OFFICE OF CLINICAL PHARMACOLOGY REVIEW MEMORANDUM

NDA Number	209405
Link to EDR	\\cdsesub1\evsprod\NDA209405
Submission Type	Resubmission
Review type	Clinical Pharmacology Review Memorandum
PDUFA Date	03/30/2020
Brand Name	A brand name has not been determined. The indicated name for the proposed product in the current submission is EV402.
Generic Name	Levonorgestrel/Ethinyl Estradiol
Dosage Form and Strength	Levonorgestrel/Ethinyl Estradiol tablets, 0.1 mg/0.02 mg
Route of Administration	Oral
Proposed Indication	Prevention for pregnancy
Applicant	Exeltis USA, Inc
Associated IND	IND (b) (4)
OCP Review Team	Jihong Shon, M.D., Ph.D. Lu Yanhui, Ph.D.

EXECUTIVE SUMMARY

EV402 consists of 28 (b) (4) tablets, 21 tablets containing 0.10 mg of levonorgestrel (LNG) and 0.02 mg of ethinyl estradiol (EE) and 7 inactive tablets. The Applicant is seeking approval via the 505(b)(2) pathway using Alesse® (LNG 0.10 mg / EE 0.02 mg, NDA 20-683 approved on April 1997) as the listed drug. The Applicant proposed to rely on the Agency's safety and efficacy findings of the listed drug. Since Alesse® is no longer marketed in the U.S., the Applicant used Lutera® (ANDA 76-625 by Mayne Pharma, Inc.), the current reference standard, as a reference product in their comparative bioavailability (bioequivalence) studies.

The Office of Clinical Pharmacology (OCP), Division of Cardiometabolic and Endocrine Pharmacology completed reviewing the clinical pharmacology information submitted for NDA 209405 (EV402) and concluded that the application was acceptable and recommended approval from the clinical pharmacology standpoint (OFFICE OF CLINICAL PHARMACOLOGY REVIEW for NDA 209405 dated February 24, 2020 in DARRTS). This decision was made mainly based on pharmacokinetic (PK) comparability of EV402 to Lutera®, the reference product, in a pivotal bioequivalence study (Study EXS-P3-236). In this review process, (b) (4) In addition, it is noted that EV402 was chewed and swallowed in all completed PK studies including the pivotal bioequivalence study. (b) (4) products, Allesse® and Lutera®. (b) (4)

(b) (4)

(b) (4) should be revised to "levonorgestrel and ethinyl estradiol tablets" and recommended the Dosage and Administration section be revised to include options for chewing and swallowing or swallowing whole (Information Request/Advice dated March 6, 2020).

The OCP concurs with the current decision and recommendation for the labeling product nomenclature based on the currently available information. The original OCP NDA review (dated February 24, 2020) still supports approval of the proposed product provided that an agreement on the language in the package insert is reached between the Applicant and the Agency.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

JIHONG SHON
03/28/2020 01:51:14 PM

YANHUI LU
03/28/2020 02:08:45 PM