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APPLICATION NUMBER:

022501Orig1s000

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

OFFICE OF CLINICAL PHARMACOLOGY REVIEW

NDA: 22-501	Submission Date(s): 04/20/2010 (Resubmission) 03/26/2009; 12/23/2009 (Original)
Brand Name	Lo Loestrin Fe®
Generic Name	WC3016 (norethindrone acetate, NA 1 mg and ethinyl estradiol, EE 10 µg tablets, ethinyl estradiol 10 µg tablets and ferrous fumarate tablets)
Reviewer	Sandhya Apparaju, Ph.D.
Team Leader	Myong Jin Kim, Pharm.D.
OCP Division	Division of Clinical Pharmacology III (DCP3)
OND Division	Division of Reproductive and Urologic products
Sponsor	Warner Chilcott
Submission Type	NDA Resubmission
Formulation; Strength(s)	Oral tablets; 1 mg /10 µg NA/EE tablets and 10 µg EE alone tablets
Indication	Prevention of pregnancy

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1 Executive Summary

The original NDA for WC3016 tablets for prevention of pregnancy (NDA 22-501) was submitted on March 26, 2009. The subject of the NDA is a low dose oral contraceptive consisting of 10 µg of EE and 1 mg of NA (WC3016 1/10 tablets) taken once daily for 24 days, followed by two daily doses of 10 µg of EE (WC3016 EE10 tablets) and ferrous fumarate tablets (75 mg) for 2 days during a 28-day regimen. Three Clinical Pharmacology studies and one phase 3 safety and efficacy trial were conducted in support of this NDA.

An optional intra-divisional Clinical Pharmacology briefing was held for this NDA on November 16, 2009. NDA was found acceptable from a Clinical Pharmacology perspective provided an agreement could be reached with the sponsor pertaining to labeling language [refer to Clinical Pharmacology review in DARRTS signed on 11/27/2009].

During the first review cycle the NDA received a complete response action (letter dated January 26, 2010) due to pending CMC issues (deficiencies identified during inspections of the drug substance manufacturing facility and a control testing laboratory). Satisfactory resolution of these deficiencies was required before the application could be approved. Labeling was not finalized at the time of complete response action.

With this NDA resubmission (submitted 04/20/2010), sponsor intends to address the unresolved deficiencies noted in the first cycle. In addition, draft labeling that incorporates edits recommended by the Division during the first review cycle has also been included for review.

Labeling review: On December 23, 2009 during the first NDA review cycle, sponsor submitted revised draft labeling and additional information in response to labeling comments sent by the Division via e-mail on December 15, 2009. The sponsor had at the time accepted most of the recommended labeling changes including Clinical Pharmacology changes to Drug Interactions (7.0), Use in Specific Populations (8.0), and Clinical Pharmacology (12.0). In addition, the sponsor provided further justification to support a labeling statement pertaining to metabolic conversion of NA to EE within this section.

Following review of the sponsor's December 23, 2009 response to labeling edits, additional labeling comments were sent to the sponsor with the second round of labeling edits in January 2010. In the NDA resubmission, sponsor has adequately addressed pending labeling comments. In addition, Minor revisions to the Clinical Pharmacology sections of the proposed draft labeling were recommended during the review of the resubmitted labeling and were accepted by the sponsor. There are no pending Clinical Pharmacology issues with regard to the proposed labeling.

1.1 Recommendation

NDA 22-501 is acceptable from a Clinical Pharmacology perspective.

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/s/

SANDHYA K APPARAJU
10/07/2010

MYONG JIN KIM
10/12/2010

OFFICE OF CLINICAL PHARMACOLOGY REVIEW

NDA: 22-501	Submission Date: 03/26/2009
Brand Name	(b) (4)
Generic Name	Norethindrone acetate (NA) & Ethinyl Estradiol (EE) tablets, and Ferrous Fumarate tablets
Reviewer	Sandhya Apparaju, Ph.D.
Team Leader	Myong Jin Kim, Pharm.D.
OCP Division	Division of Clinical Pharmacology 3
OND Division	Division of Reproductive and Urologic Products
Sponsor	Warner Chilcott, LLC
Relevant IND(s)	73,510
Submission Type; Code	Original NDA
Formulation; Strength(s)	Oral immediate release tablets; 1 mg NA + 10 µg EE, 10 µg EE, Ferrous Fumarate 75 mg
Indication	Prevention of Pregnancy

An optional intra-division level OCP briefing was held for NDA 22-501 on Monday, 16 November, 2009 from 1- 2 PM in WO Bldg 51 Conference Room 3200. Attendees included Dr's. Hae Young Ahn, Myong Jin Kim, Ron Orleans, Darrell Abernathy, Hyunjin Kim, LaiMing Lee, Jee Eun Lee, Chongwoo Yu and Sandhya Apparaju.

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