

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Application Number** 21-090

**APPROVAL LETTER**

NDA 21-090



NDA 21-090

Organon, Inc.  
Attention: Albert Mayo  
Executive Director, Regulatory Affairs  
375 Mt. Pleasant Avenue  
West Orange, NJ 07052

Dear Mr. Mayo:

Please refer to your new drug application (NDA) dated May 7, 1999, received May 7, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cyclessa™ (desogestrel/ethinyl estradiol) Tablets.

We acknowledge receipt of your submissions dated May 14, June 16, July 1, 2 and 23, August 4 and 24, September 2, October 28, December 6, 15, and 27, 1999; January 6, 7, 20, 24 and 31, February 7, 16 and 25, March 1 and 2, October 20, November 1, and December 19 and 20, 2000. Your submission of October 20, 2000 constituted a complete response to our March 7, 2000 action letter.

This new drug application provides for the use of Cyclessa™ (desogestrel/ethinyl estradiol) Tablets for the prevention of pregnancy in women who elect to use this product as a method of contraception.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert) and submitted draft labeling (immediate container and carton labels submitted). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved NDA 21-090." Approval of this submission by FDA is not required before the labeling is used.

As discussed, on March 2, 2000, and subsequently agreed by you via March 2, 2000, facsimile, the Division requests that you implement the dissolution specifications Q ~~15~~ after 15 minutes for the release specification and the specification of Q ~~30~~ after 30 minutes for the stability specification, with the Phase 4 commitment to perform dissolution testing at 15 and 30 minutes on the first 3 commercial batches of each strength of Cyclessa™ (desogestrel/ethinyl estradiol) product at 40°C/75% RH up to 6 months (at 3, 6 months) and 25°C/60% RH up to 12 months (at 3, 6, 9, and 12 months). Data are to be submitted to the Division when 12-month dissolution data are available, at which time an evaluation of the specification will be made.

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). We are waiving the pediatric study requirement for this action on this application.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

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

Sincerely,

Susan Allen, M.D.  
Director  
Division of Reproductive and Urologic Drug Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Enclosure

/s/

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Susan Allen

12/20/00 05:06:42 PM

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Application Number** 21-090

**APPROVABLE LETTER**



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

NDA 21-090

Food and Drug Administration  
Rockville MD 20857

Organon, Inc.  
Attention: Thomas Putik, Ph.D.  
Associate Director, Regulatory Affairs  
375 Mt. Pleasant Avenue  
West Orange, NJ 07052

MAR 7 2000

Dear Dr. Putik:

Please refer to your new drug application (NDA) dated May 7, 1999, received May 7, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cyclessa™ (desogestrel/ethinyl estradiol) Tablets.

We acknowledge receipt of your submissions dated May 14, June 16, July 1, 2 and 23, August 4 and 24, September 2, October 28, December 6, 15 and 27, 1999; January 6, 7, 20, 24 and 31, February 7, 16 and 25, March 1 and 2, 2000.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to submit draft labeling consistent with the enclosed labeling. This labeling includes the following areas for your consideration:

- **WARNINGS section**

Thromboembolism Disorders and Other Vascular Problems subsection

- a. Thromboembolism: Text describing the risk of venous-thromboembolism with third generation oral contraceptives.
- b. Myocardial Infarction: Text describing \_\_\_\_\_

- **PRECAUTIONS section**

**8. Drug Interaction section:** Text describing potential drug interactions and clarifying that no drug-drug interaction studies were performed with Cyclessa™ (desogestrel/ethinyl estradiol).

If additional information relating to the safety or effectiveness of this drug becomes available, additional revision of the labeling may be required.

As discussed, on March 2, 2000, and subsequently agreed by you via March 2, 2000, facsimile, the Division requests that you implement the dissolution specifications Q — after 15 minutes for the release specification and the specification of Q — after 30 minutes for the stability specification, with the Phase 4 commitment to perform dissolution testing at 15 and 30 minutes on the first 3 commercial batches of each strength of Cyclessa™ (desogestrel/ethinyl estradiol) product at 40°C/75% RH up to 6 months (at 3,6 months) and 25°C/60% RH up to 12 months (at 3, 6, 9, and 12 months). Data are to be submitted to the Division when 12-month dissolution data are available, at which time an evaluation of the specification will be made.

Under 21 CFR 314.50(d)(5)(vi)(b), we request that you update your NDA upon resubmission by submitting all safety information you have regarding your new drug. Please provide updated information as listed below. The update should cover all studies and uses of the drug including: (1) those involving indications not being sought in the present submission, (2) other dosage forms, and (3) other dose levels, etc.

1. Retabulation of all safety data including results of trials that were still ongoing at the time of NDA submission. The tabulation can take the same form as in your initial submission. Tables comparing adverse reactions at the time the NDA was submitted versus now will certainly facilitate review.
2. Retabulation of drop-outs with new drop-outs identified. Discuss, if appropriate.
3. Details of any significant changes or findings.
4. Summary of worldwide experience on the safety of this drug.
5. Case report forms for each patient who died during a clinical study or who did not complete a study because of an adverse event.
6. English translations of any approved foreign labeling not previously submitted.
7. Information suggesting a substantial difference in the rate of occurrence of common, but less serious, adverse events.

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

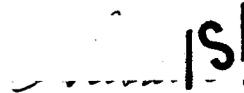
NDA 21-090

Page 3

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, call Jennifer Mercier, B.S., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

A handwritten signature in black ink, appearing to be "S. Allen", written over a horizontal line.

Susan Allen, M.D., M.P.H.

Acting Director

Division of Reproductive and Urologic Drug Products

Office of Drug Evaluation III

Center for Drug Evaluation and Research

Enclosure

**APPEARS THIS WAY  
ON ORIGINAL**