CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

19-653/S-032 & 19-697/S-029

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: 06/03/2002

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-032 & 19-697/S-029

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Reviews / Information Included in this NDA Review.

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-032 & 19-697/S-029

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 16-709/S-128
NDA 17-735/S-093
NDA 17-919/S-075
NDA 18-354/S-043
NDA 18-985/S-039
NDA 19-004/S-028
NDA 19-653/S-032
NDA 19-697/S-029

Johnson & Johnson Pharmaceutical Research & Development
Attention: Donna Panasewicz
Senior 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 application dated December 14, 2001, received December 17, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for

NDA and Supplement	Drug Name
16-709/S-0128	ORTHO-NOVUM 1/50 (norethindrone/mestranol) Tablets
17-735/S-093	MODICON 28 (norethindrone/ethinyl estradiol) Tablets
17-919/S-075	ORTHO-NOVUM 1/35 (norethindrone/ethinyl estradiol) Tablets
18-354/S-043	ORTHO-NOVUM 10/11 (norethindrone/ethinyl estradiol) Tablets
18-985/S-039	ORTHO-NOVUM 7/7/7 (norethindrone/ethinyl estradiol) Tablets
19-004/S-028	ORTHO-NOVUM 7/14 (norethindrone/ethinyl estradiol) Tablets
19-653/S-032	ORTHO-CYCLEN (norgestimate/ethinyl estradiol) Tablets
19-697/S-029	ORTHO TRI-CYCLEN (norgestimate/ethinyl estradiol) Tablets

This "Changes Being Effected" supplemental new drug application provides for the option to use the [ ] as an alternative to the [ ] used for the [ ] of green placebo tablets and to alter the manufacturing batch size of [ ] for the green placebo tablets.

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}

David Lin, 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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

David T. Lin
6/3/02 12:40:40 PM
I concur.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-032 & 19-697/S-029

CHEMISTRY REVIEW(S)

CHEMIST REVIEW
OF **SUPPLEMENT**

1. **ORGANIZATION:** DRUDP HFD-580
2. **NDA NUMBER: NDA 19-653/SCS-032**
3. **SUPPLEMENT NUMBERS/DATES:**
   Letterdate: 14-Dec-2001
   Stampdate: 17-Dec-2001
4. **AMENDMENTS/REPORTS/DATES:**
   Letterdate:
   Stampdate:
5. **RECEIVED BY CHEMIST:** 28-DEC-2001

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

9. **CHEMICAL NAME/STRUCTURE:**
   Please refer to the USP Dictionary of USAN and International Drug Names.

   see UPS Dictionary of Drug Names for structures.

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

11. **POTENCY:**
    Norgestimate 250µg/ Ethinyl Estradiol 35µg

12. **PHARMACOLOGICAL CATEGORY:**
    Progestin/Estrogen Oral Contraception

13. **HOW DISPENSED:**
    RX

14. **RECORDS & REPORTS CURRENT:**
    Yes

15. RELATED IND/NDA/DMF:
NDA 17-735/SCS-093, NDA 17-919/SCS-075, NDA 18-354/SCS-043, NDA 18-985/SCS-039, NDA 19-004/SCS 028, NDA 16-709/SCS-128, NDA 19-697/SCS-029.

16. SUPPLEMENT-CHANGES BEING EFFECTED PROVIDES FOR:
The option to use [ ] as an alternative to the [ ] used for the [ ] of green placebo tablets and to alter the manufacturing batch size of [ ] for the green placebo tablets.

17. COMMENTS
This Supplement-Changes Being effected has been filed to provide for an option to use [ ] [ ] as an alternative to the [ ] used for the [ ] of green placebo tablets and to alter the manufacturing batch size of [ ] for the green placebo tablets. The sponsor has provided the following documents to support the changes.

- A figure is included to show the difference between [ ] and [ ]. Since [ ], the sponsor has provided data to compare between the approved [ ] (Lot # PD 1878/11B544) with the proposed [ ] (Lot # PD 1879/11B545) [ ] for the proposed [ ] batches of the green placebo tablets. Data from both [ ] and [ ] are closely comparable (see chemist's review notes) and meet the acceptance criteria of critical parameters including weight, hardness, thickness and disintegration. Thus, the proposed alternate change of [ ] for the green placebo tablet is deemed satisfactory.
- Quantitative formulation for the [ ] batch size has been provided (see chemist's review notes) and the sponsor stated that the manufacturing will be performed according to the approved protocol. The provided data from one batch (Lot # PD 1879/11B545) show that the product remained within specification. In addition, another batch (Lot# PD 1878/11B544) of [ ] size has been manufactured using [ ] also remain within specifications and supports the alternate batch size of [ ]. Thus, the proposal for the alternate batch size of [ ] is deemed acceptable.
- The sponsor has committed to place the first batch of placebo tablets [ ] utilizing the [ ] on marketed product stability with whichever of the referenced oral contraceptive products it is first packaged with and to report the results in the annual report. The commitment is deemed satisfactory.

18. CONCLUSIONS AND RECOMMENDATIONS:
This CBE Supplement may be approved. **Issue an approval letter.**

19. REVIEWER NAME	**SIGNATURE**	**DATE COMPLETED**
Jila H. Boal, Ph.D. Review Chemist		30-MAY-2002

cc: Original: NDA 19-653/SCS-032
HFD-580/Division File
HFD-580/JMercier
HFD-580/DTLin/JBoal

INIT by DTLin, Ph.D.

Filename: NDA 19-653/SCS-032

2 Page(s) Withheld

Chemistry Review (19-653/S-032)

X § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Jila Boal
5/30/02 10:15:47 AM
CHEMIST

David T. Lin
5/30/02 05:11:20 PM
CHEMIST
I concur.

CHEMIST REVIEW
OF **SUPPLEMENT**

1. **ORGANIZATION:** DRUDP HFD-580
2. **NDA NUMBER: NDA 19-697/SCS-029**
3. **SUPPLEMENT NUMBERS/DATES:**
   Letterdate: 14-Dec-2001
   Stampdate: 17-Dec-2001
4. **AMENDMENTS/REPORTS/DATES:**
   Letterdate:
   Stampdate:
5. **RECEIVED BY CHEMIST:** 28-DEC-2001

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

9. **CHEMICAL NAME/STRUCTURE:**
   Please refer to the USP Dictionary of USAN and International Drug Names.

   see UPS Dictionary of Drug Names for structures.

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

11. **POTENCY:**
    Norgestimate / Ethinyl Estradiol
    180 µg / 35µg
    215 µg / 35 µg
    250µg / 35µg

12. **PHARMACOLOGICAL CATEGORY:**
    Progestin/Estrogen Oral Contraception

13. **HOW DISPENSED:**
    RX

14. **RECORDS & REPORTS CURRENT:**
    Yes

15. RELATED IND/NDA/DMF:
NDA 17-735/SCS-093, NDA 17-919/SCS-075, NDA 18-354/SCS-043, NDA 18-985/SCS-039, NDA 19-004/SCS 028, NDA 16-709/SCS-128, NDA 19-653/SCS-032.

16. SUPPLEMENT-CHANGES BEING EFFECTED PROVIDES FOR:
The option to use [ ] as an alternative to the [ ] used for the [ ] of green placebo tablets and to alter the manufacturing batch size of [ ] for the green placebo tablets.

17. COMMENTS
This Supplement-Changes Being effected has been filed to provide for an option to use [ ] [ ] as an alternative to the [ ] used for the [ ] of green placebo tablets and to alter the manufacturing batch size of [ ] for the green placebo tablets. The sponsor has provided the following documents to support the changes.

- A figure is included to show the difference between [ ] and [ ]. Since [ ], the sponsor has provided data to compare between the approved [ ] (Lot # PD 1878/11B544) with the proposed [ ](Lot # PD 1879/11B545)[ ] for the proposed [ ] batches of the green placebo tablets. Data from both[ ] and[ ] are closely comparable (see chemist's review notes) and meet the acceptance criteria of critical parameters including weight, hardness, thickness and disintegration. Thus, the proposed alternate change of[ ] for the green placebo tablet is deemed satisfactory.
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- The sponsor has committed to place the first batch of placebo tablets[ ] utilizing the [ ] on marketed product stability with whichever of the referenced oral contraceptive products it is first packaged with and to report the results in the annual report. The commitment is deemed satisfactory.

18. CONCLUSIONS AND RECOMMENDATIONS:
This CBE Supplement may be approved. **Issue an approval letter.**

19. REVIEWER NAME	**SIGNATURE**	**DATE COMPLETED**
Jila H. Boal, Ph.D. Review Chemist		30-MAY-2002

cc: Original: NDA 19-697/SCS-029
HFD-580/Division File
HFD-580/JMercier
HFD-580/DTLin/JBoal

INIT by DTLin, Ph.D.

Filename: NDA 19-697/SCS-029

2 Page(s) Withheld

Chemistry Review (19-697/S-029)

X § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

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/s/

Jila Boal
5/30/02 10:18:54 AM
CHEMIST

David T. Lin
5/30/02 05:14:03 PM
CHEMIST
I concur.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-032 & 19-697/S-029

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 16-709
NDA 17-735
NDA 17-919
NDA 18-354
NDA 18-985
NDA 19-004
NDA 19-653
NDA19-697

CBE-0 SUPPLEMENT

R.W. Johnson Pharmaceutical Research Institute
Attention: Donna Panasewicz, Director, Regulatory Affairs
920 Route 202 South
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:

NDA and Supplement	Drug Name
16-709/S-0128	ORTHO-NOVUM 1/50 (norethindrone/mestranol) Tablets
17-735/S-093	MODICON 28 (norethindrone/ethinyl estradiol) Tablets
17-919/S-075	ORTHO-NOVUM 1/35 (norehtindrone/ethinyl estradiol) Tablets
18-354/S-043	ORTHO-NOVUM 10/11 (norethindrone/ethinyl estradiol) Tablets
18-985/S-039	ORTHO-NOVUM 7/7/7 (norethindrone/ethinyl estradiol) Tablets
19-004/S-028	ORTHO-NOVUM 7/14 (norethindrone/ethinyl estradiol) Tablets
19-653/S-032	ORTHO-CYCLEN (norgestimate/ethinyl estradiol) Tablets
19-697/S-029	ORTHO TRI-CYCLEN (norgestimate/ethinyl estradiol) Tablets

Date of supplement: December 14, 2001

Date of receipt: December 17, 2001

This supplemental application was submitted as a "Supplement - Changes Being Effected." The appropriateness of reporting the proposed change as changes being effected 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 February 17, 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 please 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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Jennifer L. Mercier
12/19/01 12:40:13 PM

ORIGINAL

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

14 DEC 2001

Susan Allen, MD MPH, Director
US Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Attn.: Document Control Room 14B-03
5600 Fishers Lane
Rockville, Maryland 20852

NDA 16-709
ORTHO-NOVUM® 1/50 28 Tablets
(norethindrone/mestranol)

NDA 17-735
MODICON® 28 Tablets
(norethindrone/ethinyl estradiol)

NDA 17-919
ORTHO-NOVUM® 1/35 28 Tablets
(norethindrone/ethinyl estradiol)

NDA 18-354
ORTHO-NOVUM® 10/11 Tablets
(norethindrone/ethinyl estradiol)

NDA 18-985
ORTHO-NOVUM® 7/7/7 21 & 28 Tablets (norethindrone/ethinyl estradiol)

NDA 19-004
ORTHO-NOVUM® 7/14 Tablets
(norethindrone/ethinyl estradiol)

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

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

SUPPLEMENT – CHANGES BEING EFFECTED

NDA NO. 19-697 SER. NO. SCS029
NDA SUPPL FOR Control

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

Dear Dr. Allen:

Reference is made to the above approved New Drug Applications for our oral contraceptive and green placebo tablets. At this time, we are submitting a Changes Being Effected Supplement to provide for the option to use [ ] as an alternative to the [ ] currently used for the [ ] of green placebo tablets at our Raritan, New Jersey

facility. These green placebo tablets are packaged with the referenced products in the 28-day put-up. In addition, we are providing for an alternate manufacturing batch size of [ ] for the green placebo tablets. This new batch size will be manufactured in accordance with our approved applications. It is our intention to use the [ ] for the [ ] of green placebo tablets manufactured using the alternate [ ] batch effective immediately.

In support of this supplement, we have appended the quantitative formulation for the [ ] batch size, and comparative hardness, weight, thickness, and disintegration data for [ ] and [ ] tablets. The data demonstrates that the [ ] process utilizing the [ ] is consistent in all measurable parameters as product produced utilizing the current [ ]

We commit to place the first batch of placebo tablets [ ] utilizing the [ ] [ ] on marketed product stability with whichever of the referenced oral contraceptive products it is first packaged with and to report the results in the NDA annual report.

A field copy of this submission is being forwarded directly to the FDA district office in North Brunswick, New Jersey. We certify that the field copy is a true copy of the information contained in the archival and review copies of this supplemental application.

Should you have any questions and/or comments, please contact me directly at (908) 218-6140 or Sandy Rathborne at (908) 704-4687, or call our telephone line dedicated for FDA use at (908) 704-4600.

Sincerely,

The R.W. Johnson
Pharmaceutical Research Institute

Sandy Rathborne
for

Donna Panasewicz
Director
Regulatory Affairs

Enclosure(s)