

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
ANDA 086069Orig1s017

Name: Estradiol Vaginal Cream USP
0.01%

Sponsor: Warner Chilcott Laboratories

Approval Date: March 27, 2001

CENTER FOR DRUG EVALUATION AND RESEARCH

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ANDA 086069Orig1s017

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APPLICATION NUMBER:
ANDA 086069Orig1s017

APPROVAL LETTER

ANDA 86-069/S-017

Warner Chilcott Laboratories
Attn: Blair Harvey
Rockaway 80 Corporate Center
100 Enterprise Drive, Suite 280
Rockaway, NJ 07866

MAR 27 2001

Dear Sir:

This is in reference to your supplemental new drug application dated November 3, 2000, submitted under Section 505(j) of the Federal Food, Drug, and Cosmetic Act, regarding your abbreviated new drug application for Estradiol Vaginal Cream, USP, 0.01%.

The supplemental application, submitted as "Supplement-Changes Being Effected in 30 Days", provides for a change in the manufacturing site for the Drug Substance, Estradiol, USP.

We have completed review of this supplemental application and it is approved.

We remind you that you must comply with the requirements for an approved abbreviated new drug application described in 21 CFR 314.80-81.

The material submitted is being retained as part of your application.

Sincerely yours,

M. Smela for 3/26/01

Rashmikanth M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center of Drug Evaluation and Research

cc: ANDA 86-069/S-017
Division File
Field Copy
HFD-600/Reading File

Endorsements:

HFD-625/S. Adah/03/19/01 *Stan Adah 3/22/01*
HFD-625/M. Smela/03/19/01/3/22/01 *for M. Smela 3/26/01*
HFD-625/M. Dillahunt/PM/03/19/01/3/22/01 *Dillahunt 3/26/01*

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F/T by: DJ 3/22/01

APPROVAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 086069Orig1s017

CHEMISTRY REVIEW

ANDA
86-069/SCB017

NAME AND ADDRESS OF APPLICANT:

Warner Chilcott Laboratories
Attn: Blair Harvey
Rockaway 80 Corporate Center
100 Enterprise Drive, Suite 280
Rockaway, NJ 07866

PURPOSE OF AMENDMENT/SUPPLEMENT

Change in manufacturing site for the Drug Substance, Estradiol, USP

DATE OF SUBMISSION

November 3, 2000

PHARMACOLOGICAL CATEGORY

Treatment of vulval and vaginal atrophy

TRADE NAME

Estrace

NONPROPRIETARY NAME

Estradiol Vaginal Cream, USP, 0.01%

DOSAGE FORM

Cream

POTENCY

0.01%

Rx OR OTC

R_x

REMARKS AND CONCLUSION

Approved

REVIEWER

Steven Adah

DATE COMPLETED

March 19, 2000

cc: ANDA # 86069
Division File
Field Copy

Endorsements:

HFD-625/S. Adah/3/19/01 *Steven Adah 3/22/01*
HFD-625/K. Furnkranz/3/22/01 *K. Furnkranz 3/26/01*
HFD-625/M.Dillahunt/
v: \firmsnz\warnerch\ltrs&rev\86069s17.rev
F/T by: DJ 3/22/01

RELATED IND/NDA/DMF

N/A

STERILIZATION

N/A

LABELING

N/A

BIOEQUIVALENCY STATUS

N/A

ESTABLISHMENT INSPECTION

Acceptable – November 30, 2000

See attached summary report.

COMPONENTS, COMPOSITION, MANUFACTURING, CONTROLS

Warner Chilcott has submitted this supplement – changes being effected in 30 days to report that (b) (4) one of their approved manufacturers for Estradiol, USP will be manufacturing future lots of Estradiol at a new manufacturing site.

(b) (4)



ORDER OF REVIEW:

The application submissions covered by this review were taken in the date order of receipt

No ____ Yes X

If no, explain reason (s) below:

SPOT? Yes ____ No X
If yes, complete form

ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: **ANDA 86069/017**
Stamp: **06-NOV-2000** Regulatory Due:
Applicant: **WARNER CHILCOTT**
100 ENTERPRISE DR STE 280
ROCKAWAY, NJ 07866

Priority:
Action Goal:
Brand Name: **ESTRACE**
Established Name: **ESTRADIOL**
Generic Name:
Dosage Form: **CRM (CREAM)**
Strength: **0.01% VAGINAL**

Org Code: **600**District Goal: **06-APR-2001**

FDA Contacts: **M. DILLAHUNT (HFD-613)** **301-827-5848** , Project Manager
M. SMELA JR (HFD-625) **301-827-5848** , Team Leader

Overall Recommendation:

ACCEPTABLE on 30-NOV-2000 by M. GARCIA (HFD-322) 301-594-0095

Establishment:

(b) (4)

DMF No:

AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **30-NOV-2000**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **DRUG SUBSTANCE**
MANUFACTURER

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 086069Orig1s017

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS



WARNER CHILCOTT
LABORATORIES

November 3, 2000

Mr. Gary Buehler
Acting Director, Office of Generic Drugs
Food and Drug Administration (CDER)
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

**Special Supplement-
Changes Being Effectuated in 30 days**

NDA NO. _____ REF. NO. SCB017
NDA SUPPL FOR Facility Add / MT

Re: ANDA #86-069
Estrace® Vaginal Cream (Estradiol Vaginal Cream, USP, 0.01%)
Supplement: Change in manufacturing site for the Drug Substance, Estradiol, USP

Dear Mr. Buehler:

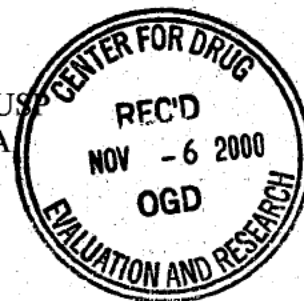
Reference is made to our abbreviated new drug application for Estrace® Vaginal Cream (Estradiol Vaginal Cream, USP, 0.01%). In accordance with the Guidance for Industry entitled "Changes to an Approved NDA or ANDA" issued November 1999 we are submitting a special supplement-changes being effected in 30 days to provide for an alternate manufacturing site for drug substance Estradiol, USP used in the manufacture of Estrace cream. This change is covered under section VI, C, 1a of the aforementioned guidance document.

(b) (4) one of our approved manufacturers of Estradiol, USP has informed us by way of Bristol-Myers Squibb Co. that future lots of Estradiol will be manufactured at a new (b) (4) facility. Bristol-Myers Squibb Co. manufactures Estrace Vaginal Cream for Warner Chilcott using Estradiol, USP supplied by (b) (4)

We have learned from (b) (4) that there has been FDA oversight regarding this change including an FDA inspection of the new (b) (4) manufacturing site in 1998.

Warner Chilcott has received notification from (b) (4) that they have submitted amendments to the relevant DMF's to the FDA. In addition, (b) (4) has prepared a report covering the introduction of the new manufacturing facility. Please refer to Attachment A for a copy of this report supporting this new manufacturing facility. This report includes

- 1) Validation of estradiol production at the new site
- 2) Stability information
- 3) Letter from FDA Office of New Drug Chemistry and Generic Drugs
- 4) Representative Certificates of Analysis for the drug substance Estradiol, USP
- 5) (b) (4) has amended the appropriate DMF, and has submitted it to FDA



ANDA #86-069

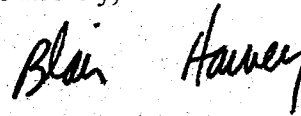
Mr. G. Buehler

Page 2

Warner Chilcott's stability commitment for this CBE-30 supplement, consists of a commitment to place the first production batch of Estrace cream in our approved container/closure system on long term stability in our ongoing program. The results of this stability study will be reported in the annual report in accordance with 21 CFR 314.81 (b)(2).

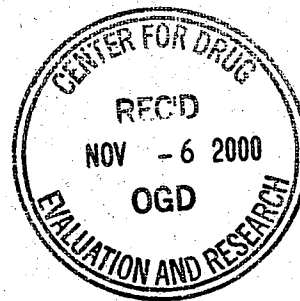
We trust that the enclosed information is satisfactory and will permit approval of this supplemental application. Our intent is put these changes in place after December 7, 2000. Please do not hesitate to contact me directly at (973) 442-3229 if you should have any questions regarding this supplement. In accordance with current FDA requirements, a field copy of this submission is being sent to our home FDA district office (New Jersey District Office).

Sincerely,



Blair Harvey
Manager, Regulatory Affairs
Warner Chilcott, Inc.

C: FDA Field Copy: Ms. Regina Brown, FDA New Jersey District Office



SPECIAL

A15.1

CBE- THIRTY (30) DAY SUPPLEMENT ROUTING FORM

This form is to accompany all CBE-30 Day supplements. Upon completion, return to the OGD Document Room

- I. To be completed by the OGD Document Room using information from the applicant Cover letter:

DATE PROCESSED: 11-7-00
APPLICATION # : N 86069 SUPPLEMENT # : SCB017

- II: To be determined by Chemistry Division Staff.

Date and initial appropriate category.

Thirty (30) Day CBEs:

Chemistry Div. Staff	Qualifies as CBE-30 (GR)	Does Not Qualify. This is a CBE-0. (DC)	Does not Qualify. This is an Annual Report (DA)	Does not Qualify. This is a Prior Approval Supp. (DN)
Chemistry/Micro Project Manager(s)	<i>M. Smeul</i> 11/24/00			
Micro and/or Labeling Team Leader (as needed)	N/A			
Chemistry Team Leader	<i>M. Smeul</i> 11/29/00			
Chemistry Div. Dir. Or Deputy* Dir.				

*Div/Deputy Director signature needed only when: 1) CBE elevated to PAS or 2) PM/TM recommend different actions,
COMMENTS:

see requested 11/24/00

- III. To Project Manager Chemistry Team 2:

Prepare letter and notify applicant by telephone when CBE is denied because it is a prior approval supplement.

DATE: _____

Notify applicant by telephone that inappropriate CBE category used.

DATE _____

Request that applicant withdraw supplement when CBE qualifies for submission as an Annual Report

DATE _____

- IV. To Document Room

Record appropriate CBE Code
File in archival submission

GR