CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-544

PHARMACOLOGY REVIEW

PHARMACOLOGY/TOXICOLOGY COVER SHEET

NDA number: 21-544
Review number: 1
Sequence number/date/type of submission: Original NDA review
Information to sponsor: Yes ( ) No (X)
Sponsor and/or agent: Barr Research, Inc
Manufacturer for drug substance. [redacted]

Reviewer name: Alex Jordan
Division name: DRUDP
HFD #: 580
Review completion date: 1/7/03

Drug:

Trade name: Seasonale
Generic name (list alphabetically): ethinyl estradiol; levonorgestrel
Code name:
Chemical name:
CAS registry number:
Mole file number:
Molecular formula/molecular weight:
Structure:

Relevant INDs/NDAs/DMFs: NDA 18-668, 18-782, ANDA 75-866

Drug class: contraceptive

Indication: contraception

Clinical formulation: ethinyl estradiol, levonorgestrel, microcrystalline cellulose, hydroxypropyl methyl cellulose, lactose, magnesium stearate, polyethylene glycol, polysorbate 80, titanium dioxide.

Route of administration: oral

Proposed use: contraception for an extended duration of 91 days.

Disclaimer: Tabular and graphical information is from sponsor's submission unless stated otherwise.

Executive Summary

I. Recommendations

A. Recommendation on Approvability: Seasonale is approvable from the standpoint of Pharmacology.

B. Recommendation for Nonclinical Studies: none

C. Recommendations on Labeling: none

II. Summary of Nonclinical Findings

A. Brief Overview of Nonclinical Findings: Seasonale consists of levonorgestrel (0.15 mg) and ethinyl estradiol (0.03 mg) to be taken orally for 91 days (84 days on, 7 days off). Nordette-21 is an approved NDA (18-668) and Portia is an approved ANDA (75-866) with the same active ingredients and the same doses. The only difference is the length of time the active drug is taken prior to 7 days off drug. Many of the chronic toxicology studies to support the safety of levonorgestrel and ethinyl estradiol were done using daily dosing up to 2 years and are sufficient to support the safety of Seasonale. No new toxicology studies are necessary and none were submitted.

B. Pharmacologic Activity: contraceptive

C. Nonclinical Safety Issues Relevant to Clinical Use: none

III. Administrative

A. Reviewer signature: _____

B. Supervisor signature: Concurrence - _____

Non-Concurrence - _____
(see memo attached)

C. cc: list:

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/s/

Alexander W. Jordan
3/4/03 08:48:15 AM
PHARMACOLOGIST