CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

19-653/S-023 & 19-697/S-019

Trade Name: Ortho-Cyclen 0.25mg/0.035mg

Ortho Tri-Cyclen 0.18mg/0.035mg, 0.215mg/0.035mg, 0.25mg/0.035mg

Generic Name: norgestimate/ethinyl estradiol tablets

Sponsor: Johnson RW

Approval Date: 09/30/1999

Indications: Ortho-Cyclen & Ortho Tri-Cyclen: For the prevention of pregnancy in women who elect to use oral contraceptives as a method of contraception.

Ortho Tri-Cyclen: For the treatment of moderate acne vulgaris in females, greater than or equal to 15 years of age, who have no known contradictions to oral contraceptive therapy, desire contraception, have achieved menarche and are unresponsive to topical anti-acne medications.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-023 & 19-697/S-019

CONTENTS

Reviews / Information Included in this NDA Review.

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Labeling	
Summary Review	
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Medical Review(s)	
Chemistry Review(s)	X
Environmental Assessment	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
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Proprietary Name Review(s)	
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-023 & 19-697/S-019

APPROVAL LETTER

20.1

NDA 19-653/S-023
NDA 19-697/S-019

SEP 30 1999

R.W. Johnson Pharmaceutical Research Institute
Attention: Donna Panasewicz
Director, Regulatory Affairs
Route 202
P.O. Box 300
Raritan, NJ 08869-0602

Dear Ms. Panasewicz:

Please refer to your supplemental new drug applications dated May 14, 1999, received May 17, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ortho-Cyclen® (noregestimate/ethinyl estradiol) Tablets, Ortho Tri-Cyclen® (noregestimate/ethinyl estradiol) Tablets.

We note that these supplements were submitted as 'Special Supplement - Changes Being Effected' under 21 CFR 314.70(c).

These supplemental new drug applications provide for an additional analytical testing laboratory site. Your submission stated June 14, 1999 as the implementation date for the change.

We have completed the review of these supplemental applications and they are 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, contact Jennifer Mercier, Regulatory Project Manager, at (301) 827-4260.

Sincerely, 9/30/99

for

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

cc:
Archival NDAs 19-653, 19-697
HFD-580/Div. Files
HFD-580/J.Mercier
HFD-580/Reviewers and Team Leaders
HFD-095/DDMS-IMT
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: JM/September 27, 1999
Initialed by: Rumble9.28.99/Lin9.29.99/Rhee9.29.99/Rarick9.29.99
final: September 30, 1999
filename: 19697SMU.WPD

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-023 & 19-697/S-019

CHEMISTRY REVIEW(S)

SEP 24 1999

20.1

CHEMIST REVIEW
OF **SUPPLEMENT**

1. **ORGANIZATION:** DRUDP HFD-580
2. **NDA NUMBER:** 19-697/SCM-019
3. **SUPPLEMENT NUMBERS/DATES:**
   Letterdate: 14-MAY-1999
   Stampdate: 17-MAY-1999
4. **AMENDMENTS/REPORTS/DATES:**
   Letterdate:
   Stampdate:
5. **RECEIVED BY CHEMIST:** 19-MAY-1999

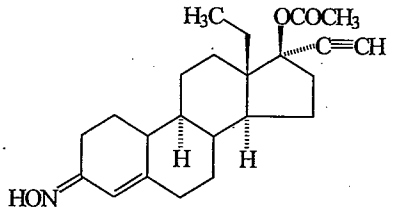
6. **APPLICANT NAME AND ADDRESS:**
   R.W. Johnson Pharmaceutical Research Institute
   920 Route 202 South
   P.O. Box 300
   Raritan, NJ 08869-0602

7. **NAME OF DRUG:**
   Ortho Tri-Cyclen Tablets

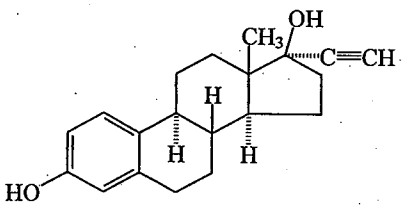
8. **NONPROPRIETARY NAME:**
   Norgestimate/ethinyl estradiol (NGM/EE)

9. **CHEMICAL NAME/STRUCTURE:**

a. Norgestimate: a) (+)-13-Ethyl-17-hydroxy-18,19-dinor-17α-pregn-4-en-20-yn-3-one oxime acetate
b) 18,19-Dinor-17-pregn-4-en-20-yn-3-one,17-(acetyloxy)-13-ethyl-, oxime, (17α)-(+)



b. Ethinyl estradiol: a) 19-Nor-17α-pregn-1,3,5(10)-trien-20-yne-3,17-diol
b) 19-Norpregna-1,3,5(10)-trien-20-yne-3,17-diol, (17α)



10. **DOSAGE FORM(S):**
    Tablet

11. **POTENCY:**
    180 µg /35 µg, 215 µg /35 µg, and 250 µg /35 µg Norgestimate/ethinyl estradiol

12. **PHARMACOLOGICAL CATEGORY:**
    Progestin, estrogen/Contraception

13. HOW DISPENSED:
RX

14. RECORDS & REPORTS CURRENT:
Yes

15. RELATED IND/NDA/DMF:
NDA 19-653/SCM-023

16. SUPPLEMENT PROVIDES FOR:
An additional analytical testing laboratory site.

17. COMMENTS
This supplement has been filed to provide for an additional analytical testing laboratory site at [ ]. The sponsor has met all the criteria for this supplement to qualify as a CBE supplement under PAC-ALTS (Postapproval Changes-Analytical Testing Laboratory Sites). An EER was submitted on September 23, 1999 and returned as acceptable on September 23, 1999, based on profile (see attached EER).

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. Review Chemist	9/24/99	24-SEP-1999

cc: Original: NDA 19-697/SCM-019
HFD-580/Division File
HFD-580/JMercier
HFD-580/MRhee/DLin

INIT by MJ Rhee 9/24/99

Filename: S19697.019 (doc)

23-SEP-1999 FDA CDER EES Page 1 of 1
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

Application: NDA 19697/019
Stamp: 17-MAY-1999
Regulatory Due: 17-SEP-1999
Applicant: JOHNSON RW
RT 202 SOUTH
RARITAN, NJ 088690602
Priority: 3S
Org Code: 580

Action Goal:
District Goal: 13-AUG-1999
Brand Name: ORTHO TRI-CYCLEN
Estab. Name:
Generic Name: ETHINYL ESTRADIOL/NORGESTIMATE

Dosage Form: (TABLET)
Strength: SEE COMMENTS

Application Comment: THE TABLET STRENGTHS ARE: 180 MG /35 MG, 215 MG /35 MG, AND 250 MG /35 MG NORGESTIMATE/ETHINYL ESTRADIOL. THIS SUPPLEMENT IS FOR AN ADDITIONAL ANALYTICAL TESTING SITE. IT IS RELATED TO NDA 19-653/S-023. (on 23-SEP-1999 by D. LIN (HFD-580) 301-827-4230)

FDA Contacts:
J. MERCIER (HFD-580) 301-827-4260 , Project Manager
D. LIN (HFD-580) 301-827-4230 , Review Chemist
M. RHEE (HFD-580) 301-827-4237 , Team Leader

Overall Recommendation: ACCEPTABLE on 23-SEP-1999 by S. FERGUSON (HFD-324) 301-827-0062

Establishment: [redacted]

DMF No: AADA:
Responsibilities: FINISHED DOSAGE RELEASE TESTER
FINISHED DOSAGE STABILITY TESTER
Profile: CTL OAI Status: NONE
Estab. Comment: THIS SITE HAS HAD A SATISFACTORY CGMP INSPECTION WITHIN THE PAST TWO YEARS. (on 23-SEP-1999 by D. LIN (HFD-580) 301-827-4230)

Milestone Name	Date	Req. Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	23-SEP-1999				LINDAV
OC RECOMMENDATION	23-SEP-1999			ACCEPTABLE BASED ON PROFILE	FERGUSONS

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-023 & 19-697/S-019

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-697/S-019

MAY 19 1999

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

Attention: Donna Panasewicz
Director, Regulatory Affairs

Dear Ms. Panasewicz:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: ORTHO TRI-CYCLEN®

NDA Number: 19-697

Supplement Number: S-019

Date of Supplement: May 14, 1999

Date of Receipt: May 17, 1999

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on July 16, 1999 in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Office of Drug Evaluation III
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

Terri F. Rumble
Chief, Project Management Staff
Division of Reproductive and Urologic
Drug Products, HFD-580
Office of Drug Evaluation III
Center for Drug Evaluation and Research

cc:
Original NDA 19-697/S-019
HFD-580/Div. Files
HFD-580/CSO/Mercier

SUPPLEMENT ACKNOWLEDGEMENT

ORIGINAL

NDA NO. 19697 REF. NO. SCM-01

NDA SUPPL FOR CBE sit

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

MAY 14 1999

Lisa Rarick, M.D.
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Office of Drug Evaluation II
Attn: Document Control Room 14B -03
5600 Fishers Lane
Rockville, Maryland 20857

NDA 19-653
ORTHO-CYCLEN® Tablets
(norgestimate/ethinyl estradiol)

Please cross refer to:

NDA 19-697
ORTHO TRI-CYCLEN® Tablets
(norgestimate/ethinyl estradiol)

CHANGES BEING EFFECTED IN 30 DAYS
PAC-ATLS Submission

Dear Dr. Rarick:

Reference is made to the above listed approved New Drug Applications for our norgestimate and ethinyl estradiol oral contraceptive products. Pursuant to 21 CFR 314.70 (a) and the Guidance for Industry - PAC-ATLS: Postapproval Changes - Analytical Testing Laboratory Sites, we are hereby submitting, in duplicate, a Changes Being Effected In 30 Days Supplement to provide for an additional analytical testing laboratory site.

At this time, we are providing for the following analytical testing site to perform routine release, stability and validation (process, packaging, etc.) testing of ORTHO-CYCLEN® and ORTHO TRI-CYCLEN® Tablets by the methods described in NDA 19-653 and NDA 16-697:

[ ]

We have determined that [ ] has the capability to perform testing by the current approved methods for this product. All postapproval commitments related to the test methods for the above referenced products have been fulfilled. [ ] has had a satisfactory current good manufacturing practice (CGMP) inspection within the past two (2) years.

N:\ORTHO_CY\LTR[ ]SUP399.DOC/1

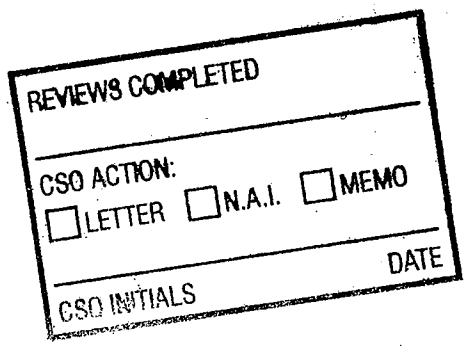
In accordance with 21 CFR Part 314.70 (a), identical field copies of this supplemental application have been filed with our local FDA District Offices.

Should you have any questions or comments concerning this submission, please contact me directly at (908) 218-6140 or call our telephone line dedicated for FDA use at (908) 704-4600.

Sincerely,

The R. W. Johnson
Pharmaceutical Research Institute

Donna Panasewicz
Director
Regulatory Affairs



Field Copy: Newark District Office, North Brunswick
San Juan District Office, San Juan, Puerto Rico