CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

19-697/S-025

Trade Name: 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: 08/30/2000

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

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:

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-697/S-025

APPROVAL LETTER

NDA 19-697/S-025

AUG 3 0 2000

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

Dear Ms. Panasewisz:

Please refer to your supplemental new drug application dated August 17, 2000, received August 18, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ORTHO TRI-CYCLEN® Tablets (norgestimate/ethinyl estradiol).

This "Changes Being Effected in 30 days" supplemental new drug application provides for the reduction of the expiration date of the norgestimate 0.180 mg/ethinyl estradiol 0.035 mg strength component in ORTHO TRI-CYCLEN® Tablets from 36 to 24 months. Therefore, the actual expiration date of the ORTHO TRI-CYCLEN® product package is 24 months.

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, Regulatory Project Manager, at (301) 827-4260.

Sincerely,

8/30/00

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 NDA 19697/
HFD-580/Div. Files
HFD-580/J.Best/Mercier
HFD-580/Lin/Rhee
HFD-095/DDMS-IMT
HFD-093/DDMS-IST
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: JAB/August 28, 2000
Initialed by:Rumblet,08.30.00/Lin,08.28.00/Rhee,08.28.00/Shames, 08.28.00
final:JAB/August 30, 2000
filename: N19697S25Apltr.doc

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-697/S-025

CHEMISTRY REVIEW(S)

AUG 24 2000

CHEMIST REVIEW
OF **SUPPLEMENT**

1. **ORGANIZATION:** DRUDP HFD-580
2. **NDA NUMBER:** 19-697/SCE-025
3. **SUPPLEMENT NUMBERS/DATES:**
   Letterdate: 17-AUG-2000
   Stampdate: 18-AUG-2000
4. **AMENDMENTS/REPORTS/DATES:**
   Letterdate:
   Stampdate:
5. **RECEIVED BY CHEMIST:** 24-AUG-2000

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:**
    N/A

16. SUPPLEMENT PROVIDES FOR:

Reducing the expiration date of the norgestimate 0.180 mg/ethinyl estradiol 0.035 mg strength component in the Ortho Tri-Cyclen regiment to 24 months. Consequently, the entire Ortho Tri-Cyclen product package will have an expiration date of two years from the date of manufacture.

17. COMMENTS

This supplement has been filed to reduce the expiration date of the 0.180 mg norgestimate/0.035 mg ethinyl estradiol strength tablet in the Ortho Tri-Cyclen regimen to 24 months from currently approved 36 months. The Ortho Tri-Cyclen regimen consists of three different strength tablets: 1) 0.180 mg norgestimate/0.035 mg ethinyl estradiol, 2) 0.215 mg norgestimate/0.035 mg ethinyl estradiol, and 3) 0.250 mg norgestimate/0.035 mg ethinyl estradiol. Since the 0.180 mg norgestimate/0.035 mg ethinyl estradiol strength tablet is one component of the entire product package, the entire Ortho Tri-Cyclen product will have a 24 month expiration date.

The reason for this request to reduce the expiration date is due to the possibility that the total impurities specification (NMT [ ]%) could be exceeded at 36 months. The only impurity detected thus far is [ ] and this impurity level has exceeded the [ ]% limit only in the 0.180 mg norgestimate/0.035 mg ethinyl estradiol strength tablet at the final testing point of 36 months. The reason for the higher level of [ ] in one of the tablet strengths is being investigated. Data will be provided once the sponsor completes the investigation.

Based on the information provided, the proposed reduction in the expiration date to 24 months from 36 months is acceptable.

18. CONCLUSIONS AND RECOMMENDATIONS:

This CBE-30 Supplement may be approved. **Issue an approval letter.**

19. REVIEWER NAME	**SIGNATURE**	**DATE COMPLETED**
David T. Lin, Ph.D. Review Chemist	8/24/00	24-AUG-2000

cc: Original: NDA 19-697/SCE-025
HFD-580/Division File
HFD-580/JBest
HFD-580/MRhee/DLin

INIT by MJ Rhee 8/24/00

Filename: S19697.025 (doc)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-697/S-025

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

NDA 19-697/S-025

CBE-30 SUPPLEMENT

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

AUG 22 2000

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:

Name of Drug Product: ORTHO TRI-CYCLEN® Tablets (norgestimate/ethinyl estradiol)

NDA Number: 19-697

Supplement Number: S-025

Date of Supplement: August 17, 2000

Date of Receipt: August 18, 2000

This supplemental application, submitted as a "Changes Being Effected" supplement, proposes the following change: the reduction of the expiration data of the norgestimate 0.180 mg/ethinyl estradiol 0.035 mg strength component in ORTHO TRI-CYCLEN® Tablets to 24 months. Changes of the kind that you have proposed cannot be put into effect immediately upon submission of the supplement. However, **this** change may be implemented and distribution of the affected drug product may commence 30 days after FDA receives your submission.

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 October 17, 2000 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be February 18, 2001.

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

Sincerely,

8/22/00

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

cc:
Archival NDA 19-697
HFD-580/Div. Files
HFD-580/J.Best
HFD-580/Reviewers and Team Leaders

HFD-358/D.MorleyDISTRICT OFFICE

Drafted by: JAB/August 21, 2000
Initialed by:Rumble,08.21.00
final:JAB/August 22, 2000
filename: N19697S25Acltr.doc

CBE-30 SUPPLEMENT ACKNOWLEDGEMENT (AC)

Noted 8/30/00 See Chem. Rev. dated 8/24/00. TC 8/24/00

ORIGINAL

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

AUG 17 2000

noted 8/30/00 RVB

Susan Allen, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and Urologic
Drug Products, HFD 580
Attn: Document Control Room 14B-04
5600 Fishers Lane
Rockville, Maryland 20857-1706

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

NDA NO. 19697 REF. NO. 025
NDA SUPPL FOR Expiration
SPECIAL SUPPLEMENT
CHANGES BEING EFFECTED

Dear Dr. Allen:

This letter is to inform you that effective immediately, we are reducing the expiration date of the norgestimate 0.180 mg /ethinyl estradiol 0.035 mg strength component in our ORTHO TRI-CYCLEN regimen to 24 months and that consequently, the actual ORTHO TRI-CYCLEN product package will have an expiration date of two years from the date of manufacture. Based upon our current stability trend, there exists the possibility that at the current expiration date of 36 months, our specification of not more that [ ]% for the total impurities may be exceeded. The only impurity we have detected has been [ ]. The impurity level is only exceeded in the norgestimate 0.180 mg/ethinyl estradiol 0.035 mg strength and thus far we have exceeded it only at the final testing point of 36 months. This increase has no effect on the efficacy or safety of ORTHO TRI-CYCLEN® Tablets.

Please be advised that we are currently conducting an investigation of this matter. Once the investigation is completed, we will provide FDA with our findings.

A field copy of this submission is being forwarded directly to the FDA district offices 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 require any additional information, please contact me at (908) 218-6140 or call our telephone line dedicated for FDA use at (908) 704-4600.

Sincerely,

Donna Panasewicz
Director
Regulatory Affairs

REVIEWS COMPLETED

CSO ACTION:
☑ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS 8/30/00 DATE

N:\ORTHOTRI\LTR\CBE REDUCTION OF EXP DATING.DOC/1