

Application Number 21-090

CHEMISTRY REVIEW(S)

MEMORANDUM

To: NDA 21-090 (Cyclessa Tablets)
From: Ali Al-Hakim, Review Chemist, HFD-180
Subject: Organon Inc. request to withdraw New Jersey Site (quality control testing) from the NDA
Date: November 16, 2000

The applicant submitted an amendment dated November 07, 2000 requesting that the following site, which involves in quality control testing for the drug product, should be withdrawn from the NDA:

Organon Inc.
375 Mount Pleasant Avenue
West Orange
New Jersey 07052

Therefore, the above site will be deleted from the Establishment Evaluation System (EES).

Ali Al-Hakim, Ph.D.

Review Chemist, HFD-180

**APPEARS THIS WAY
ON ORIGINAL**

cc:
Orig. NDA 21-090
HFD-580/Division File
HFD-180/AAI-Hakim
HFD-580/CSO/Mercier/MRhee
R/D Init by: MJ Rhee
AA. 11/16/2000 C:\MSWord\NDA\21090.Mem

Summary of Chemistry Review of NDA 21-090

A. Drug Substance:

The drug substance, desogestrel (DSG), is a synthetic progestin compound and has been used in other products. It is _____ in compliance to cGMP.

Another drug substance, ethinyl estradiol (EE) is also a synthetic estrogen and has been widely used in oral contraceptives and is known to be much more potent estrogen than estradiol. It is _____ of which facility is in compliance to cGMP

The _____ of desogestrel and ethinyl estradiol, respectively, and are deemed adequate to support this NDA.

B. Drug Product:

This oral contraceptive presents triphasic regimen containing 7 light yellow tablets (100µg/25µg of DSG/EE), 7 orange tablets (125µg/25µg of DSG/EE), 7 red tablets (150µg/25µg of DSG/EE), and 7 green placebo tablets.

They are manufactured, packaged, and tested by Organon N.V. in Netherland and also tested by Organon, Inc. in NJ. Organon, Inc., in PA carries out the final packaging and distribution. All these facilities are in compliance to cGMP.

The quality of the tablets are controlled by tests; appearance, identification, diameter, thickness, hardness, weight, disintegration, loss on drying, moisture content, dissolution (interim specifications, Q= _____ @15 min at release and Q= _____ @30min for shelf life), assay, content uniformity, related steroids, and microbial limits. All the respective specifications are deemed appropriate except for the dissolution specifications. The firm made a commitment to settle a final dissolution specification after they collect dissolution data from their first three commercial production batches during their stability studies.

The tablets are packaged into a blister card which is made of PVC film and aluminum foil. The blister pack is housed in a polypropylene compact and packaged further in a laminated aluminum sachet. They are considered to be adequate for protecting the product during the shelf life.

Based on real time data of the product up to 36 months, 36-month of expiry date is granted.

The tradename, Cyclessa, has been accepted by OPDRA, and adequate chemistry information is presented in the labeling and labels of primary as well as secondary packaging.

C. Conclusion and Recommendation:

As recommended by the primary reviewer, this NDA may be approved from chemistry, manufacturing, and controls point of view.

S 3/6/00

 Moo-Jhong Rhee, Ph.D.
 Chemistry Team Leader
 For the Division of reproductive and Urologic Drug Products
 DNDC II, Office of New Drug Chemistry

/s/

Ali Al-Hakim
11/16/00 02:12:27 PM
CHEMIST

Moo-Jhong Rhee
11/17/00 04:48:27 PM
CHEMIST

APPEARS THIS WAY
ON ORIGINAL

DIVISION OF REPRODUCTIVE AND UROLOGICAL DRUG PRODUCTS
HFD-580

Review of Chemistry, Manufacturing, and Controls

NDA #: 21-090

CHEM.REVIEW #: 2

REVIEW DATE: 03/03/2000

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Amendment	01/24/2000	01/27/2000	01/27/2000
Amendment	02/16/2000	02/17/2000	02/17/2000
Amendment	03/02/2000	03/02/2000(Fax)	03/03/2000

NAME & ADDRESS OF APPLICANT:

ORANON INC.
375 Mt. Pleasant Avenue
West Orange, NJ 07052

DRUG PRODUCT NAME

Proprietary: Cyclessa™

Nonproprietary/USAN: Desogestrel and Ethinyl Estradiol

Code Name/#: CTR 77

Chem.Type/Ther.Class: 4/S

ANDA Suitability Petition/DESI/Patent Status: Not Applicable

PHARMACOL.CATEGORY/INDICATION:

Prevention of pregnancy in women who elect to use oral contraceptives as a method of contraception.

DOSAGE FORM:

Tablets

STRENGTHS:

3 different strengths:

100 µg desogestrel /25 µg ethinyl estradiol

125 µg desogestrel /25 µg ethinyl estradiol

150 µg desogestrel /25 µg ethinyl estradiol

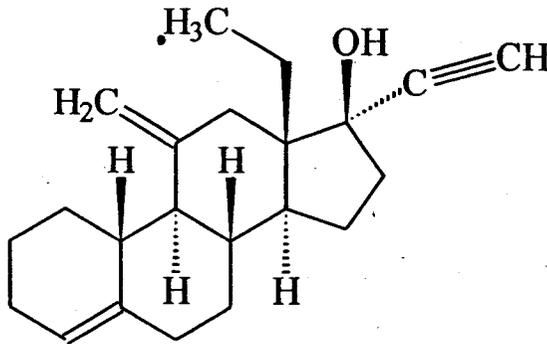
(In addition to placebo)

ROUTE OF ADMINISTRATION: Oral

DISPENSED: Rx OTC

**CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA,
MOL.WT:**

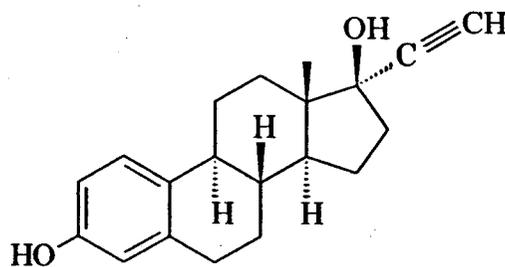
13-ethyl-11-methylene-18,19-dinor-17 α -pregn-4-en-20-yn-17-ol (desogestrel)



Molecular Formula: C₂₂H₃₀O

Molecular weight: 310.48

19-nor-17 α -pregna-1,3,5 (10)-trien-20-yne-3,17-diol (ethinyl estradiol)



Molecular Formula: C₂₀H₂₄O₂

Molecular Weight: 296.4

SUPPORTING DOCUMENTS:

The following is the list of the Drug Master Files related to the application.

DMF / Type	Subject/Item Reviewed	Holder	Status	Review Date and Reviewer Name	Letter Date
			Adequate	03/02/1999 Mujahid L. Shaikh	N/A
			Adequate	11/10/1998 David T. Lin	N/A
			Adequate	7/22/1997 David T. Lin and	N/A
			Adequate	09/30/1999 Ali Al-Hakim	N/A
			Adequate	01/05/2000 Ali Al-Hakim	N/A
			Adequate	02/24/1999 Ray Frankewich	N/A
			Adequate	10/22/1999 Jila Boal	N/A

RELATED DOCUMENTS:

NDA 20-713

CONSULTS:

Trade name to OPDRA

Dissolution specification to Biopharmaceutics

**APPEARS THIS WAY
ON ORIGINAL**

**THIS SECTION
WAS
DETERMINED
NOT
TO BE
RELEASABLE**

44 pages

G. ESTABLISHMENT INSPECTION

Establishment Evaluation Requests (EER) of all the sites involved in manufacturing, packaging and testing of the drug product have been submitted. EER report dated 10/04/1999 indicated that all sites were inspected and found acceptable. Copy of the report is provided below

04-OCT-1999

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Page 1 of 2

Application: NDA 21090/000
Stamp: 07-MAY-1999 Regulatory Due: 07-MAR-2000
Applicant: ORGANON INC
375 MT PLEASANT AVE
WEST ORANGE, NJ 07052

Priority: IS
Action Goal: _____
Brand Name: _____

Orig Code: 580
District Code: 07-LAN-2000

Established Name:
Generic Name: DESOGETRELETHINYL ESTRADIOL
100UG DSG/2
Dosage Form: TAB (TABLET)
Strength: 100 UG DSG/25 UG EE

FDA Contacts: J. MERCIER (HFD-580) 301-827-4260 , Project Manager
D. LIN (HFD-580) 301-827-4230 , Review Chemist
M. RHEE (HFD-580) 301-827-4237 , Team Leader

Overall Recommendation:

ACCEPTABLE on 08-JUL-1999 by M. EGAS (HFD-322) 301-594-0095

Establishment: _____ DMF No: _____
AADA No: _____

fine

Profile: CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 06-JUL-1999
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Responsibilities: _____

Establishment: _____ DMF No: _____
AADA No: _____

fine

Profile: CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 06-JUL-1999
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Responsibilities: _____

Establishment: 2211109
ORGANON INC SUB AKZONA INC
375 MT PLEASANT AVE
WEST ORANGE, NJ 07052

DMF No: _____
AADA No: _____

Not good 10/3/00

Profile: CTL OAI Status: NONE
Last Milestone: OC RECOMMENDATION

Responsibilities: FINISHED DOSAGE RELEASE
TESTER

04-OCT-1999

Page 2 of 3

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

**FINISHED DOSAGE STABILITY
TESTER**

Milestone Date: 06-JUL-1999
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Establishment: 2529406
ORGANON INC SUB AKZONA INC
6350 HEDGEWOOD DR
ALLENTOWN, PA 18103

DMF No:
AADA No:

fine

Profile: TCM OAI Status: NONE Responsibilities: **FINISHED DOSAGE PACKAGER**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: 06-JUL-1999
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Establishment: 9610342
ORGANON NV
KLOOSTERSTRAAT 6, 5340-BH
OSS, NL

DMF No:
AADA No:

fine

Profile: TCM OAI Status: NONE Responsibilities: **FINISHED DOSAGE
MANUFACTURER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE
TESTER
FINISHED DOSAGE STABILITY
TESTER**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: 08-JUL-1999
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

**APPEARS THIS WAY
ON ORIGINAL**

**Number of Pages
Redacted** 2



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Commercial Information