CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

21-180/S-002

Trade Name: Ortho Evra

Generic Name: norelgestromin/ethinyl estradiol transdermal system

Sponsor: Ortho-McNeil Pharmaceutical, Inc.

Approval Date: August 09, 2002

Indications: For the prevention of pregnancy.

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APPLICATION NUMBER:

21-180/S-002

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	**X**
Approvable Letter	
Labeling	
Summary Review	
Officer/Employee List	
Office Director Memo	
Cross Discipline Team Leader Review	
Medical Review(s)	
Chemistry Review(s)	**X**
Environmental Assessment	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/Biopharmaceutics Review(s)	
Risk Assessment and Risk Mitigation Review(s)	
Proprietary Name Review(s)	
Administrative/Correspondence Document(s)	**X**

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APPLICATION NUMBER:

21-180/S-002

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-180/S-002

Johnson & Johnson Pharmaceutical Research & Development
Attention: Sheila Alexander
Director, Regulatory Affairs
920 Route 202 South
P.O. Box 300
Raritan, NJ 08869-0602

Dear Ms. Alexander:

Please refer to your supplemental new drug application dated February 19, 2002, received February 20, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ORTHO-EVRA™ (norelgestromin/ethinyl estradiol transdermal system).

This "Changes Being-Effected in 30 days" supplemental new drug application provides for a site change for the manufacture of the drug substance ethinyl estradiol.

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 Jennifer Mercier, B.S., 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

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/s/

Moo-Jhong Rhee
8/9/02 11:05:49 AM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-180/S-002

CHEMISTRY REVIEW(S)

DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS
REVIEW OF CHEMISTRY MANUFACTURING AND CONTROLS
CHEMIST'S REVIEW #1

1. NDA NUMBER: 21-180

2. NAME AND ADDRESS OF APPLICANT
   Johnson & Johnson Pharmaceutical Research & Development, LLC
   920 Route 202 South
   P.O. Box 300
   Raritan, New Jersey 08869-0602

3. SUPPLEMENT NUMBER/DATE/DATE ASSIGNED
   SCM-002 /2-19-02/2-20-02

4. NAME OF THE DRUG: ORTHO EVRA

5. NONPROPRIETARY NAME: Norelgesrtomin/Ethinyl estradiol Transdermal Drug Delivery System

6. SUPPLEMENT PROVIDES FOR: Site change for the manufacture of drug substance "Ethinyl estradiol"

7. AMENDMENTS/REPORTS/ DATE: None

8. PHARMACOLOGICAL CATEGORY
   Combination estrogen/progestin, prevention of pregnancy

9. HOW DISPENSED
   Prescription

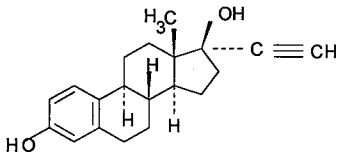
10. RELATED IND/NDA/DMF/SUPPLEMENT
    DMF [ ]

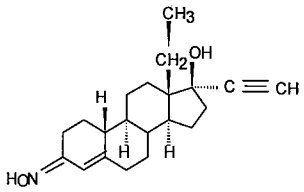
11. DOSAGE FORM : Transdermal

12. POTENCY
Norelgestromin/Ethinyl estradiol (6.0 mg/0.75 mg per 20 cm^2) delivering 150 µg norelgestromin, and 20 µg ethinyl estradiol per day.

13. CHEMICAL NAME AND STRUCTURE

Norelgestromin - (17α)-17-hydroxy- 13-ethyl-18,19-dinorpregn-4-en-20-yn-3-one-3-oxime
Ethinyl estradiol - 19-Norpregna-1,3,5(10)-trien-20-yne-3,17-diol, (17α)





Ethinyl estradiol
Molecular wt: 296.40

Norelgestromin
Molecular weight: 327.47

14. COMMENTS

As a part of the agreement between the FDA and [ ], the supplement was submitted as CBE supplement contingent on specific information to be submitted in the DMF [ ]. The information submitted in the DMF (amendment, dated 11-29-99) was in accordance with the letter to [ ], dated 7-20-1999 by the ONDC and OGD directors. The DMF amendment was reviewed by Dr. N.Takiar and found adequate to support ANDA 75-804. For details see DMF [ ], Chemistry Review # 8, dated 12-16-99, by Dr. N Takiar.

15. CONCLUSIONS AND RECOMMENDATIONS: The supplement may be approved. Please issue an "Approval" letter.

Reviewed By: Amit K. Mitra, Ph.D, 8-8-02

R/D INIT. BY: Moo-Jhong Rhee, Ph.D

CC: A. K. MITRA/HFD-580
M.J.RHEE/HFD-580
J.MERCIER/HFD-580
NDA 21-180

Redacted 1 page(s)

of trade secret and/or

confidential commercial

information from

Chemistry Review

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: **NDA 21180/002**
Priority: **14S**
Org Code: **580**
Stamp: **20-FEB-2002** Regulatory Due: **20-AUG-2002**
Action Goal:
District Goal: **16-JUL-2002**
Applicant: **ORTHO MCNEIL PHARM**
1000 ROUTE 202 SOUTH
RARITAN, NJ 088690602
Brand Name: **ORTHO EVRA(NORELGESTROMIN/ETHINYL ESTRAD**
Established Name:
Generic Name: **NORELGESTROMIN/ETHINYL ESTRADIOL**
Dosage Form: **FLM (TRANSDERMAL SYSTEM)**
Strength: **NRG/EE (150/20 MCG/DAY)**

FDA Contacts: **A. MITRA** **(HFD-580)** **301-827-4238** **, Review Chemist**

Overall Recommendation:

ACCEPTABLE on 01-MAR-2002 by GARCIAM

Establishment: [redacted]
DMF No: [ ]
AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **26-FEB-2002**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: **DRUG SUBSTANCE MANUFACTURER**

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/s/

Amit K. Mitra
8/8/02 02:58:19 PM
CHEMIST

Moo-Jhong Rhee
8/8/02 03:06:28 PM
CHEMIST
I concur

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-180/S-002

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-180

CBE-30 SUPPLEMENT

Johnson & Johnson Pharmaceutical Research & Development
Attention: Donna Panasewicz
Senior Director, Regulatory Affiars
920 P.O. Box 300
Raritan, NJ 08869-0602

Dear Ms. Panasewicz:

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:	ORHTO-EVRA™ (noregstromin/ethinyl estradiol) Tansdermal Patch
NDA Number:	21-180
Supplement number:	S-002
Date of supplement:	February 19, 2002
Date of receipt:	February 20, 2002

This supplemental application was submitted as a "Supplement - Changes Being Effected in 30 days." The appropriateness of reporting the proposed change as changes being effected in 30 days is under review.

Unless we notify you within 60 days of the 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 20, 2002 in accordance with 21 CFR 314.101(a).

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service/Courier/Overnight Mail:
Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Attention: Division Document Room, 17B20
5600 Fishers Lane
Rockville, Maryland 20857

If you have any question contact me at (301) 827-4260.

Sincerely,

Jennifer Mercier
Regulatory Project Manager
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

cpms, rpm, or chem tl signature block

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/s/

Jennifer L. Mercier
2/22/02 04:49:17 PM