD-510
Rockville, MD 20857

Sincerely yours,

*Harold Headspeth*Harold Headspeth for
Supervisory Consumer Safety Officer
Division of Metabolism and Endocrine Drug Products
Center for Drug Evaluation and Research