CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204654Orig1s000

CHEMISTRY REVIEW(S)

Initial Quality Assessment
Branch IV
Division of New Drug Quality Assessment II

OND Division:	Division of Reproductive and Urologic Products
NDA:	204654
Applicant:	Warner Chilcott
Stamp Date:	27-Sep-2012
PDUFA Date:	26-Jul-2013
Trademark:	None provided
Established Name:	Norethindrone acetate/Ethinyl estradiol/Ferrous Fumarate
Dosage Form:	Tablet
Route of Administration:	Oral
Indication:	Prevention of pregnancy
CMC Lead:	Donna F. Christner, Ph.D.

	YES	NO
ONDQA Fileability:	X	☐
Comments for 74-Day Letter	☐	X

Summary and Critical Issues:

A. Summary

The applicant has provided the following information on the drug product:

> (b) (4) is a 28-tablet oral contraceptive regimen consisting of the following (see Figure 1):
>
> - Twenty-four (b) (4) chewable tablets [norethindrone acetate (NA), 1.0 mg and ethinyl estradiol (EE), 10 µg per tablet],
> - Two WC3016 (b) (4) tablets (EE, 10 µg per tablet),
> - Two ferrous fumarate tablets, containing 75 mg of ferrous fumarate per tablet.
>
> The formulation for (b) (4) chewable tablets is based on a previously approved formulation, WC3016 (b) (4) in Lo Loestrin (NDA 22-501). The main difference between the two target product profiles was that (b) (4) tablets are intended to be chewable. The WC3016-(b) (4) tablets and the ferrous fumarate tablets are previously approved products in NDA 22-501.

The (b) (4) 1/10 chewable tablet formulation was based on the approved formulation for Lo Loestrin Fe 1 mg NA/10 mcg EE tablets (referred to in the NDA as **WC3016 1/10 tablets** or by its formulation **WC3016 (b) (4) tablets**); a flavor and (b) (4) were added to (b) (4) 1/10 chewable tablets. The WC3016 EE10 tablets are identical to Lo Loestrin Fe 10 mcg EE tablets. Lo Loestrin Fe received approval as an oral contraceptive on October 21, 2010 under NDA 022501.

The drug product is provided in a standard (b) (4) blister pack. The chewable combination tablets are contained in the first 24 wells of the blister pack, while the nonchewable ethinyl estradiol

tablets are contained in blister wells 25-26 and the inert, nonchewable ferrous fumarte tablets are in blister wells 27-28. The blister packaging is the same as used in the approved product under NDA 22501

B. Critical issues for review

All specifications are set based on the approved NDA 22501. Since these are immediate release tablets and the specifications are based on an approved NDA, consultation to ONDQA BioPharm may not be necessary. It is the primary reviewer's decision on whether a BioPharm review is warranted.

The combination tablet has only 6 months of stability data submitted in support of a 12 month expiration dating period. Although 6 months of data are less than what is currently recommended by ONDQA, based on the fact that the formulation is almost identical to an approved formulation except for the addition of sweetener and flavor,the amount of information is deemed adequate to allow review and to determine if 12 months of expiration dating period are appropriate.

C. Comments for 74-Day Letter

No comments to be conveyed at this time.

D. Recommendation:

This NDA is fileable from a CMC perspective. Gene Holbert, Ph.D. is assigned as the primary reviewer.

REGULATORY BRIEFING RECOMMENDATION: Branch level.

_____
Donna F. Christner, Ph.D.

Established/Proper Name:

Norethindrone acetate and ethinyl estradiol chewable tablets, ethinyl estradiol tablets and ferrous fumarate tablets

NDA Number: 204654 **Type: 5**

Applicant: Warner Chilcott

Letter Date: 27-Sep-2012

Stamp Date: 27-Sep-2012

The following parameters are necessary in order to initiate a full review, i.e., complete enough to review but may have deficiencies. On **initial** overview of the NDA application for filing:

A. GENERAL				
	Parameter	**Yes**	**No**	**Comment**
1.	Is the CMC section organized adequately?	X		
2.	Is the CMC section indexed and paginated (including all PDF files) adequately?	X		
3.	Are all the pages in the CMC section legible?	X		
4.	Has all information requested during the IND phase, and at the pre-NDA meetings been included?	X		

B. FACILITIES*				
	Parameter	**Yes**	**No**	**Comment**
5.	Is a single, comprehensive list of all involved facilities available in one location in the application?	X		
6.	For a naturally-derived API only, are the facilities responsible for critical intermediate or crude API manufacturing, or performing upstream steps, specified in the application? If not, has a justification been provided for this omission? **This question is not applicable for synthesized API.**		X	N/A

7.	Are drug substance manufacturing sites identified on FDA Form 356h or associated continuation sheet? For each site, does the application list: • Name of facility, • Full address of facility including street, city, state, country • FEI number for facility (if previously registered with FDA) • Full name and title, telephone, fax number and email for on-site contact person. • Is the manufacturing responsibility and function identified for each facility?, and • DMF number (if applicable)	X		
8.	Are drug product manufacturing sites are identified on FDA Form 356h or associated continuation sheet. For each site, does the application list: • Name of facility, • Full address of facility including street, city, state, country • FEI number for facility (if previously registered with FDA) • Full name and title, telephone, fax number and email for on-site contact person. • Is the manufacturing responsibility and function identified for each facility?, and • DMF number (if applicable)	X		

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