CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

19-653/S-024 & 19-697/S-021

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: 01/05/2000

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-024 & 19-697/S-021

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Reviews / Information Included in this NDA Review.

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APPLICATION NUMBER:

19-653/S-024 & 19-697/S-021

APPROVAL LETTER

NDA 12-728/S-190
NDA 16-709/S-125
NDA 16-954/S-088
NDA 17-488/S-105
NDA 17-489/S-088
NDA 17-735/S-088
NDA 17-919/S-070
NDA 18-354/S-039
NDA 18-985/S-034
NDA 19-653/S-024
NDA 19-697/S-021

JAN 5 2000

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

Dear Ms. Panasewicz:

Please refer to your supplemental new drug applications dated November 3, 1999, received November 8, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for:

NDA 12-728/S-190	Ortho-Novum® 1/50 21 Tablets (norethindrone/mestranol)
NDA 16-709/S-125	Ortho-Novum® 1/50 28 Tablets (norethindrone/mestranol)
NDA 16-954/S-088	Micronor® 28 Tablets (norethindrone)
NDA 17-488/S-105	Modicon® 21 Tablets (norethindrone/ethinyl estradiol)
NDA 17-489/S-088	Ortho-Novum® 1/35 21 Tablets (norethindrone/ethinyl estradiol)
NDA 17-735/S-088	Modicon® 28 Tablets (norethindrone/ethinyl estradiol)
NDA 17-919/S-070	Ortho-Novum® 1/35 28 Tablets (norethindrone/ethinyl estradiol)
NDA 18-354/S-039	Ortho-Novum® 10/11 21&28 Tablets (norethindrone/ethinyl estradiol)
NDA 18-985/S-034	Ortho-Novum® 7/7/7 21&28 Tablets (norethindrone/ethinyl estradiol)
NDA 19-653/S-024	Ortho-Cyclen® Tablets (noregestimate/ethinyl estradiol)
NDA 19-697/S-021	Ortho Tri-Cyclen® Tablets (noregestimate/ethinyl estradiol)

These "Changes Being Effected in 30 days" supplemental new drug applications provide for an alternate secondary packaging.

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, call Jennifer Mercier, B.S., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

1/5/2000

Moo-Jhong Rhee, Ph.D.
Team Leader for Division of Reproductive and Urologic Drug Products
Division of New Drug Chemistry II
Center for Drug Evaluation and Research

cc:
Archival NDAs 12-728, 16-709, 16-954, 17-488, 17-489, 17-735, 17-919, 18-354, 18-985, 19-653, 19-697
HFD-580/Div. Files
HFD-580/J.Mercier
HFD-580/Rhee/Lin
HFD-095/DDMS-IMT
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: JM/January 3, 2000
Initialed by: Rumble1.4.00/Lin1.4.00/Rhee1.5.00/Rarick1.5.00
final: January 5, 2000
filename: 12728APM.WPD

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-024 & 19-697/S-021

CHEMISTRY REVIEW(S)

CHEMIST REVIEW
OF **SUPPLEMENT**

1. **ORGANIZATION:** DRUDP HFD-580
2. **NDA NUMBER:** 19-653/SCP-024
3. **SUPPLEMENT NUMBERS/DATES:**
   Letterdate: 03-NOV-1999
   Stampdate: 08-NOV-1999
4. **AMENDMENTS/REPORTS/DATES:**
   Letterdate:
   Stampdate:
5. **RECEIVED BY CHEMIST:** 12-NOV-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-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)

see UPS Dictionary of Drug Names for structures.

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

11. **POTENCY:**
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 12-728/SCP-190, NDA 16-709/SCP-125, NDA 16-954/SCP-088, NDA 17-488/SCP-105, NDA 17-489/SCP-088, NDA 17-735/SCP-088, NDA 17-919/SCP-070, NDA 18-354/SCP-039, NDA 18-985/SCP-034, NDA 19-697/SCP-021

16. SUPPLEMENT PROVIDES FOR:
An alternate secondary packaging material.

17. COMMENTS
This supplement has been filed to provide for an alternate secondary packaging material ([ ] gauge [ ]/INK/ADHESIVE/[ ] gauge [ ]; Cohesive: [ ] adhesive [ ] or [ ] [ ]). This packaging component is supplied by [ ] and only used as an overwrap for the primary blister packaged tablets. In addition this material does not come in direct contact with the drug product. The packaging material is a two layer sheet composed of [ ]. Between these two [ ] layers is a proprietary adhesive and ink. The sheet is used as a pouch in which the blister packs are placed into and then [ ]. The cohesive used for sealing is a [ ] adhesive [ ] or a [ ] adhesive. The [ ] adhesive is the one currently being used in the approved secondary packaging material, but the sponsor wants the option of being able to use the [ ] adhesive which provides a [ ] seal. A light transmission test was performed on this material following USP 23 <661> for containers. The results show that the observed light transmission is less than 1% of transmittance and does not exceed the limits given for plastic containers (classes I-IV). Based on these results the proposed material appears to be equivalent to the current secondary packaging material.

The sponsor has committed to placing one batch of each product packaged with the proposed overwrap material in the product stability program.

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		16-DEC-1999

cc: Original: NDA 19-653/SCP-024
HFD-580/Division File
HFD-580/JMercier
HFD-580/MRhee/DLin

INIT by MJ Rhee

Filename: S19653.024 (doc)

JAN - 3 2000

CHEMIST REVIEW
OF **SUPPLEMENT**

1. **ORGANIZATION:** DRUDP HFD-580
2. **NDA NUMBER:** 19-697/SCP-021
3. **SUPPLEMENT NUMBERS/DATES:**
   Letterdate: 03-NOV-1999
   Stampdate: 08-NOV-1999
4. **AMENDMENTS/REPORTS/DATES:**
   Letterdate:
   Stampdate:
5. **RECEIVED BY CHEMIST:** 12-NOV-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)

see UPS Dictionary of Drug Names for structures.

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 12-728/SCP-190, NDA 16-709/SCP-125, NDA 16-954/SCP-088, NDA 17-488/SCP-105, NDA 17-489/SCP-088, NDA 17-735/SCP-088, NDA 17-919/SCP-070, NDA 18-354/SCP-039, NDA 18-985/SCP-034, NDA 19-653/SCP-024

16. SUPPLEMENT PROVIDES FOR:

An alternate secondary packaging material.

17. COMMENTS

This supplement has been filed to provide for an alternate secondary packaging material ([ ]gauge [ ]/INK/ADHESIVE/[ ]gauge [ ]; Cohesive: [ ] adhesive [ ] or [ ] [ ]). This packaging component is supplied by [ ] and only used as an overwrap for the primary blister packaged tablets. In addition this material does not come in direct contact with the drug product. The packaging material is a two layer sheet composed of [ ]. Between these two [ ] layers is a proprietary adhesive and ink. The sheet is used as a pouch in which the blister packs are placed into and then [ ]. The cohesive used for sealing is a [ ] adhesive [ ] or a [ ] adhesive. The [ ] adhesive is the one currently being used in the approved secondary packaging material, but the sponsor wants the option of being able to use the [ ] adhesive which provides a [ ] seal. A light transmission test was performed on this material following USP 23 <661> for containers. The results show that the observed light transmission is less than 1% of transmittance and does not exceed the limits given for plastic containers (classes I-IV). Based on these results the proposed material appears to be equivalent to the current secondary packaging material.

The sponsor has committed to placing one batch of each product packaged with the proposed overwrap material in the product stability program.

18. CONCLUSIONS AND RECOMMENDATIONS:

This CBE Supplement may be approved. **Issue an approval letter.**

19. REVIEWER NAME
David T. Lin, Ph.D.
Review Chemist

SIGNATURE
12/16/99

DATE COMPLETED
16-DEC-1999

cc: Original: NDA 19-697/SCP-021
HFD-580/Division File
HFD-580/JMercier
HFD-580/MRhee/DLin

INIT by MJ Rhee 1/3/00

Filename: S19697.021 (doc)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-024 & 19-697/S-021

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-697/S-021

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

NOV 15 1999

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® 21& 28 Tablets

NDA Number: 19-697

Supplement Number: S-021

Date of Supplement: November 03, 1999

Date of Receipt: November 08, 1999

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on January 01, 2000 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-021
HFD-580/Div. Files
HFD-580/CSO/ J. Mercier

SUPPLEMENT ACKNOWLEDGEMENT

ORIGINAL

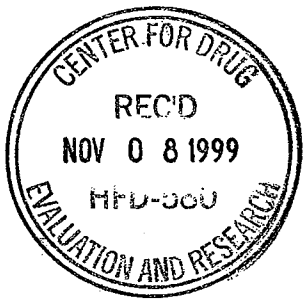
NDA NO. 19-697 REF. NO. 021

NDA SUPPL FOR SCP

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

NOV - 3 1999

Dr. Lisa Rarick
US Food and Drug Administration
Center for Drug Evaluation & Research
Division of Reproductive and
Urologic Drug Products, HFD-580
Office of Drug Evaluation II
Att: Document Control Room 14B-03
5600 Fishers Lane
Rockville, MD 20857



NDA 12-728
ORTHO-NOVUM® 1/50 ☐ 21 Tablets

Please Cross Refer to:

NDA 16-709
ORTHO-NOVUM® 1/50 ☐ 28 Tablets

NDA 16-954
MICRONOR® 28 Tablets

NDA 17-488
MODICON® 21 Tablets

NDA 17-489
ORTHO-NOVUM® 1/35 ☐ 21 Tablets

NDA 17-735
MODICON® 28 Tablets

NDA 17-919
ORTHO-NOVUM® 1/35 ☐ 28 Tablets

NDA 18-354
ORTHO-NOVUM® 10/11 ☐ 21 & 28 Tablets

NDA 18-985
ORTHO-NOVUM® 7/7/7 ☐ 21 & 28 Tablets

NDA 19-653
ORTHO-CYCLEN® ☐ 21 & 28 Tablets

NDA 19-697
ORTHO TRI-CYCLEN® 21 & 28 Tablets

SPECIAL SUPPLEMENT:
Changes Being Effected

Dear Dr. Rarick:

Reference is made to the above listed approved New Drug Applications. At this time, we are submitting a "Special Supplement – Changes Being Effected" to provide for a change in a secondary packaging component for our blister packaged oral

contraceptive tablet products. We are providing for the following alternate [ ] overwrap material to be used as secondary packaging:

Supplier	Material
[ ]	/ gauge [ ] /INK/ADHESIVE/ / gauge [ ] Cohesive: [ ] adhesive [ ] or [ ]

Light transmission testing for this material was performed and the results indicate that the material is comparable to those currently used for overwrapping the primary blister packages of our oral contraceptive products. The results of this testing are included with this submission. One batch of each product packaged with this new overwrap material will be placed in our marketed product stability program.

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