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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##Reviews / Information Included in this NDA Review.

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APPLICATION NUMBER:
21-180/S-002

APPROVAL LETTER
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-Effect 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,

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
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: Norelgestromin/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/ND/DMF/SUPPLEMENT
    DMF

11. DOSAGE FORM: Transdermal

12. POTENCY
    Norelgestromin/Ethinyl estradiol (6.0 mg/0.75 mg per 20 cm²) 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)

![Chemical structures of Norelgestromin and Ethinyl Estradiol]

Ethinyl estradiol
Molecular wt: 296.40

Norelgestromin
Molecular weight: 327.47

14. COMMENTS

As a part of the agreement between the FDA and the ONDC, 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 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
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of trade secret and/or
confidential commercial
information from

Chemistry Review
FVA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 21180/002
Applicant: ORTHO MCNEIL PHARM
1000 ROUTE 202 SOUTH
RARITAN, NJ 088690602

Priority: 14S
Org Code: 580
Action Goal: ORTHO
District Goal: 16-JUL-2002
Brand Name: EVRA(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: □ □
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
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™ (noregestromin/ethinyl estradiol) Transdermal 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
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/s/

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