

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-490**

**CHEMISTRY REVIEW(S)**



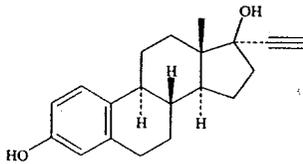
**NDA 21-490**

**Ovcon 35**

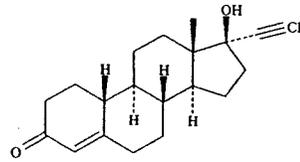
**Warner Chilcott**

**AMIT K. MITRA, Ph.D**

**REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS**



**Ethinyl estradiol**



**Norethindrone**



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1. NDA 21-490
2. REVIEW #: 3
3. REVIEW DATE: 04-NOV-2003
4. REVIEWER: Amit K. Mitra, Ph.D
5. PREVIOUS DOCUMENTS:

<u>Previous Documents</u>	<u>Document Date</u>
Original	29-MAR-2002
Amendments	16-MAY-2002
	16-AUG-2002
	17-OCT-2002
	09-DEC-2002
	12-DEC-2002
	19-DEC-2002
	07-JAN-2003
	22-JAN-2003

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Amendment	17-OCT-2003
Amendment	30-SEP-2003
Amendment	29-SEP-2003
Amendment	20-AUG-2003
Amendment	1-AUG-2003
Amendment	13-MAY-2003



## CHEMISTRY REVIEW



### Chemistry Assessment Section

7. NAME & ADDRESS OF APPLICANT:

Name: Warner Chilcott  
Address: Rockaway 80 Corporate Center  
Representative: Mr. Alvin Howard  
Telephone: (973)443-3233

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Ovcon 35
- b) Non-Proprietary Name (USAN): Norethindrone and ethinyl estradiol tablet, chewable
- c) Code Name/# (ONDC only): N/A
- d) Chem. Type/Submission Priority (ONDC only):
  - Chem. Type: 3
  - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: NA

10. PHARMACOL. CATEGORY: Contraception

11. DOSAGE FORM: Chewable tablet

12. STRENGTH/POTENCY: 0.4 mg norethindrone and 0.035 mg ethinyl estradiol

13. ROUTE OF ADMINISTRATION: Oral



## CHEMISTRY REVIEW



Chemistry Assessment Section

14. Rx/OTC DISPENSED:  Rx  OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM)

SPOTS product – Form Completed

Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT: ; Norethindrone-19-Norpregn-4-en-20-yn-3-one, 17-hydroxy-, 17 (•);  $C_{20}H_{26}O_2$ ; 298.42. Ethinyl estradiol-19-Norpregna-1,3,5(10)-trien-20-yne-3,17-diol, (17•),  $C_{20}H_{24}O_2$ , 296.40.

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs: See Chemistry Review #1, adequate

B. Other Documents: None

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	NA		
EES	Acceptable	04-NOV-2003	Ms. D. Ambrogio
Pharm/Tox	Satisfactory	23-JAN-2003	Dr. A. Jordan
Biopharm	NA		
LNC	NA		
Methods Validation	Will be initiated		
Division of Medical Errors and Technical Support (DMETS)	Trademark "Ovcon 35 " satisfactory.	3-JUL-2003	Ms. L. Y. Kim-Jung
EA	Categorical exclusion granted	14-JAN-2003	Dr. A. K. Mitra
Microbiology	Satisfactory	18-OCT-2002	Dr. S.Langille



# The Chemistry Review for NDA 21-490

## The Executive Summary

### I. Recommendations

#### A. Recommendation and Conclusion on Approvability

The application is recommended to be approved

#### B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

Warner Chilcott is to provide the lot numbers of the blister lots that do not contain the storage conditions within \_\_\_\_\_ post approval. The \_\_\_\_\_

\_\_\_\_\_, therefore, the sponsor was requested and agreed on placing the storage conditions on the blister card. However, the sponsor has approximately \_\_\_\_\_ supply of blister foil that do not contain the storage conditions. Therefore, the sponsor was requested to provide the lot numbers for those batches without the storage conditions on the blister card so that they can be identified quickly, if needed. **The sponsor agreed to supply the lot numbers corresponding to the product in blister cards without storage conditions printed on the label within \_\_\_\_\_ post approval.**

### II. Summary of Chemistry Assessments

#### A. Description of the Drug Product(s) and Drug Substance(s)

The drug product "Ovcon 35", is an immediate release chewable tablet formulation. The drug product is proposed to be available in only one dosage strength containing 0.4 mg norethindrone and 0.035 mg ethinyl estradiol per tablet. The tablets are packed into a blister card to contain 28 tablets, 21 of that contain 0.4 mg norethindrone and 0.035 mg ethinyl estradiol. The remaining 7 tablets are placebos and contain only inactive ingredients. The appearance of the active and placebo tablets are distinctly different and the difference is adequate for proper identification of active vs. placebo tablets. Ovcon 35 is indicated for the prevention of pregnancy in women. The women would start with the white tablets (21 tablets one each for 21 days) and followed by 7 green placebo tablets (once a day). The next pack of 28 tablets should be started after the last "reminder" tablet.

The drug is formulated in a tablet dosage form using \_\_\_\_\_ ethinyl estradiol and norethindrone. Both drug substances are monographed in the USP. The drug substances are \_\_\_\_\_

\_\_\_\_\_ The details of the Chemistry, Manufacturing and Controls of the



## CHEMISTRY REVIEW



### Chemistry Assessment Section

norethindrone and ethinyl estradiol are documented in DMFs — and — respectively, and those DMFs are adequate to support the NDA. The sponsor of the NDA has referenced to DMF for adequate information on the container closure system for the drug substance.

All excipients are compendial except for the color and flavors. The sponsor has provided the specifications for various colors and flavor used in the formulation. The sponsor has adequately addressed all the deficiencies listed in the Chemistry Review #2, dated 27-JAN-2003.

#### **B. Description of How the Drug Product is Intended to be Used**

The recommended dose for the drug product is 1 active tablet/per day for 21 days followed by 1 placebo tablet per day for 7 days. Only one strength of the tablet is proposed (0.4 mg norethindrone and 0.035 mg ethinyl estradiol) with 21 active and 7 placebo tablets in a blister card. The blister card containing 28 tablets is stored in a green rectangular compact. The recommended dose is one tablet per day and it is the maximum daily dose. The drug product is recommended to be chewed or swallowed.

The stability data from ~ production scale lots were used for determination of expiration date. Based on the stability data provided, an expiration date of 18 months is granted. The sponsor's storage conditions "store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F)" is satisfactory to the reviewer.

#### **C. Basis for Approvability or Not-Approval Recommendation**

The sponsor has adequately addressed all the Chemistry deficiencies. Therefore, the application may be approved.

### **III. Administrative**

#### **A. Reviewer's Signature**

#### **B. Endorsement Block**

A. K. Mitra, Ph.D/  
M. J. Rhee, Ph.D/  
K. Anderson/

#### **C. CC Block**

NDA 21-490/Division File

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this page is the manifestation of the electronic signature.**  
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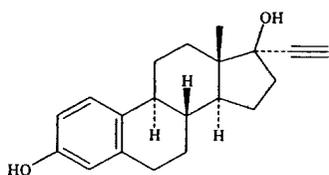
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CHEMIST

Moo-Jhong Rhee  
11/5/03 11:44:19 AM  
CHEMIST  
I concur

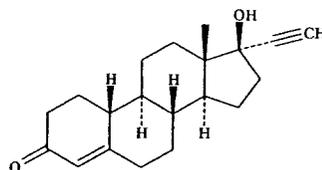
**NDA 21-490**  
**Ovcon 35 Chewable**

**Warner Chilcott**

**AMIT K. MITRA, Ph.D**  
**REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS**



**Ethinyl estradiol**



**Norethindrone**



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1. NDA 21-490
2. REVIEW #: 2
3. REVIEW DATE: 27-JAN-2003
4. REVIEWER: Amit K. Mitra, Ph.D
5. PREVIOUS DOCUMENTS:

Previous Documents

Document Date

Original  
Amendments

29-MAR-2002  
16-MAY-2002  
16-AUG-2002  
  
17-OCT-2002  
09-DEC-2002  
12-DEC-2002  
19-DEC-2002  
07-JAN-2003

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed

Document Date

Amendment

22-JAN-2003



Executive Summary Section

7. NAME & ADDRESS OF APPLICANT:

Name: Warner Chilcott  
Address: Rockaway 80 Corporate Center  
Representative: Mr. Alvin Howard  
Telephone: (973)443-3233

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Ovcon 35
- b) Non-Proprietary Name (USAN): Norethindrone and ethinyl estradiol chewable tablet.
- c) Code Name/# (ONDC only): N/A
- d) Chem. Type/Submission Priority (ONDC only):
  - Chem. Type: 3
  - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: NA

10. PHARMACOL. CATEGORY: Contraception

11. DOSAGE FORM: Chewable tablet

12. STRENGTH/POTENCY: 0.4 mg norethindrone and 0.035 mg ethinyl estradiol

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED:  Rx  OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM)

SPOTS product – Form Completed



## Executive Summary Section

  x   Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT: ; Norethindrone-19-Norpregn-4-en-20-yn-3-one, 17-hydroxy-, 17 ( $\alpha$ );  $C_{20}H_{26}O_2$ ; 298.42. Ethinyl estradiol-19-Norpregna-1,3,5(10)-trien-20-yne-3,17-diol, (17 $\alpha$ ),  $C_{20}H_{24}O_2$ , 296.40.

## 17. RELATED/SUPPORTING DOCUMENTS:

**A. DMFs: See Chemistry Review #1, adequate**

**B. Other Documents: None**

## 18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	NA		
EES	Withhold	23-AUG-2002	Mr. B. Hartman
Pharm/Tox	Satisfactory	23-JAN-2003	Dr. A. Jordan
Biopharm	NA		
LNC	NA		
Methods Validation	Will be initiated		
Division of Medical Errors and Technical Support (DMETS)	Trademark "Ovcon 35" — satisfactory. The other pertinent DMETS comments were incorporated in the review of the labeling section	20-NOV-2002	Ms. A. R. Mahmud
EA	Categorical exclusion granted		Dr. A. K. Mitra
Microbiology	Satisfactory	18-OCT-2002	Dr. S.Langille



# The Chemistry Review for NDA 21-371

## The Executive Summary

### I. Recommendations

#### A. Recommendation and Conclusion on Approvability

The application is approvable pending resolution of all the deficiencies recorded in the Draft Deficiency letter.

#### B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

Warner Chilcott is to provide the lot numbers of the blister lots that do not contain the storage conditions within — post approval.

### II. Summary of Chemistry Assessments

#### A. Description of the Drug Product(s) and Drug Substance(s)

The drug product "Ovcon 35 —", is an immediate release chewable tablet formulation. The drug product is proposed to be available in only one dosage strength containing 0.4 mg norethindrone and 0.035 mg ethinyl estradiol per tablet. The tablets are blister packed into a blister card containing 28 tablets, 21 of that contain 0.4 mg norethindrone and 0.035 mg ethinyl estradiol. The remaining 7 tablets are placebos and contain only inactive ingredients. The appearance of the active and placebo tablets are distinctly different and the difference is adequate for proper identification of active vs. placebo tablets. Ovcon 35 chewable is indicated for the prevention of pregnancy in women. The women would start with the white tablets (21 tablets one each for 21 days) and followed by 7 green placebo tablets (once a day). The next pack of 28 tablets should be started after the last "reminder" tablet.

The drug is formulated in a tablet dosage form using — ethinyl estradiol and norethindrone. Both drug substances are monographed in the USP.

The drug substances are —

The details of the CMC of the norethindrone and ethinyl estradiol are documented in DMFs — and — respectively and those DMFs are adequate to support the NDA. The sponsor of the NDA has referenced adequate information on the container closure system for the drug substance.

All excipients are compendial except for the color and flavors. The sponsor was also requested to provide the specifications for various colors and flavor used in the formulation. The sponsor has adequately addressed all the deficiencies listed in the



Executive Summary Section

Chemistry Review #1, dated 10-JAN-2003 except for the Information Request in the Draft Deficiency Section of the review.

**B. Description of How the Drug Product is Intended to be Used**

The recommended dose for the drug product is 1 active tablet/per day for 21 days and 1 placebo tablet per day for 7 days. Only one strength of the tablet is proposed (0.4 mg norethindrone and 0.035 mg ethinyl estradiol) with 21 active and 7 placebo tablets in a blister card. The blister card containing 28 tablets is stored in a green rectangular compact. The recommended dose is one tablet per day and it is the maximum daily dose. The drug product is recommended to be chewed or swallowed.

The stability data from — production scale lots were used for determination of expiration date. The stability data indicate that the —

— A potency of — of label claim was determined in a lot of tablet at the — stability point for —. In the — lot, a — potency to — of label ( — of initial) was reported at the 18 months time point. Moreover, — lots failed the acceptance criteria for ethinyl estradiol potency under accelerated conditions ( — 40°C/75%RH). Therefore, the reviewer recommends a tentative shelf life of — based on Chemistry Review #1, until satisfactory real time data from — lots are available for extension of shelf life further. The sponsor's storage conditions "store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F)" is satisfactory to the reviewer.

**C. Basis for Approvability or Not-Approval Recommendation**

The sponsor has not adequately addressed the information requested in the Draft Deficiency Section of the review with respect to the shelf life of the drug product. —, the reviewer recommends a — 1 specification — the drug product. The Office of Compliance (OC) has provided an overall "Withhold" recommendation for the facilities. The NDA is approvable pending satisfactory response from the Office of Compliance, and satisfactory responses for the information requested in the Draft Deficiency section of the review.



### **III. Administrative**

#### **A. Reviewer's Signature**

#### **B. Endorsement Block**

A. K. Mitra, Ph.D/

M. J. Rhee, Ph.D/

K. Anderson/

#### **C. CC Block**

NDA 21-490/Division File

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Moo-Jhong Rhee  
1/29/03 03:47:52 PM  
CHEMIST  
I concur

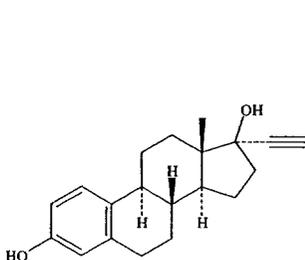
**NDA 21-490**

**Ovcon 35**

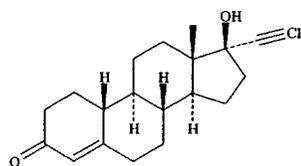
**Warner Chilcott**

**AMIT K. MITRA, Ph.D**

**REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS**



**Ethinyl estradiol**



**Norethindrone**



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# Chemistry Review Data Sheet

1. NDA 21-490
2. REVIEW #: 1
3. REVIEW DATE: 10-JAN-2003
4. REVIEWER: Amit K. Mitra, Ph.D

5. PREVIOUS DOCUMENTS:

Previous Documents

None

Document Date

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed

Original

Amendments

Document Date

29-MAR-2002

16-MAY-2002

16-AUG-2002

17-OCT-2002

09-DEC-2002

12-DEC-2002

19-DEC-2002

07-JAN-2003

7. NAME & ADDRESS OF APPLICANT:

Name:

Warner Chilcott

**CHEMISTRY REVIEW**

Executive Summary Section

Address: Rockaway 80 Corporate Center  
Representative: Mr. Alvin Howard  
Telephone: (973)443-3233

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Ovcon 35
- b) Non-Proprietary Name (USAN): Norethindrone and ethinyl estradiol chewable tablet.
- c) Code Name/# (ONDC only): N/A
- d) Chem. Type/Submission Priority (ONDC only):
  - Chem. Type: 3
  - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: NA

10. PHARMACOL. CATEGORY: Contraception

11. DOSAGE FORM: Chewable tablet

12. STRENGTH/POTENCY: 0.4 mg norethindrone and 0.035 mg ethinyl estradiol

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED:  Rx  OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM)

SPOTS product – Form Completed

Not a SPOTS product



## Executive Summary Section

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT: ; Norethindrone-19-Norpregn-4-en-20-yn-3-one, 17-hydroxy-, 17 ( $\alpha$ );  $C_{20}H_{26}O_2$ ; 298.42. Ethinyl estradiol-19-Norpregna-1,3,5(10)-trien-20-yne-3,17-diol, (17 $\alpha$ ),  $C_{20}H_{24}O_2$ , 296.40.

## 17. RELATED/SUPPORTING DOCUMENTS:

## A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE <sup>1</sup>	STATUS <sup>2</sup>	DATE REVIEW COMPLETED	COMMENTS
-	II			1	Adequate	09-DEC-2002	Reviewer: Dr. A. K. Mitra
-	II			3	Adequate	19-JUL-2002	Reviewer: Dr. N. Taikar
-	III			3	Adequate	5-MAY-2002	Reviewer: Dr. E. Chikhale
-	IV			1	Adequate	10-JAN-2003	Reviewer: Dr. A. K. Mitra
-	III			1	Adequate	14-DEC-2002	Reviewer: Dr. A. K. Mitra

<sup>1</sup> Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

<sup>2</sup> Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: None

**CHEMISTRY REVIEW**

## Executive Summary Section

## 18. STATUS:

<b>CONSULTS/ CMC RELATED REVIEWS</b>	<b>RECOMMENDATION</b>	<b>DATE</b>	<b>REVIEWER</b>
Biometrics	NA		
EES	Withhold	23-AUG- 2002	Mr. B. Hartman
Pharm/Tox	Pending		Dr. A. Jordan
Biopharm	NA		
LNC	NA		
Methods Validation	Will be initiated		
Division of Medical Errors and Technical Support (DMET)	Trademark "Ovcon 35 " satisfactory. The other pertinent OPDRA comments were incorporated in the review of the labeling section	20-NOV- 2002	Ms. A. R. Mahmud
EA	Categorical exclusion granted		Dr. A. K. Mitra
Microbiology	Satisfactory	18-OCT- 2002	Dr. S.Langille



# The Chemistry Review for NDA 21-371

## The Executive Summary

### I. Recommendations

#### A. Recommendation and Conclusion on Approvability

The application is approvable pending resolution of all the deficiencies recorded in the Draft Deficiency letter.

#### B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

None

### II. Summary of Chemistry Assessments

#### A. Description of the Drug Product(s) and Drug Substance(s)

The drug product "Ovcon 35", is an immediate release chewable tablet formulation. The drug product is proposed to be available in only one dosage strength containing 0.4 mg norethindrone and 0.035 mg ethinyl estradiol per tablet. The tablets are blister packed into a blister card containing 28 tablets, 21 of that contain 0.4 mg norethindrone and 0.035 mg ethinyl estradiol. The remaining 7 tablets are placebos and contain only inactive ingredients. The appearance of the active and placebo tablets are distinctly different and the difference is adequate for proper identification of active vs. placebo tablets. Ovcon 35 is indicated for the prevention of pregnancy in women. The women would start with the white tablets (21 tablets one each for 21 days) and followed by 7 green placebo tablets (once a day). The next pack of 28 tablets should be started after the last "reminder" tablet.

The drug is formulated in a tablet dosage form using — ethinyl estradiol and norethindrone. Both drug substances are monographed in the USP. The drug substances are —

Therefore, the sponsor is not being asked to adopt particle size specifications for the drug substances. The details of the CMC of the norethindrone and ethinyl estradiol are documented in DMFs — respectively and those DMFs are adequate to support the NDA. The sponsor of the NDA is being asked to provide the container/closure used for storage of the drug substances ethinyl estradiol and norethindrone.

All excipients are compendial except for the color and flavors. The sponsor was also requested to provide the specifications for various colors and flavor used in the formulation.

## Executive Summary Section

The sponsor has adopted \_\_\_\_\_ as an in-process control \_\_\_\_\_  
\_\_\_\_\_ The sponsor has not adopted critical in-process controls such as \_\_\_\_\_  
\_\_\_\_\_ ) to establish uniformity throughout the lot. The drug  
product is a chewable tablet; therefore, \_\_\_\_\_ are important  
parameters. Therefore, in-process control or regulatory specifications of those  
attributes are being sought. Several deficiencies were recorded based on Chemistry  
Review #1, and the sponsor needs to respond to those deficiencies. Clinical studies  
were not conducted on the proposed formulation. Instead, the sponsor chose to  
conduct a bioequivalence study comparing the current formulation with the proposed  
formulation, a safety study to assess the potential of irritation from the chewable  
tablet. Those information were reviewed by the OCPB and Clinical reviewers. See  
OCPB and Clinical reviews for details.

**B. Description of How the Drug Product is Intended to be Used**

The recommended dose for the drug product is 1 active tablet/per day for 21 days  
and 1 placebo tablet per day for 7 days. Only one strength of the tablet is proposed  
(0.4 mg norethindrone and 0.035 mg ethinyl estradiol) with 21 active and 7 placebo  
tablets in a blister card. The blister card containing 28 tablets is stored in a green  
rectangular compact. The recommended dose is one tablet per day and it is the  
maximum daily dose. The drug product is recommended to be chewed or  
swallowed.

The stability data from \_\_\_\_\_ production scale lots were used for determination of  
expiration date. The stability data indicate that the drug product \_\_\_\_\_  
ethinyl estradiol during storage at 25°C/60%RH. A potency of \_\_\_\_\_ of label claim  
was determined in \_\_\_\_\_ of tablet at the \_\_\_\_\_ stability point for \_\_\_\_\_. In the  
\_\_\_\_\_ lot, \_\_\_\_\_ ethinyl estradiol potency to \_\_\_\_\_ of initial) was  
reported at the \_\_\_\_\_ time point. The extrapolated shelf life are calculated by  
the reviewer are approximately \_\_\_\_\_, for the \_\_\_\_\_ lots. Moreover, both  
lots failed the acceptance criteria for ethinyl estradiol under accelerated conditions  
(40°C/75%RH). Therefore, a tentative shelf life of \_\_\_\_\_ can be granted for the  
drug product based on the real time data. The sponsor's storage conditions "store at  
25°C (77°F); excursions permitted to 15-30°C (59-86°F)" is satisfactory to the  
reviewer.

**C. Basis for Approvability or Not-Approval Recommendation**

The NDA is approvable pending satisfactory response to the Information Request  
presented at the end of the review. The major deficiencies with the application are  
lack of stability data to support the \_\_\_\_\_ shelf life requested by the sponsor. A  
maximum of \_\_\_\_\_ of shelf life can be granted based on the stability data  
provided. The acceptance criteria for the ethinyl estradiol and norethindrone related  
substances were arbitrarily set. The sponsor needs to revise the acceptance criteria  
for the related substances based on the safety and manufacturing capability.



### **III. Administrative**

#### **A. Reviewer's Signature**

#### **B. Endorsement Block**

A. K. Mitra, Ph.D./

M. J. Rhee, Ph.D./

K. Anderson/

#### **C. CC Block**

NDA 21-490/Division File

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/s/

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Amit K. Mitra  
1/14/03 08:01:19 AM  
CHEMIST

Moo-Jhong Rhee  
1/14/03 10:23:17 AM  
CHEMIST  
I concur

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