CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

19-653/S-016 & 19-697/S-011

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: 08/02/1996

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-016 & 19-697/S-011

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APPLICATION NUMBER:

19-653/S-016 & 19-697/S-011

APPROVAL LETTER

ORIGINAL

NDA 19-653/S-016
NDA 19-697/S-011

AUG 2 1996

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

Dear Ms. Panasewicz:

Please refer to your April 1, 1996, supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for:

> Ortho-Cyclen (norgestimate and ethinyl estradiol) Tablets, NDA 19-653; and
> Ortho-TriCyclen (norgestimate and ethinyl estradiol) Tablets, NDA 19-697.

These supplemental applications provide for a final dissolution specification, Q= 80% at 20 min (0.025% Tween), for both drug substances.

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, please contact Ms. Christina Kish at 310-827-4271.

Sincerely,

Helen W. Davies 8/02/96

Helen W. Davies, Ph.D.
Chemistry Team Leader
Division of New Drug Chemistry II
Office of New Drug Chemistry, OPS
@ Division of Reproductive and Urologic
Drug Products (HFD-580)
Center for Drug Evaluation and Research

cc:
Orig. NDA's (2)
HFD-580(2)
DISTRICT OFFICE
HFD-80
HFD-580/HDavies/MRhee
HFD-580/CKish/7.5.96/n19653ap.s16
concurrences:LPauls 7.31.96/MRhee 7.31.96/HDavies 7.31.96

SUPPLEMENT APPROVAL (S/AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-016 & 19-697/S-011

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW

1. Organization
DMEDP HFD-510

2. NDA Number
19-653

JUL - 2 199

3. Name amd Address of Applicant
The R.W. Johnson
Pharmaceutical Research Institute
Route 202, P.O. Box 300
Raritan, NJ 08869-0602
908-704-4038

4. Supplement
S-016
7-2-96

ORIGINAL

5. Name of Drug
Ortho-Cyclen

6. Nonproprietary Name
Norgestimate/EE tablets

7. Supplement Provides For
A final dissolution specification, Q=80% at 20 min (0.025% Tween), for both drug substances.

8. Amendment

9. Pharmacological Category
Oral contraceptive

10. How Dispensed
RX

11. Related
NDA 19-697 (S-011)

12. Dosage form
Tablets for oral administration

13. Potency
250μg/35μg (norgestimate/EE)

14. Chemical Name and Structure
Norgestimate: 18,19-dinor-17-pregn-4-en-20-yn-3-on, 17-(acetyloxy)-13-ethyl-, oxime,(17α)-(+)-

Empirical Formula: $C_{23}H_{31}NO_3$ MW: 369.50

Ethinyl Estradiol: 19-nor-17-α-pregna-1,3,5-(10)-trien-20-yne-3,17-diol
Empirical Formula: $C_{22}H_{30}O$ MW: 296.41

15. Comments
This special supplement was submitted to notify the Agency of the final specification of the dissolution test, Q=80% 20 min for both drug substances. The Biopharm review supports the use of this specification. See Biopharm's review for detail.

16. Conclusion and Recommendation
This supplement is approvable. Issue an approval letter.

17. Name
Moo-Jhong Rhee, Ph.D.

Reviewer's Signature

Date
7-2-96

Distribution	Original Jacket	Reviewer/CSO	Division File
R/D initialed by			
SL.253	H. Davis 7/2/96		

CHEMIST'S REVIEW

1. Organization
DMEDP HFD-510

2. NDA Number
19-697

3. Name amd Address of Applicant
The R.W. Johnson
Pharmaceutical Research Institute
Route 202, P.O. Box 300
Raritan, NJ 08869-0602
908-704-4038

4. Supplement
S-011
4-1-96

5. Name of Drug
Ortho Tri-Cyclen

6. Nonproprietary Name
Norgestimate/EE tablets

7. Supplement Provides For
A final dissolution specification, Q=80% at 20 min (0.025% Tween), for both drug substances.

8. Amendment

9. Pharmacological Category
Oral contraceptive

10. How Dispensed
RX

11. Related
NDA 19-653 (S-016)

12. Dosage form
Tablets for oral administration

13. Potency
180μg/35μg, 215μg/35μg, 250μg/35μg (norgestimate/EE)

14. Chemical Name and Structure
Norgestimate: 18,19-dinor-17-pregn-4-en-20-yn-3-on, 17-(acetyloxy)-13-ethyl-, oxime,(17α)-(+)-
Empirical Formula: $C_{23}H_{31}NO_3$ MW: 369.50
Ethinyl Estradiol: 19-nor-17-α-pregna-1,3,5-(10)-trien-20-yne-3,17-diol
Empirical Formula: $C_{22}H_{30}O$ MW: 296.41

15. Comments
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16. Conclusion and Recommendation
This supplement is approvable. Issue an approval letter.

17. Name
Moo-Jhong Rhee, Ph.D.

Reviewer's Signature

Date
7-2-96

Distribution **Original Jacket** **Reviewer/CSO** **Division File**
R/D initialed by
SL.252 H Davis 7/2/96

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-016 & 19-697/S-011

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

Date APR 30 1996

NDA No. 19-697

The R.W. Johnson Pharmaceutical Research Inst.
Division of Ortho Pharmaceutical Corporation
920 Route 202 South
P.O. Box 300
Raritan, New Jersey 08869-0602

Attention: Donna Panasewicz, Manager, Regulatory Affairs

Dear Sir/Madam:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: ORTHO TRI-CYCLEN(Norgestimate + Ethinyl Estradiol)

NDA Number: 19-697

Supplement Number: S-011

Date of Supplement: April 1, 1996

Date of Receipt: April 16, 1996

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on JUN 15 1996 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 Metabolic and Endocrine Drug Products
Attention: Document Control Room
5600 Fishers Lane, HFD-510
Rockville, MD 20857

Sincerely yours,

Chief, Project Management Staff
Division of Metabolic and Endocrine Drug Products
Office Drug Evaluation II
Center for Drug Evaluation and Research

FORM FDA 3217g (11/95)

PREVIOUS EDITION IS OBSOLETE

★ U.S. GPO: 1995-404-897/20718

NDA NO. 19697 REP. NO. 011

NDA ORIG. SCF

ORIGINAL

NDA SUPPLEMENT

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

APR 01 1996

Solomon Sobel, M.D.
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Review II, HFD #510
ATTN: Document Control Room #14B-03
5600 Fishers Lane
Rockville, Maryland 20857-1706

Special Supplement - Changes Being Effected

NDA 19-653
ORTHO CYCLEN® (Norgestimate/Ethinyl Estradiol) Tablets
NDA 19-697
ORTHO TRI-CYCLEN® (Norgestimate/Ethinyl Estradiol) Tablets

Dear Dr. Sobel,

Reference is made to our supplemental new drug applications for ORTHO-CYCLEN, NDA 19-653 (S-009) and ORTHO TRI-CYCLEN, NDA 19-697 (S-002) submitted July 26, 1993 which provided for a new non-alcoholic based dissolution method, (DM91-020). Further reference is made to your approval letter dated February 16, 1995 in which it was requested that we establish a final dissolution specification after additional data are accrued for one year using dissolution method DM91-020.

At this time we are submitting our final dissolution specifications for norgestimate and ethinyl estradiol applicable to both product release and stability testing. The specifications are as follows:

CSO: please let this be reviewed by Biopharm
MPM 5/1/96

Norgestimate:	Q=80% at 20 minutes
Ethinyl Estradiol:	Q=80% at 20 minutes.

As discussed at a meeting held with the agency on September 14, 1995 regarding Dissolution Method DM 91-020 we continue to experience variability in our dissolution results and our investigation into the reason for the variability as well as the increase in S2 testing since employing this method is on-going. Upon completion of our investigation we plan to discuss our findings and future steps with the agency.

Should you have any questions , you may contact me at (908) 704-4600 a number designated for FDA use only or if you prefer you may contact me directly at (908) 218-6140.

CENTER FOR DRUG REC'D APR 16 1996 HFD-510 EVALUATION AND RESEARCH

Very truly yours,
The R.W. Johnson Pharmaceutical Research Institute

Donna M. Panasewicz
Manager
Regulatory Affairs

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO
DATE
CSO INITIALS

cc: John Hunt

Noted telephonically 5/2/96

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