CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

19-653/S-035 & 19-697/S-032

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: 01/03/2003

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-035 & 19-697/S-032

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Reviews / Information Included in this NDA Review.

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Pharmacology Review(s)	
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-035 & 19-697/S-032

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-653 / S035
NDA 19-697 / S032

Johnson & Johnson Pharmaceutical Research & Development, L.L.C.
Attention: Sandy Rathborne
Manager, Regulatory Affairs
1000 Route 202 South
P.O. Box 300
Raritan, New Jersey 08869-0602

Dear Ms. Rathborne:

Please refer to your supplemental new drug applications dated October 18, 2002, received October 31, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ortho-Cyclen® and Ortho Tri-Cyclen® (norgestimate/ethinyl estradiol) Tablets.

These "Changes Being Effected in 30 days" supplemental new drug applications provide for an option to use [ ] as an alternative to the [ ] used for the [ ] of Ortho-Cyclen® and Ortho Tri-Cyclen® at the Manati, Puerto Rico facility.

We have completed our review of these supplemental new drug applications and they are approved.

We remind you that you must comply with the reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Karen Anderson, N.P., Regulatory Project Manager, at (301) 827-4259.

Sincerely,

{See appended electronic signature page}

David T. Lin, Ph.D.
Chemistry Team Leader for
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
1/3/03 09:48:38 AM
I concur.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-035 & 19-697/S-032

CHEMISTRY REVIEW(S)

CHEMIST REVIEW
OF **SUPPLEMENT**

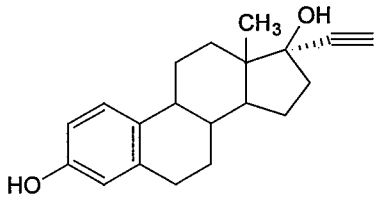
1. **ORGANIZATION:** DRUDP, HFD-580
2. **NDA NUMBER:** 19-653/SCS 035
3. **SUPPLEMENT NUMBERS/DATES:**
   Letterdate: 18-Oct-2002
   Stampdate: 31-Oct-2002
4. **AMENDMENTS/REPORTS/DATES:**
   Letterdate:
   Stampdate:
5. **RECEIVED BY CHEMIST:** 02-Nov-2002

6. **APPLICANT NAME AND ADDRESS:** Ortho-McNeil Pharmaceuticals, Inc.
   1000 Route 202 South
   P.O. Box 300
   (908)-704-9757

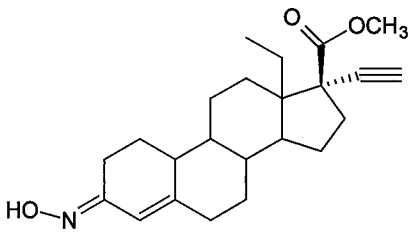
7. **NAME OF DRUG:** Ortho-Cyclen

8. **NONPROPRIETARY NAME:** Norgestimate/Ethinyl estradiol

9. **CHEMICAL NAME/STRUCTURE:**



Ethinyl estradiol (EE)



Norgestimate (NGM)

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

Norgestimate (NGM): (+)-13-Ethyl-17-hydroxy-18,19-dinor-17α-pregn-4-en-20-yne-3-one oxime acetate

10. **DOSAGE FORM(S):** Oral tablets

11. **POTENCY:** 250 mcg/35 mcg (NGM/EE)

12. **PHARMACOLOGICAL CATEGORY:** Estrogen/Progestin, Oral contraceptive

13. **HOW DISPENSED:** Rx

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

15. **RELATED IND/NDA/DMF:** NDA 19-697/SCS 032

16. SUPPLEMENT PROVIDES FOR: The option of using [ ] for [ ] of drug product at the Manati, Puerto Rico manufacturing site.

17. SPECIAL PRODUCTS: YES _ NO _X__.
(If yes, fill out the form for special products and deliver to TIA through team leader for data entry)

18. COMMENTS: Please refer to attached Comments Section.

19. CONCLUSIONS AND RECOMMENDATIONS:
This CBE-30 supplement may be **approved**. Issue an Approval Letter.

20. REVIEWER NAME	**SIGNATURE**	**DATE COMPLETED**
Sarah C. Pope, Ph.D.		13-Nov-2002

cc: Original: NDA 19-653/SCS-035
HFD-580/Division File
HFD-580/D. Spell-Lesane
HFD-580/D.T. Lin/S. Pope

2 Page(s) Withheld

Chemistry Review (19-653/S-035)

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

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

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/s/

Sarah Pope
12/10/02 10:01:10 AM
CHEMIST

David T. Lin
12/10/02 10:24:06 AM
CHEMIST
I concur.

CHEMIST REVIEW
OF **SUPPLEMENT**

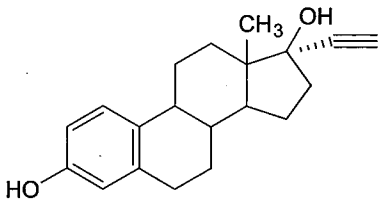
1. **ORGANIZATION:** DRUDP, HFD-580
2. **NDA NUMBER:** 19-697/SCS 032
3. **SUPPLEMENT NUMBERS/DATES:**
   Letterdate: 18-Oct-2002
   Stampdate: 31-Oct-2002
4. **AMENDMENTS/REPORTS/DATES:**
   Letterdate:
   Stampdate:
5. **RECEIVED BY CHEMIST:** 02-Nov-2002

6. **APPLICANT NAME AND ADDRESS:** Ortho-McNeil Pharmaceuticals, Inc.
   1000 Route 202 South
   P.O. Box 300
   (908)-704-9757

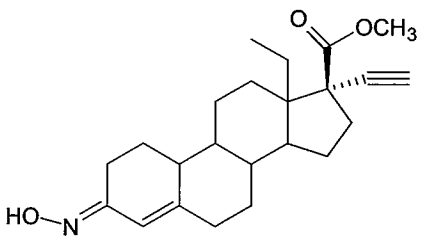
7. **NAME OF DRUG:** Ortho Tri-Cyclen

8. **NONPROPRIETARY NAME:** Norgestimate/Ethinyl estradiol

9. **CHEMICAL NAME/STRUCTURE:**



Ethinyl estradiol (EE)



Norgestimate (NGM)

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

Norgestimate (NGM): (+)-13-Ethyl-17-hydroxy-18,19-dinor-17α-pregn-4-en-20-yne-3-one oxime acetate

10. **DOSAGE FORM(S):** Oral tablets

11. **POTENCY:** 180 mcg/35 mcg, 215 mcg/35 mcg, and 250 mcg/35 mcg (NGM/EE)

12. **PHARMACOLOGICAL CATEGORY:** Oral contraceptive

13. **HOW DISPENSED:** Rx

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

15. **RELATED IND/NDA/DMF:** NDA 19-653/SCS 035

16. SUPPLEMENT PROVIDES FOR: The option of using [ ] for [ ] of drug product at the Manati, Puerto Rico manufacturing site.

17. SPECIAL PRODUCTS: YES _ NO _X__.
(If yes, fill out the form for special products and deliver to TIA through team leader for data entry)

18. COMMENTS: Please refer to attached Comments Section.

19. CONCLUSIONS AND RECOMMENDATIONS:
This CBE-30 supplement may be **approved**. Issue an Approval Letter.

20. REVIEWER NAME	**SIGNATURE**	**DATE COMPLETED**
Sarah C. Pope, Ph.D.		13-Nov-2002

cc: Original: NDA 19-697/SCS-032
HFD-580/Division File
HFD-580/D. Spell-Lesane
HFD-580/DLin/SPope

2 Page(s) Withheld

Chemistry Review (19-697/S-032)

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

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

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/s/

Sarah Pope
12/10/02 09:59:26 AM
CHEMIST

David T. Lin
12/10/02 10:20:28 AM
CHEMIST
I concur.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-035 & 19-697/S-032

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Johnson & Johnson
PHARMACEUTICAL RESEARCH
& DEVELOPMENT, L.L.C.

11 NOV 2002

920 U.S. Highway 202, P.O. Box 300
Raritan NJ 08869

RECEIVED
NOV 12 2002
FDR/CDER

Daniel Shames, MD, Acting Director
US Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation III
Division of Reproductive and Urologic Drug Products, HFD-580
Attn.: Document Control Room 14B-04
5600 Fishers Lane
Rockville, Maryland 20857-1706

ORIGINAL
20-653/S-082-WD
NDA SUPPL AMENDMENT

K. Anders NP
pm 11/21/02

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

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

WITHDRAWAL OF SUPPLEMENTS

Dear Dr. Shames:

Reference is made to the above-approved New Drug Applications for our oral contraceptive and green placebo tablets. Reference is further made to our Changes Being Effected in 30 Days supplemental applications dated 18 October 2002 (copy of cover letter is attached). The supplements provided for the option to use [ ] as an alternative to the [ ] [ ] used for the [ ] of **green placebo** tablets at our **Manati, Puerto Rico** facility and for an alternate batch size of [ ] for the manufacture of these tablets.

Finally, reference is made to a telephone conversation of 06 November 2002 between Dr. David Lin of your Division and Ms. Sandy Rathborne of Johnson & Johnson Pharmaceutical Research & Development, L.L.C. in which Dr. Lin advised Ms. Rathborne that these changes should not be submitted as supplements as had previously been agreed with FDA. Rather, this information,

should be reported in the next NDA annual reports. Dr. Lin further advised that for administrative purposes these supplements should be withdrawn.

At this time, on behalf of Ortho-McNeil Pharmaceutical, Inc., and at the request of Dr. Lin, we are withdrawing these supplements in accordance with 21 CFR 314.65 and hereby advise the Agency that we will be reporting these changes in the next NDA annual reports for the above referenced approved New Drug Applications.

A field copy of this submission is being forwarded directly to the FDA district office in San Juan, Puerto Rico. We certify that the field copy is a true copy of the information contained in the archival and review copies of this Withdrawal of Supplemental Applications.

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

Sincerely,

Johnson & Johnson Pharmaceutical Research & Development, L.L.C.

Sandy Rathborne

Sandy Rathborne
Manager, Regulatory Affairs
Global Chem-Pharm.

Att.

Johnson & Johnson
PHARMACEUTICAL RESEARCH
& DEVELOPMENT, L.L.C.

NDA NO. 19697 REF NO. 032
NDA SUPPL FOR SCS

920 U.S. Highway 202, P.O. Box 300
Raritan NJ 08869

ORIGINAL

RECEIVED 18 OCT 2002

OCT 31 2002

FDA/CDER

Reviewed on 26-Nov-02 see DFS Sarah C. Pope

Daniel Shames, MD, Acting Director
US Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation III
Division of Reproductive and Urologic Drug Products, HFD-580
Attn.: Document Control Room 14B-04
5600 Fishers Lane
Rockville, Maryland 20857-1706

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

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

SUPPLEMENT – CHANGES BEING EFFECTED IN 30 DAYS

Dear Dr. Shames:

Reference is made to our approved New Drug Application(s)19-653 and 19-697 for ORTHO-CYCLEN® (250 µg norgestimate/35 µg ethinyl estradiol) Tablets and ORTHO TRI-CYCLEN® (180, 215 and 250 µg norgestimate/35 µg ethinyl estradiol) Tablets, respectively. Reference is further made to our Changes Being Effected in 30 Days supplemental application dated 25 July 2001 and approved 16 January 2002 (Attachment #1). The supplement provided for the option to use [ ] as an alternative to the [ ] [ ] used for the [ ] of ORTHO-CYCLEN and ORTHO TRI-CYCLEN Tablets at our **Raritan, New Jersey facility**.

At this time, on behalf of Ortho-McNeil Pharmaceutical, Inc., we are submitting a Changes Being Effected in 30 Days supplement to provide for the option to use the [ ] as an alternative to the [ ] currently used for the [ ] of these two products at our **Manati, Puerto Rico facility.**

In support of this change, we have appended the following:

- **Attachment 1:**
  - 25 July 2001 submission letter and 16 January 2002 approval letter
- **Attachment 2:**
  - A description of the [ ]
- **Attachment 3:**
  - Comparative hardness, weight, thickness, and disintegration data for [ ] and [ ] for our 215 µg norgestimate/35 µg ethinyl estradiol containing tablets (the mid-strength tablet in our triphasic product, ORTHO TRI-CYCLEN Tablets).

The same study parameters were followed for Manati as that of the study conducted to support the Raritan submission, with the exception of the tablet strength. The Raritan study was conducted utilizing the 250 µg norgestimate/35 µg ethinyl estradiol tablet, which represents the high strength tablet in the triphasic product. All three norgestimate/ethinyl estradiol tablet strengths are manufactured using the same method of manufacture. In addition, the formulations are identical at both the Raritan and Manati.

The appended data demonstrate that the [ ] process utilizing the [ ] is consistent in all measurable parameters as product produced utilizing the current [ ] [ ] and that there is no change in the, quality of the products.

A field copy of this submission is being forwarded directly to the FDA district office in North Brunswick, New Jersey and San Juan, Puerto Rico. 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) 704-4687, or call our telephone line dedicated for FDA use at (908) 704-4600.

Sincerely,

Johnson & Johnson Pharmaceutical Research & Development, L.L.C.

Sandy Rathborne
Manager, Regulatory Affairs
Global Chem-Pharm.

Enclosure(s)