CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-180

ADMINISTRATIVE DOCUMENTS
CORRESPONDENCE

NDA 21-180

ORTHO EVRA®
(norelgestromin/ethinyl estradiol) Transdermal Patch

R.W. Johnson Pharmaceutical Research Institute
1, 4S

PM: Jennifer Mercier
HFD-580
7-4260

Submission Date: December 21, 2000
Primary Goal Date: October 21, 2001
Secondary Goal Date: December 21, 2001

/S/ 9/24/01

Advisory Committee Meeting

N/A

NDA 21-180

ORTHO EVRA®
(norelgestromin/ethinyl estradiol) Transdermal Patch

R.W. Johnson Pharmaceutical Research Institute
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PM: Jennifer Mercier
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/S/
9/24/01

Federal Register Notice

N/A

NDA 21-180
ORTHO EVRA (norgestimate/ethinyl estradiol) Tablets

3S

R.W. Johnson

PM: Jennifer Mercier
7-4260
HFD-580

Submission Date: August 25, 2000
Goal Date: June 25, 2001

Administration Section

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

USER FEE COVER SHEET

See Instructions on Reverse Before Completing This Form

1. APPLICANT'S NAME AND ADDRESS

The R.W. Johnson Pharmaceutical Research Institute
920 Route 202 South
P.O. Box 300
Raritan, New Jersey 08869-0602

2. TELEPHONE NUMBER *(Include Area Code)*
(908) 704-4812

3. PRODUCT NAME
ORTHO EVRA™ (norelgestromin and ethinyl estradiol transdermal system)

4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?
IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW:

☒ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO_____
(APPLICATION NO. CONTAINING THE DATA).

5. USER FEE I.D. NUMBER
3894

6. LICENSE NUMBER / NDA NUMBER
NDA 21-180

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92
(Self Explanatory)

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
(See item 7, reverse side before checking box.)

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act
(See item 7, reverse side before checking box.)

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act
(See item 7, reverse side before checking box.)

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY
(Self Explanatory)

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? ☐ YES ☒ NO
(see reverse if answered YES)

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0297)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please **DO NOT RETURN** this form to this address.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Ramon Polo, PhD	Director, Regulatory Affairs	DEC 2 1 2000

FORM FDA 3397 (5/98)

EDMS-USRA-6057556

THE R.W. JOHNSON
PHARMACEUTICAL RESEARCH INSTITUTE
ROUTE 202, P.O. BOX 300, RARITAN, NEW JERSEY 08869-0602

DEC - 4 2000

Mellon Bank
525 William Penn Way
Three Mellon Center
27th Floor (FDA 360909) room 153-2713
PO Box 360909
Pittsburgh, PA 15259-0001

NDA 21-180
ORTHO EVRA™
(norelgestromin/
ethinyl estradiol transdermal system)

USER FEE NO. 3894

Dear Sir/Madam:

Enclosed please find a company check in the amount of $285,740.00 to cover User Fee expenses for ORTHO EVRA™ (norelgestromin and ethinyl estradiol) Transdermal Contraceptive System, NDA 21-180. ORTHO EVRA™ is indicated for the prevention of pregnancy. A completed unsigned User Fee Cover Sheet (Form FDA 3397) is also enclosed. The signed and dated User Fee Cover Sheet will accompany the original NDA submission.

If you have any questions regarding this information, please contact me at (908) 704-4812, contact Valerie Donnelly at (908) 704-5891 or call our telephone line dedicated for FDA use at (908) 704-4600.

Sincerely,

Valerie P Donnelly for/

Ramon Polo, Ph.D.
Director
Regulatory Affairs

Enclosures

cc: Jennifer Mercier, CSO @ DRUDP (FDA/CDER HFD-580)

Number of Pages Redacted 101

❖❖❖

Draft Labeling
(not releasable)

42 pages
59 pages
101

NDA 21-180

ORTHO EVRA®
(norelgestromin/ethinyl estradiol) Transdermal Patch

R.W. Johnson Pharmaceutical Research Institute
1, 4S

PM: Jennifer Mercier
HFD-580
7-4260

Submission Date: December 21, 2000
Primary Goal Date: October 21, 2001
Secondary Goal Date: December 21, 2001

Class Labeling

N/A
This is a new molecular entity.

/S/

Number of Pages Redacted 131

❖❖❖

Draft Labeling
(not releasable)

SECTION I 50 pages
II 59 pages
III 22 pages

NDA 21-180

ORTHO EVRA®
(norelgestromin/ethinyl estradiol) Transdermal Patch

R.W. Johnson Pharmaceutical Research Institute
1, 4S

PM: Jennifer Mercier
HFD-580
7-4260

Submission Date: December 21, 2000
Primary Goal Date: October 21, 2001
Secondary Goal Date: December 21, 2001

/S/ 11/6/01

Foreign Labeling

N/A

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

2 pages

CONSULTATION RESPONSE
Office of Post-Marketing Drug Risk Assessment
(OPDRA; HFD-400)

DATE RECEIVED:	DUE DATE:	OPDRA CONSULT #:
February 23, 2001	May 1, 2001	01-0054

TO: Susan Allen, M.D.
Director, Division of Reproductive and Urologic Drug Products
HFD-580

THROUGH: Jennifer Mercier, Project Manager
HFD-580

PRODUCT NAME:	MANUFACTURED BY:
Ortho-Evra (Norelgestromin and Ethinyl Estradiol Transdermal System) 6 mg/0.75 mg **NDA #: 21-180**	R.W. Johnson Pharmaceutical Research Institute

SAFETY EVALUATOR: Carol Holquist, R.Ph.

SUMMARY: In response to a consult from the Division of Reproductive and Urologic Drug Products (HFD-580), OPDRA conducted a re-review of the proposed proprietary name "Ortho-Evra" and reviewed the pouch, carton, and insert labeling for possible interventions that might minimize user error.

OPDRA RECOMMENDATION: OPDRA has no objections to the use of the proprietary name "Ortho-Evra" (see checked box below). In addition, OPDRA recommends implementation of the labeling revisions outlined in section III of the review in order to minimize the potential for medication errors.

☑ FOR NDA/ANDA WITH ACTION DATE BEYOND 90 DAYS OF THIS REVIEW
This name must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary names/NDAs from the signature date of this document. A re-review request of the name should be submitted via e-mail to "OPDRAREQUEST" with the NDA number, the proprietary name, and the goal date. OPDRA will respond back via e-mail with the final recommendation.

FOR NDA/ANDA WITH ACTION DATE WITHIN 90 DAYS OF THIS REVIEW
OPDRA considers this a final review. However, if the approval of the NDA is delayed beyond 90 days from the date of this review, the name must be re-evaluated. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary names/NDA's from this date forward.

FOR PRIORITY 6 MONTH REVIEWS
OPDRA will monitor this name until approximately 30 days before the approval of the NDA. The reviewing division need not submit a second consult for name review. OPDRA will notify the reviewing division of any changes in our recommendation of the name based upon the approvals of other proprietary names/NDAs from this date forward.

Jerry Phillips, R.Ph.
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment
Phone: (301) 827-3242
Fax: (301) 480-8173

Martin Himmel, M.D.
Deputy Director
Office of Post-Marketing Drug Risk Assessment
Center for Drug Evaluation and Research
Food and Drug Administration

Office of Post-Marketing Drug Risk Assessment
HFD-400; Rm. 15B03
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: **March 30, 2001**

NDA NUMBER: **21-180**

NAME OF DRUG: **Ortho Evra**
(Norelgestromin and Ethinyl Estradiol Transdermal System) 6 mg/0.75 mg

NDA HOLDER: **The R.W. Johnson Pharmaceutical Research Institute**

I. INTRODUCTION

This consult was written in response to a request from the Division of Reproductive and Urologic Drug Products (HFD-580), for reassessment of the proposed proprietary drug name, Ortho Evra, regarding potential name confusion with other proprietary/established drug names as well as unapproved pending names. In addition, the pouch, carton, and insert labeling were reviewed for possible interventions that might minimize user error.

BACKGROUND

The Labeling and Nomenclature Committee (LNC) initially reviewed the proprietary name Evra on September 28, 1998, and concluded the name was acceptable. The sponsor later revised the proprietary name to "Ortho Evra". Ortho Evra was submitted to OPDRA for review in the IND phase and concluded the proprietary name was acceptable on October 2, 2000 (see OPDRA Consult 00-0142).

PRODUCT INFORMATION

Ortho Evra is a combination transdermal contraceptive patch that contains 6 mg of norelgestromin and 0.75 mg ethinyl estradiol. This transdermal system uses a 28-day, four-week cycle. A new patch is applied each week for three weeks (21 total days) and week four is patch-free. The product will be available in folding cartons of 1 cycle each (3 patches) and in folding cartons containing a single patch that is intended for use as a replacement in the event that a patch is inadvertently lost or destroyed.

II. RISK ASSESSMENT

The proprietary name Ortho Evra was originally evaluated by OPDRA in the IND phase. At that time three prescription analysis studies were conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name. Most incorrect interpretations of the name were misspelled and/or phonetic variations of Ortho Evra.

In addition, an Expert Panel discussion was held by OPDRA to gather professional opinions on the safety of the proprietary name. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of OPDRA Medication Errors Prevention Staff and representation from the Division of Drug Marketing and Advertising Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

The following drug products were identified for their potential sound-alike and/or look alike properties relative to Ortho Evra:

Ortho-Cept	Tablets, monophonic=c 30 mcg Ethinyl Estradiol and 1.5 mg Norethindrone	One tablet daily.	S/A, L/A per OPDRA
Ortho-Est	Tablets 1.25 mg Na. Estrone Sulfate	One tablet daily.	S/A, L/A per OPDRA
Ortho-Novum	Tablets 50 mcg Mestranol and 1 mg Norethindrone	One tablet daily.	S/A per OPDRA
Ortho-Tri-Cyclen	Tablets, Triphasic Norethindrone and Ethinyl Estradiol	One tablet daily.	LA per OPDRA
Ortho-Gynol	Gel 1% Octoxynol 9	As directed.	S/A per OPDRA
Ortho-Novum	Tablets, triphasic Norethindrone and Ethinyl Estradiol	One tablet daily.	S/A per OPDRA
*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike)			

Following an overall risk assessment it was determined that the potential for confusion between Ortho Evra and the above listed products were unlikely.

APPEARS THIS WAY
ON ORIGINAL

Upon reassessment of this proprietary name the medication error staff of OPDRA conducted a search of several standard published drug product reference texts[i,ii,iii] as well as several FDA databases[iv] for existing drug names which sound alike or look alike to Ortho Evra to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted[v]. An additional Expert Panel discussion was conducted to review all findings from the searches. No additional prescription studies were conducted. The Expert Panel concluded that there were no products approved that had not been previously identified as a potential sound-alike/look-alike name.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

In the review of the pouch, carton and insert labeling for Ortho Evra, OPDRA has attempted to focus on safety issues relating to possible medication errors. We have identified several areas of possible improvement, in the interest of minimizing potential user error.

A. GENERAL COMMENT

1.

2.

B. POUCH LABELING

1. See GENERAL COMMENTS above.

2. Insert "Usual Dosage" prior to the statement "See patient instructions. Apply...".

C. FOLDING CARTON LABELING

See GENERAL COMMENTS.

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[i] MICROMEDEX Healthcare Intranet Series, 2000, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Index Nominum, and PDR/Physician's Desk Reference (Medical Economics Co. Inc, 2000).

[ii] American Drug index, 42nd Edition, 1999, Facts and Comparisons, St. Louis, MO.

[iii] Facts and Comparisons, 2001, Facts and Comparisons, St. Louis, MO.

[iv] COMIS, The Established Evaluation System [EES], the Labeling and Nomenclature Committee [LNC] database of Proprietary name consultation requests, New Drug Approvals 98-00, and online version of the FDA Orange Book.

[v] WWW location http:// www.uspto.gov/tmdb/index.html.

D. REPLACEMENT PATCH FOLDING CARTON LABELING

1. See GENERAL COMMENTS.

2. [redacted] /cle.

E. PACKAGE INSERT LABELING

1. See GENERAL COMMENTS.

2. [redacted]

3. [redacted]

IV. RECOMMENDATIONS

OPDRA has no objections to the use of the proprietary name, Ortho Evra. OPDRA recommends implementation of the above labeling revisions in order to minimize the potential for medication errors.

OPDRA would appreciate feedback of the final outcome of this consult. We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact the project manager, Sammie Beam, R.Ph., at 301-827-3231.

Carol Holquist, R.Ph.
Safety Evaluator
Office of Postmarketing Drug Risk Assessment (OPDRA)

Concur:

Jerry Phillips, R.Ph.
Associate Director for Medication Error Prevention
Office of Postmarketing Drug Risk Assessment (OPDRA)

/s/

Carol Holquist
4/2/01 10:04:30 AM
PHARMACIST

Jerry Phillips
4/2/01 02:13:59 PM
DIRECTOR

Martin Himmel
4/4/01 11:37:19 AM
MEDICAL OFFICER

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Jerry Phillips
\ssociate Director, Medication Error Prevention
Office of Post Marketing Drug Risk Assessment, HFD-400
(Rm. 15B-03, PKLN Bldg.)

FROM:
Susan Allen, M.D.
Director, Division of Reproductive and Urologic Drug Products
HFD-580

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
February 15, 2001		21-180	Labeling	December 21, 2000

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Ortho-Evra (norelgestromin/ethinyl estradiol)	Standard	1S	May 1, 2001

NAME OF FIRM: RW Johnson Pharmaceutical Research Institute

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Please see attached material for your review. Please address any comments or questions to Jennifer Mercier 7-4249.

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one) ☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

/s/

Jennifer L. Mercier
2/15/01 03:09:20 PM

APPEARS THIS WAY
ON ORIGINAL

NDA 21-180

ORTHO EVRA®
(norelgestromin/ethinyl estradiol) Transdermal Patch

R.W. Johnson Pharmaceutical Research Institute
1, 4S

PM: Jennifer Mercier
HFD-580
7-4260

Submission Date: December 21, 2000
Primary Goal Date: October 21, 2001
Secondary Goal Date: December 21, 2001

/S/

Application Integrity Policy

N/A

NDA 21-180

ORTHO EVRA®
(norelgestromin/ethinyl estradiol) Transdermal Patch

R.W. Johnson Pharmaceutical Research Institute
1, 4S

PM: Jennifer Mercier
HFD-580
7-4260

Submission Date: December 21, 2000
Primary Goal Date: October 21, 2001
Secondary Goal Date: December 21, 200

/S/
9/04/01

Advertising Information

N/A

NDA 21-180

ORTHO EVRA®
(norelgestromin/ethinyl estradiol) Transdermal Patch

R.W. Johnson Pharmaceutical Research Institute
1, 4S

PM: Jennifer Mercier
HFD-580
7-4260

Submission Date: December 21, 2000
Primary Goal Date: October 21, 2001
Secondary Goal Date: December 21, 2001

/S/

Post-Marketing Commitments

N/A

Edited November 20, 2001
Dd/smc
FDA Approval of Ortho Evra

FDA has approved -- a contraceptive patch that releases hormones for seven days each (A patient uses a patch every week for 3 weeks and has a patch free- week the fourth week for the 4th week during which she will start her period.) The patch is intended for birth control or pregnancy prevention and provides a convenient form for women who do not want to take a pill everyday. If used properly the product is highly effective in preventing pregnancy. The patch contains both a progestin and estrogen.

Ortho Evra works in a similar fashion to oral contraceptives to provide protection against pregnancy and is *highly* effective if used properly. The new product provides another alternative to oral contraceptives for women for pregnancy prevention. With use of Ortho Evra blood levels of the hormone are less variable.

APPEARS THIS WAY
ON ORIGINAL

How does Ortho Evra compare to other contraceptives?

Ortho Evra is a new delivery system for hormonal contraception. The progestin component norelgestromin is a new chemical entity and is the

active metabolite of norgestimate (orthocyclen and orthotricyclen), a progestin contained in some oral contraceptives.

APPEARS THIS WAY
ON ORIGINAL

Is Ortho Evra approved for use in other countries? No

What advantage does Ortho Evra have over other contraceptives?

Advantages include that it does not require taking an active pill every day for 21 days or receiving injections.

APPEARS THIS WAY
ON ORIGINAL

How effective is this new contraceptive product?

Like oral contraceptives, one out of every 100 women who use the product appropriately (as directed) for a year, will become pregnant. The product is just as effective as oral contraceptives, no better or worse. For women who weigh more than 198 pounds, it appears, based on clinical trials, to be less effective.

APPEARS THIS WAY
ON ORIGINAL

How does Ortho Evra work?

The hormones from the patch are absorbed into the blood stream through the skin and work the same as oral contraceptives, by inhibiting ovulation, thickening cervical mucus, and changing the uterine lining.

What company is manufacturing and distributing the product in the United States? Ortho McNeil

APPEARS THIS WAY
ON ORIGINAL

How should the product be handled or stored by consumers?

Store at room temperature in the protective pouch, and the patch should be applied to the skin immediately after removal from the pouch.

Do not store in a refrigerator or freezer.

APPEARS THIS WAY
ON ORIGINAL

Johnson & Johnson

OFFICE OF
GENERAL COUNSEL

ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, N.J. 08933-7003

Phone (732)524-2641
Fax (732)524-5866

May 5, 2000

Re: ORTHO EVRA™ NDA No. 21-180
Information Required in accordance with 21 CFR § 314.53

Pursuant to the provisions of 21 CFR § 314.53, attached hereto please find patent information for the above identified application.

Attached item 13 lists 2 patents. The undersigned declares that U.S. Patent Nos. 5,876,746 and 5,972,377, owned by Applicant's parent company, Ortho-McNeil Pharmaceutical, Inc., cover the composition of the drug product and the method of use of the drug product which is the subject of this application for which approval is being sought.

A claim of patent infringement could be asserted if a person not licensed by the owner of the patents listed above engaged in the manufacture, use or sale of the drug product of this application for which approval is sought.

Respectfully submitted,

Kenneth J. Dow
Registered Patent Attorney
Reg, No, 32,890

misc\evra cert letter

ITEM 13: PATENT INFORMATION

NDA 21-180 ORTHO EVRA™ (ethinyl estradiol/norelgestromin) Transdermal System

Information Required in Accordance with 21 CFR§314.53

ORTHO EVRA™ (ethinyl estradiol/norelgestromin) Transdermal System is protected by the following:

US Patent No.	Patent Type	Expiration Date	Owner
5,876,746	Drug Product Method of Use	June 7, 2015	Ortho-McNeil Pharmaceutical, Inc.
5,972,377	Drug Product Method of Use	June 7, 2015	Ortho-McNeil Pharmaceutical, Inc.

APPEARS THIS WAY
ON ORIGINAL

EXCLUSIVITY SUMMARY for NDA # 21-180 SUPPL #

Trade Name ORTHO EVRA (norelgestromin/ethinyl estradiol transdermal system)

Generic Name norelgestromin/ethinyl estradiol

Applicant Name R.W. Johnson Pharmaceuticals HFD- 580

Approval Date

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

   a) Is it an original NDA? YES/_X_/ NO /___/

   b) Is it an effectiveness supplement? YES /___/ NO /_X_/

      If yes, what type(SE1, SE2, etc.)?

   c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

      YES /_X_/ NO /___/

      If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

      If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES /_X_/ NO /___/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

5 years

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /___/ NO /_X_/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC Switches should be answered No - Please indicate as such).

YES /___/ NO /_X_/

If yes, NDA # _____ Drug Name

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /_X_/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA #

NDA #

NDA #

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /_X_/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # 19-697 norgestimate/ethinyl estradiol

NDA # 19-653 norgestimate/ethinyl estradiol

NDA #

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /_X_/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis

for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /_X_/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /_X_/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /___/

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /_X__/

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, CONT-002

Investigation #2, CONT-003

Investigation #3, Study # CONT-004

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1	YES /___/	NO /_X_/
Investigation #2	YES /___/	NO /_X_/
Investigation #3	YES /___/	NO /_X_/

If you have answered "yes" for one or more investigations, identify each such investigation and the

NDA in which each was relied upon:

NDA # _____ Study #
NDA # _____ Study #
NDA # _____ Study #

(b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /_X_/

Investigation #2 YES /___/ NO /_X_/

Investigation #3 YES /___/ NO /_X_/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # _____ Study #

NDA # _____ Study #

NDA # _____ Study #

(c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #_1_, __CONT-002

Investigation #_2_, __CONT-003

Investigation #_3_, __CONT-004

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of

the study.

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(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1	
IND # ——— YES /_X_/	NO /___/ Explain:
Investigation #2	
IND # ——— YES /_X_/	NO /___/ Explain:
Investigation #3	
IND # ——— YES /_X_/	NO /___/ Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1	
YES /___/ Explain _____	NO /___/ Explain _____
_____	_____
_____	_____
Investigation #2	

YES /___/ Explain _____ | NO /___/ Explain _____

_____ | _____

_____ | _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /_X_/

If yes, explain: _____

_____

_____

_____

Signature of Preparer Date
Title:

Signature of Office of Division Director Date

cc:
Archival NDA
HFD- /Division File
HFD- /RPM
HFD-093/Mary Ann Holovac

Form OGD-011347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

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Florence Houn
11/19/01 05:07:00 PM

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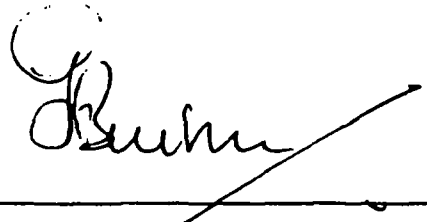
ITEM 16: DEBARMENT CERTIFICATION

The R.W. Johnson Pharmaceutical Research Institute hereby certifies that it did not and will not use in any capacity the services of any person debarred under sections 306 of the Federal Food, Drug and Cosmetic Act in connection with this application.



Graham Burton, MD
Vice President, Global Regulatory Affairs and Quality Assurance
The R.W. Johnson Pharmaceutical Research Institute
Route 202, P.O. Box 300
Raritan, NJ 08869-0602

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-180

R.W. Johnson Pharmaceutical Research Institute
Attention: Ramon Polo, Ph.D.
Director, Regulatory Affairs
920 Route 202 South
P.O. Box 300
Raritan, NJ 08869-0602

Dear Dr. Polo:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ORTHO EVRA™ (norelgestromin/ethinyl estradiol transdermal system).

We are confirming that the Office of Post-Approval Drug Risk Assessment (OPDRA) has accepted your tradename and the Division concurs with the acceptability of the proposed tradename.

If you have any questions, call Jennifer Mercier, Regulatory Project Manager, at (301) 827-4260.

Sincerely,

Daniel Shames, M.D.
Acting Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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Daniel A. Shames
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-180

DISCIPLINE REVIEW LETTER

The R.W. Johnson Pharmaceutical Research Institute
Attention: Ramon Polo, Ph.D.
Director, Regulatory Affairs
920 Route 202 South
P.O. Box 300
Raritan, NJ 08869-0602

Dear Dr. Polo:

Please refer to your December 21, 2000 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ORTHO EVRA™ (norelgestromin and ethinyl estradiol) transdermal system.

We also refer to your submissions dated February 9, 14, March 6, 23, 27, July 19, August 27, 30 and September 6, 2001.

Our review of the Chemistry, Manufacturing and controls section of your submission is complete, and we have identified the following deficiencies.

Drug Substance (norelgestromin):

1. Please submit the information on the type of bag used during stability studies of norelgestromin.

2. Based on the ICH recommendations, the acceptance criteria for total impurities in the drug substance, norelgestromin should be tightened to [redacted], unless justified.

3. [redacted]

Drug Substance (ethinyl estradiol):

1. The acceptance criteria for total impurity for ethinyl estradiol related substances should be tightened to [redacted] based on the analysis of the data provided, unless justified.

Release liner manufactured by [redacted]

1. Submit the following information on the release liner from [redacted]
   - manufacturers of the components
   - chemical formula of the components

- specifications of the components with a clear description of the test methods or a reference. Typical specification for the polyester substrate that include thickness, tensile and elongation properties. Typical specification for the coating material should include molecular weight, % solids
- a detailed description of the manufacturing process including a batch formula.

2. Submit a certificate of analysis with coating weight and subsequent adhesion values, since those are parts of the specification.

3. Provide labeling information of the jumbos and slit roll prior to shipping, and the storage conditions for the finished product.

Non woven backing film:

1. Provide test methods and acceptance criteria of polyethylene terephthalate and ———

2. Adopt specifications (acceptance criteria and test methods) for thickness, air permeability, and tensile strength of the nonwoven film, since those properties are important for manufacturability, permeability of the drug and penetration enhancer, and control of cold flow.

3. Provide labeling information of the jumbos and slit roll of the backing film prior to shipping, and the storage conditions for the finished product.

Lauryl lactate:

1. Provide a typical batch formula for the manufacture of ——— including the quantitative composition of each ingredient used in the manufacture of ———

2. Clarify the analytical result reported for purity of ——— used in the manufacture of drug product lot # 01607. It is reported to be ——— (Volume 5, page 283 of the NDA); however, the acceptance criterion described in Volume 4, page 71 is ———

3. Provide the packaging and labeling of the ——— prior to shipping.

Drug Product:
Regulatory specification

1. The appearance specification should state lack of presence of crystals since the crystals are not available for absorption. The appearance specification should also include a statement of insignificant cold flow.

2. Adopt a specification for the purity ——— used for release rate studies.

Container closure system

1. The proposal to introduce alternate pouch based on meeting the specification alone is not acceptable.

Stability:

1. Please identify the manufacturers of each of the release liners and backings used in the primary stability studies. If there are backings and release liners that were not used in any stability studies, they should be withdrawn from the NDA, unless supported by the stability data.

2. Update the degradation products specifications of the drug product with all identified individual related substances including those reported in the amendment dated 7-19-01, as applicable based on ICH recommendation.

3. The proposal of extending the shelf life based on primary stability data is not acceptable. The stability commitment should be revised to "the extension of shelf life will be based on real time data from three commercial production lots".

Labeling:

1.

2.

3. Provide a disposal procedure for the transdermal patch in the "How Supplied" section, since the drug product, when disposed, would contain a large quantity of the residual drugs and it may pose hazard by accidental use.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

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 2, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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/s/

Moo-Jhong Rhee
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-180

DISCIPLINE REVIEW LETTER

R.W. Johnson Research Pharmaceutical Institute
Attention: Ramon Polo, Ph.D.
Director, Regulatory Affairs
920 Route 202 South
P.O. Box 300
Raritan, NJ 08869-0602

Dear Dr. Polo:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ORTHO-EVRA™ (norelgestromin/ethinyl estradiol) Transdermal Contraceptive System.

Our review of the Microbiology section of your submission is complete, and we have identified the following deficiencies:

Concerning the quantitative portion of the Microbial Limits Test for the ORTHO-EVRA Trandermal Contraceptive System, please note that the use of the "recovery factor" and its application to the result of Microbial Limits Tests may not be necessary or desirable. Since variation in microbial counts are commonly accepted as normal in the aerobic plate count method, the use of "recovery factors" as described may only result in a false sense of precision.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

If you have any questions, call Jennifer Mercier, B.S., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

{See appended electronic signature page}
Terri Rumble
Chief, Project Management Staff
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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Terri F. Rumble
4/17/01 04:55:19 PM

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NDA 21-180

R.W. Johnson Pharmacuetical Research Institute
Attention: Ramon Polo, Ph.D.
Director, Regulatory Affairs
920 Route 202 South
P.O. Box 300
Raritan, NJ 08869-0602

Dear Dr. Polo:

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

Name of Drug Product:	Ortho Evra™ (norelgestromin/ethinyl estardiol transdermal system)
Review Priority	Classification: Standard (S)
Date of Application:	December 21, 2000
Date of Receipt:	December 21, 2000
Our Reference Number:	NDA 21-180

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 February 4, 2001 in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be October 20, 2001 and the secondary user fee goal date will be December 20, 2001.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). If you have not already fulfilled the requirements of 21 CFR 314.55 (or 601.27), please submit your plans for pediatric drug development within 120 days from the date of this letter unless you believe a waiver is appropriate. Within approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will make a determination whether to grant or deny a request for a waiver of pediatric studies during the review of the application. In no case, however, will the determination be made later than the date action is taken on the application. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.
Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you

should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will review your pediatric drug development plan and notify you of its adequacy. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

Under 21 CFR 314.102(c) of the new drug regulations, you may request an informal conference with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the application's ultimate approvability. Alternatively, you may choose to receive such a report by telephone.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. All communications concerning this NDA 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, call Jennifer Mercier, B.S., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

Terri Rumble
Chief, Project Management Staff
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

/s/

Dornette Spell-LeSane
12/27/00 11:33:28 AM

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THE R.W. JOHNSON
PHARMACEUTICAL RESEARCH INSTITUTE
920 Route 202, P.O. Box 300 Raritan, NJ 08869-0602

Fax Cover Sheet

Date:	November 16, 2001	**Pages:**	
To:	Jennifer Mercier	**From:**	Karen Futterknecht K.F.
Dept.:	FDA	**Dept.:**	Regulatory Affairs
Fax #:	301-827-4267	**Fax #:**	908-722-5113
Telephone #:	301-827-4249	**Telephone #:**	908-704-4912

Comments:

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THE R.W. JOHNSON
PHARMACEUTICAL RESEARCH INSTITUTE
ROUTE 202, P.O. BOX 300, RARITAN, NEW JERSEY 08869-0602

16 NOV 2001

Susan Allen, MD, Director
Division of Reproductive and Urologic
Drug Products HFD-580

Center for Drug Evaluation and Research
Food and Drug Administration
Attn.: Document Control Room 14B-04

5600 Fishers Lane
Rockville, Maryland 20857-1706

NDA 21-180
ORTHO EVRA™
(norelgestromin/ethinyl estradiol transdermal system)

AMENDMENT TO A PENDING APPLICATION;
Labeling

Dear Dr. Allen:

Reference is made to our pending NDA 21-180 for ORTHO EVRA™. Reference is also made to the Patient Package Insert, Brief Summary amended to the pending application on 08 May 2001. At this time we would like to amend the NDA and remove this item since this labeling will not be used to draft a Brief Patient Summary, for use in advertising. The DDMAC/advertising piece will be pulled from information in the USPI, which includes physician labeling and detailed patient labeling.

If you have questions regarding this information please contact me at (908)-704-4812 or Valerie Donnelly at (908)-704-5891 or our dedicated number for FDA use (908)-704-4600.

Sincerely,

The RW Johnson Pharmaceutical Research Institute

Valerie A Donnelly for

Ramon Polo Ph.D.
Director
Regulatory Affairs

Fax Copy to Jennifer Mercier

N:cygnus\n111601labeling