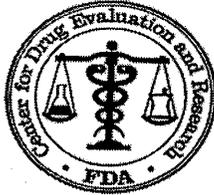


**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-871

PHARMACOLOGY REVIEW



DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

PHARMACOLOGY/TOXICOLOGY REVIEW AND EVALUATION

NDA NUMBER: 21-871
SERIAL NUMBER: 000
DATE RECEIVED BY CENTER: April 18, 2005
DRUG NAME: Loestrin® 24 (norethindrone acetate/ethinyl
estradiol) Tablets
INDICATION: Prevention of Pregnancy
SPONSOR: Warner Chilcott
DOCUMENTS REVIEWED: Volume 1.1
REVIEW DIVISION: Division of Reproductive and Urologic Products
PHARM/TOX SUPERVISOR: Lynnda Reid, Ph.D.
DIVISION DIRECTOR: Daniel Shames, M.D.
PROJECT MANAGER: Nenita Christomo

Date of review submission to Division File System (DFS): January 12, 2006

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EXECUTIVE SUMMARY

I. Recommendations

- A. Recommendation on approvability: From a Pharmacology/Toxicology viewpoint, NDA 21-871 is recommended for Approval.
- B. Recommendation for nonclinical studies: none
- C. Recommendations on labeling: Labeling for Carcinogenesis, Mutagenesis, Impairment of Fertility; Pregnancy and Nursing Mothers will be identical to the label for Loestrin® Fe 1/20 Tablets.

II. Summary of nonclinical findings

- A. Brief overview of nonclinical findings: There were no new nonclinical studies submitted in support of this application. Norethindrone acetate and ethinyl estradiol are well known chemical entities and there are no novel inactive ingredients.
- A. Pharmacologic activity: Ethinyl estradiol and norethindrone acetate are synthetic hormones which act as contraceptives by suppressing gonadotropin secretion. The primary effect of this action is inhibition of ovulation primarily mediated by the progestin component of the combination. The concomitant administration of the estrogen allows regular withdrawal bleeding and less breakthrough bleeding.
- B. Nonclinical safety issues relevant to clinical use: none

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2.6 PHARMACOLOGY/TOXICOLOGY REVIEW**2.6.1 INTRODUCTION AND DRUG HISTORY****NDA number:** 21-871**Review number:** 1**Sequence number/date/type of submission:** N000 dated April 15, 2005**Information to sponsor:** Yes () No (x)**Sponsor and/or agent:** Warner Chilcott, Rockaway, NJ**Manufacturer for drug substance:** _____**Reviewer name:** Lynnda Reid, Ph.D.**Division name:** Reproductive and Urologic Drug Products**HFD #:** 580**Review completion date:** January 12, 2006**Drug:**

Trade name: Loestrin® 24

Generic name: norethindrone acetate/ethinyl estradiol

Relevant INDs/NDAs/DMFs: NDA 17-354**Drug class:** synthetic hormones progestin and estrogen**Indication(s):** prevention of pregnancy**Clinical formulation:**

<u>Component</u>	<u>Grade</u>	<u>Amount (mg) per Tablet</u>
Norethindrone Acetate	USP	1.0
Ethinyl Estradiol	USP	0.02
Acacia _____	NF	_____
Lactose _____	NF	_____
Magnesium Stearate	NF	_____
Starch _____	NF	_____
Confectioner Sugar's	USP	_____
Talc _____	USP	_____

Route of administration: oral

Proposed use: Loestrin® 24 provides a continuous dosing regimen consisting of treatment cycles of Loestrin 1/20 tablets for 24 consecutive days followed by 4 days on placebo tablets containing 75-mg ferrous fumarate.

Drug History: Loestrin® 24 Tablets are the same tablets marketed as Loestrin Fe 1/20. Loestrin-24 differs from Loestrin Fe 1/20 only in the number of days on active pills, 24 days for Loestrin-24 and 21 days for Loestrin Fe 1/20, followed by 4 and 7 days of ferrous fumarate tablets, respectively.

Studies reviewed within this submission: None.

OVERALL CONCLUSIONS AND RECOMMENDATIONS

Conclusions: From a Pharmacology/Toxicology perspective, we recommend approval.

Unresolved toxicology issues: None

Recommendations: None

Suggested labeling: Labeling for Carcinogenesis, Mutagenesis, Impairment of Fertility; Pregnancy and Nursing Mothers will be identical to the label for Loestrin Fe 1/20.

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/s/

Lynnda Reid
1/12/2006 03:05:31 PM
PHARMACOLOGIST

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