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APPLICATION NUMBER: 21-065

PHARMACOLOGY REVIEW(S)

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## REVIEW AND EVALUATION OF PHARMACOLOGY/TOXICOLOGY DATA

KEY WORDS: menopause, HRT

Reviewer Name: Alex Jordan

Division Name: DRUDP

HFD= 580

Review Completion Date: 8/10/99

Review number: 1

IND/NDA number: 21-065

Serial number/date/type of submission: 12/16/98; Original NDA

Information to sponsor: Yes ( ) No (X)

Sponsor (or agent): Parke-Davis

Manufacturer for drug substance: Duramed, Cincinnati, Ohio

### Drug:

Code Name:

Generic Name: norethindrone acetate and ethinyl estradiol

Trade Name: FemHRT

Chemical Name:

CAS Registry Number: NA 51-98-9; EE 57-63-6

Molecular Formula/ Molecular Weight:

Structure:

Relevant INDs/NDAs/DMFs: IND [redacted]

Drug Class: contraceptive steroids

Indication: Treatment of moderate to severe vasomotor symptoms associated with menopause, treatment [redacted] and prevention of osteoporosis.

Clinical formulation: [redacted] 1.0 mg norethindrone acetate, [redacted] 5 or [redacted] ug ethinyl estradiol, calcium stearate, lactose, microcrystalline cellulose, and starch.

Route of administration: oral

Proposed clinical protocol or Use: see indication

### OVERALL SUMMARY AND EVALUATION:

Introduction: FemHRT consists of [redacted] 1.0 mg NA and 5 ug EE and [redacted] There are at least two approved oral contraceptives with NA and EE, both with higher doses. Loestrin has a dosage strength of 1.5 mg NA and 30 ug EE and Norlestrin has a dosage strength of 2.5 mg NA and 50 ug of EE. The sponsor was told that no preclinical studies were needed and none were submitted.

Safety Evaluation: There are no preclinical safety concerns.

Clinical Relevance of Safety Issues:

Other Clinically Relevant Issues:

Conclusions: No safety concerns from pharmacology standpoint.

Communication Review:

- Labeling Review (NDA): Label is satisfactory
- Investigator's Brochure/Informed consent review (IND):

RECOMMENDATIONS: Pharmacology recommends approval of FemHRT for treatment of postmenopausal vasomotor symptoms; [redacted] and osteoporosis.

Reviewer signature/team leader signature [Concurrence/Non-concurrence]

RECEIVED SUBMITTER LETTER [redacted] REPORT CROSS-REFERENCE  
SECTION 3 FROM INDMT

[redacted signature box]

8/10/99

cc: list

NDA 21-065

HFD-580

AJordan

REVIEWER'S COMMENTS

APPEARS THIS WAY  
ON ORIGINAL

ALL COMPLIANCE INFORMATION BEING