CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 20-472/S-004

Trade Name: Estring 2 mg

Generic Name: estradiol vaginal ring

Sponsor: Pharmacia and Upjohn Company

Approval Date: 07/24/2001

Indications: For the treatment of urogenital symptoms associated with post-menopausal atrophy of the vagina (such as dryness, burning, pruritus and dyspareunia) and/or the lower urinary tract (urinary urgency and dysuria).

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-472/S-004

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Reviews / Information Included in this NDA Review.

Approval Letter	X
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Summary Review	
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Cross Discipline Team Leader Review	
Medical Review(s)	
Chemistry Review(s)	X
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Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
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Proprietary Name Review(s)	
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APPLICATION NUMBER:

NDA 20-472/S-004

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-472/S-004

APPROVAL LETTER

Pharmacia & Upjohn
Attention: Daniel G. Chirby, M.Sc.
Regulatory Manager
7000 Portage Road
Kalamazoo, MI 49001-0199

Dear Mr. Chirby:

Please refer to your supplemental new drug application dated January 30, 2001, received January 31, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ESTRING, (estradiol vaginal ring) 2mg.

This "Changes Being Effected" supplemental new drug application provides for the addition of an alternate manufacturing site of the drug substance in ESTRING.

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

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, call Dornette Spell-LeSane, NP-C, Regulatory Project Manager, at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Moo-Jhong Rhee, Ph.D.
Chemistry Team Leader, for the
Division of Reproductive and Urologic
Drug Products, (HFD-580)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Moo-Jhong Rhee
7/24/01 10:37:40 AM

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APPLICATION NUMBER:

NDA 20-472/S-004

CHEMISTRY REVIEW(S)

CHEMIST REVIEW
OF **SUPPLEMENT**

1. **ORGANIZATION:** DRUDP HFD-580
2. **NDA NUMBER:** 20-472/SCM-004
3. **SUPPLEMENT NUMBERS/DATES:**
   Letterdate: 30-JAN-2001
   Stampdate: 31-JAN-2001
4. **AMENDMENTS/REPORTS/DATES:**
   Letterdate:
   Stampdate:
5. **RECEIVED BY CHEMIST:** 09-FEB-2001

6. **APPLICANT NAME AND ADDRESS:**
   Pharmacia & Upjohn Co.
   7000 Portage Road
   Kalamazoo, MI 49001

7. **NAME OF DRUG:**
   Estring

8. **NONPROPRIETARY NAME:**
   Estradiol Vaginal Ring

9. **CHEMICAL NAME/STRUCTURE:**
   estra-1,3,5(10)-triene-3,17β-diol hemihydrate

   See USP Dictionary of Drug Names for structures.

10. **DOSAGE FORM(S):**
    Vaginal ring

11. **POTENCY:**
    2 mg

12. **PHARMACOLOGICAL CATEGORY:**
    Estrogen/Treatment of urogenital symptoms associated with post-menopausal atrophy of the vagina

13. **HOW DISPENSED:**
    RX

14. **RECORDS & REPORTS CURRENT:**
    Yes

15. **RELATED IND/NDA/DMF:**
    None

16. **SUPPLEMENT PROVIDES FOR:**
    Addition of an alternate manufacturing site for the estradiol drug substance in Estring Vaginal Ring.

17. **COMMENTS**
    See review notes.

18. CONCLUSIONS AND RECOMMENDATIONS:
This CBE Supplement may be approved. **Issue an approval letter.**

19. REVIEWER NAME **SIGNATURE** **DATE COMPLETED**
David T. Lin, Ph.D. 16-JUL-2001
Review Chemist

cc: Original: NDA 20-472/SCM-004
HFD-580/Division File
HFD-580/DSpell-LeSane
HFD-580/MRhee/DLin

INIT by MJ Rhee

Filename: S20472.004 (doc)

Redacted 1 page(s)

of trade secret and/or

confidential commercial

information from

Chemistry Review (20-472/S-004)

Appendix A
(EER)

06-JUN-2001

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

Application: NDA 20472/004
Stamp: 31-JAN-2001
Regulatory Due: 31-JUL-2001
Applicant: PHARMACIA AND UPJOHN
7000 PORTAGE RD
KALAMAZOO, MI 490010199
Priority: 3S
Org Code:

Action Goal:
District Goal: 26-APR-2001
Brand Name: ESTRING (ESTRADIOL) VAGINAL RING 2MG
Estab. Name:
Generic Name: ESTRADIOL
Dosage Form: (DRUG DELIVERY SYSTEM)
Strength: 2 MG

FDA Contacts: D. LIN (HFD-580) 301-827-4230 , Review Chemist
M. RHEE (HFD-580) 301-827-4237 , Team Leader

Overall Recommendation: ACCEPTABLE on 03-APR-2001 by M. GARCIA (HFD-322) 301-594-0095

Establishment: [redacted]

DMF No: [redacted]
AADA:
Responsibilities: DRUG SUBSTANCE MANUFACTURER
Profile: CSN
OAI Status: NONE
Estab. Comment:

Milestone Name	Date	Req. Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	02-APR-2001				LINDAV
OC RECOMMENDATION	03-APR-2001			ACCEPTABLE BASED ON PROFILE	EGASM

06-JUN-2001

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

26-APR-2001

31-JUL-2001
PHARMACIA AND UPJOHN
3S
580
Priority:
Org Code:

Application Comment: THIS IS A CBE SUPPLEMENT FOR AN ALTERNATE ESTRADIOL DRUG SUBSTANCE MANUFACTURING FACILITY. (on 02-APR-2001 by D. LIN (HFD-580) 301-827-4230)

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

David T. Lin
7/16/01 03:12:30 PM
CHEMIST
New estradiol manufacturing site

Moo-Jhong Rhee
7/17/01 01:52:16 PM
CHEMIST
I concur

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-472/S-004

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20472/S-004

CBE-0 SUPPLEMENT

Pharmacia & Upjohn Company
Attention: Daniel Chirby, M.Sc.
7000 Portage Road
Kalamazoo, MI 49001

Dear: Mr. Chirby

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product:	ESTRING, (estradiol vaginal ring) 2mg.
NDA Number:	20-472
Supplement Number:	S-004
Date of Supplement:	January 30, 2001
Date of Receipt:	January 31, 2001

This supplemental application, submitted as a "Supplement - Changes Being Effected" supplement, proposes the following change: the addition of an alternate manufacturing site of the drug substance in ESTRING.

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on April 2, 2001 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be July 31, 2001.

Please cite the application number listed above at the top of the first page of any communications concerning this application. All communications concerning this supplemental application should be addressed as follows:

U.S. Postal/Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, please call me at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Dornette Spell-LeSane, NP-C, MHA
Regulatory Project Manager
Division of Reproductive and
Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

/s/

Dornette Spell-LeSane
2/3/01 02:33:08 PM