CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

19-697/S-010

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: 02/14/1996

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

19-697/S-010

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Reviews / Information Included in this NDA Review.	
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Medical Review(s)	
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Microbiology Review(s)	
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-697/S-010

APPROVAL LETTER

NDA 19-653/S-015
NDA 19-697/S-010

FEB 14 1996

R.W. Johnson Pharmaceutical Research Institute
Attention: Ms. Isabel B. Drzeweicki
Senior Director, Regulatory Affairs
Route 202, P.O. Box 300
Raritan, N.J. 08869-0602

Dear Ms. Drzewiecki:

Please refer to your November 21, 1995, 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

We also refer to your amendments dated January 16 and 19, 1996.

These supplemental applications provide for a modification to in-process testing of the bulk tablets for average tablet weight, hardness, and thickness.

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 310-443-3520.

Sincerely,

Helen W. Davies 2/15/96

Helen W. Davies, Ph.D.
Acting Supervisory Chemist I
Division of New Drug Chemistry II
Office of New Drug Chemistry, OPS
@ Division of Metabolism and
Endocrine Drug Products (HFD-510)
Center for Drug Evaluation and Research

cc:
Orig. NDA's (2)
HFD-510(2)
DISTRICT OFFICE
HFD-80
HFD-510/HDavies/MRhee
HFD-510/CKish/2.5.96/n19653ap.s15
concurrences:MRhee 2.7.96/HDavies 2.7.96/LPauls for EGalliers 2.14.96

SUPPLIMENT APPROVAL (S/AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-697/S-010

CHEMISTRY REVIEW(S)

ORIGINAL

FEB - 5 1996

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-010
11-21-95

5. Name of Drug
Ortho Tri-Cyclen

6. Nonproprietary Name
Norgestimate/EE tablets

7. Supplement Provides For
A modification to in-process testing of the bulk tablets for average tablet weight, hardness, and thickness.

8. Amendment
1-16-96
1-19-96

9. Pharmacological Category
Oral contraceptive

10. How Dispensed
RX

11. Related
NDA 19-653 (S-015)

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: [ ] MW: 296.41

15. Comments
In this "Special Supplement", the firm proposed to modify their current in-process testing of average weight, hardness, and thickness. In the supplement, current analytical laboratory procedures and current processing procedures are briefly described together with the proposed modified procedure. [ ]

[redacted]

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

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

Reviewer's Signature

Date
2-5-96

Distribution **Original Jacket** **Reviewer/CSO** **Division File**
R/D initialed by
SL.242
H. Davies
2/5/96

Redacted 1 page(s)

of trade secret and/or

confidential commercial

information from

Chemistry Review : 19-697/S-010

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-697/S-010

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

ORIGINAL

NDA [illegible]

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

JAN 16 1996

Noted
K Rehaya
1/24/96

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

Amendment to Supplement

16-653 ORTHO CYCLEN® ☐ 21 & 28 Tablets
16-697 ORTHO TRI-CYCLEN® ☐ 21 & 28 Tablets

Dear Dr. Sobel:

Reference is made to a Special Supplement, Changes Being Effected submitted on November 21, 1995 to the above listed NDA's for our norgestimate\ethinyl estradiol containing oral contraceptive tablet products. Further reference is made to a telephone conversation on January 5, 1996 between Dr. Moo Jhong Rhee of your division and Mrs. Donna Panasewicz of the R. W. Johnson Pharmaceutical Research Institute in which Dr. Rhee requested clarification regarding our supplement. At this time we wish to provide the clarification requested by Dr. Rhee on our modification to the in-process testing procedures for these products.

[redacted]

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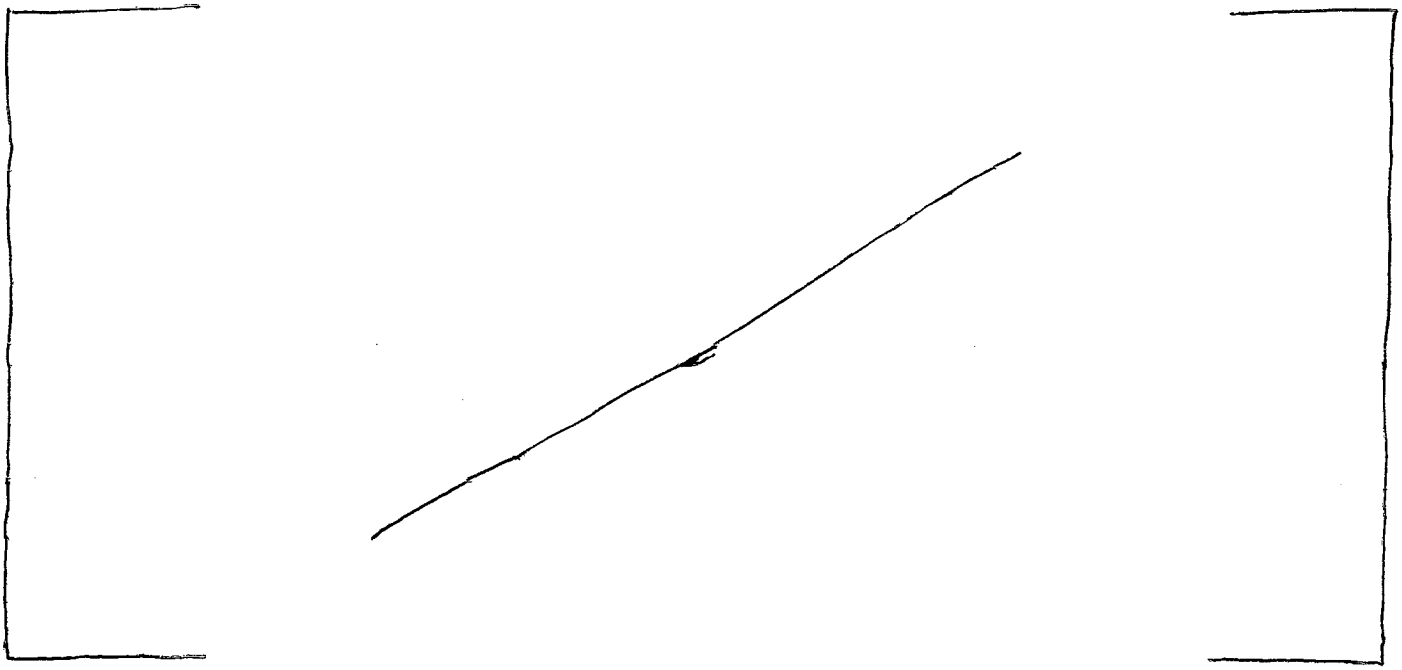
JAN 16 1996



We trust that we have responded to all of Dr. Rhee's questions and will be in contact with him within the next week to discuss the implementation of this change.

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

Very truly yours,

The R. W. Johnson
Pharmaceutical Research Institute

Donna M. Panasewicz
Manager
Regulatory Affairs

REVIEWS COMPLETED

CSO ACTION:

☐ LETTER ☐ N.A.I.

CSO INITIALS DATE

n:\ortho_cy\ltr\dp0156.mip

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

Date NOV 29 1995

NDA No. 19-697

THE R.W. JOHNSON PHARMACEUTICAL RESEARCH INSTITUTE
Division of Ortho Pharmaceutical Corporation
U.S. Route 202, P.O. Box 300
Raritan, New Jersey 08869-0602

Attention: Donna M. Panasewicz

Dear Sir/Madam:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: ORTHO TRI-CYCLEN

NDA Number: 19-697

Supplement Number: S-010

Date of Supplement: November 21, 1995

Date of Receipt: November 22, 1995

Unless we find the application not acceptable for filing, the filing date will be 60 days from the receipt date above.

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Attention: Document Control Room 14B-03
5600 Fishers Lane, HFD-510
Rockville, MD 20857

Sincerely yours,

for Brad Collins

Supervisory Consumer Safety Officer
Division of Metabolism and Endocrine Drug Products
Center for Drug Evaluation and Research

19697 ORIGINAL

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

NOV 2 1 1995

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

19-653 ORTHO CYCLEN® ☐ 21 & 28 Tablets
19-697 ORTHO TRI-CYCLEN® ☐ 21 & 28 Tablets

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
NOV 2 2 1995
HFD-510

Dear Dr. Sobel:

Reference is made to the above listed approved NDAs for our norgestimate/ethinyl estradiol containing oral contraceptive products. At this time we wish to inform you of a modification to our in-process testing of the bulk tablets associated with this NDAs, including green placebo tablets.

Our current procedure as listed in our NDAs is for our Processing Department personnel to perform in-process tests for average tablet weight, thickness and hardness. These tests are repeated by our Quality Assurance Laboratory on composite samples.

In order to enhance the quality of our products, have better control of our process and immediately identify process [ ] we are increasing the amount of in-process sampling we will be conducting on our [ ] tablets as follows:

TEST	CURRENT ANALYTICAL LABORATORY PROCEDURE	CURRENT PROCESSING PROCEDURE	MODIFIED PROCEDURE
Average Tablet Weight			
Hardness			

TEST	CURRENT ANALYTICAL LABORATORY PROCEDURE	CURRENT PROCESSING PROCEDURE	MODIFIED PROCEDURE
Thickness	[redacted]		[redacted]

Additionally, we will be utilizing the results obtained by our Processing personnel to support final disposition of a given lot of product. Quality Assurance will no longer be repeating the above listed tests. A protocol which specifically delineates the requirements for training/qualification of the Processing personnel has been internally reviewed and approved. All test results generated by Processing will be reviewed by Quality Assurance and final disposition of a lot remains the responsibility of Quality Assurance.

At this time, we are internally qualifying Processing personnel and plan to implement this change in thirty (30) days from your receipt of this notification.

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

Very truly yours,

The R.W. Johnson
Pharmaceutical Research Institute

Donna M. Panasewicz
Manager
Regulatory Affairs

REVIEWS COMPLETED

CSO ACTION:

☐ LETTER ☐ N.A.I.

CSO INITIALS DATE

DMP:lg

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