CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 21040

PHARMACOLOGY REVIEW(S)

FEB 17 1999

REVIEW AND EVALUATION OF PHARMACOLOGY/TOXICOLOGY DATA:

KEY WORDS: estradiol; norgestimate
Reviewer Name: Alex Jordan
Division Name: DRUDP
HFD#580
Review Completion Date: 2/17/99

Review number: 1
IND/NDA number: NDA 21-040
Serial number/date/type of submission: November, 1998
Information to sponsor: Yes ( ) No (X)
Sponsor (or agent): R.W. Johnson Pharmaceutical Research Inst.
Manufacturer for drug substance: Same?

Drug:

Code Name:
Generic Name: estradiol and norgestimate
Trade Name: Ortho-Prefest
Chemical Name:
CAS Registry Number:
Molecular Formula/ Molecular Weight:
Structure:

Relevant INDs/NDAs/DMFs:

Drug Class:

Indication: Indication: Hormone replacement therapy (HRT)

Clinical formulation: The drug consists of two hormones, both taken as oral tablets. 17Bestradiol, taken alone for three days at a time and estradiol + norgestimate, taken together for three days at a time. These three day periods alternate. The doses are 1 mg estradiol and 90 ug norgestimate (NGM).

Route of administration: Oral

Proposed clinical protocol or Use:

Previous clinical experience: Approved drugs

Disclaimer -- use of sponsor's material

Introduction and drug history:

Studies reviewed within this submission: The sponsor has performed no pharmacology or toxicology studies with this combination and has referred to two approved NDA's, 19-653, Ortho-Cyclen (250 ug NGM and 35 ug ethinyl estradiol) and NDA 19-697, Ortho Tri-Cyclen (180 – 250 ug NGM + 35 ug EE). The use of estradiol instead of EE is not a problem. Estradiol is the natural estrogen and is also an approved drug. No differences in the toxicity of norgestimate + EE and norgestimate + 17B-estradiol would be expected.

OVERALL SUMMARY AND EVALUATION:

Introduction:
Safety Evaluation: The two drugs are approved and are used in doses equal to or less than the approved doses. There are no safety issues with the combination.

Clinical Relevance of Safety Issues:
Other Clinically Relevant Issues:
Conclusions:

Communication Review:
- Labeling Review (NDA): Labeling should be standard format
- Investigator's Brochure/Informed consent review (IND):

RECOMMENDATIONS:

Internal comments: Pharmacology recommends approval of NDA 21-040
External Recommendations (to sponsor):
Draft letter Content for Sponsor:
Future development or NDA issues:
Reviewer signature/team leader signature [Concurrence/Non-concurrence]

/S/ 2/17/99

cc: list HFD-580; AJordan/DMoore
Draft date (# of drafts):
Memorandum of Non-concurrence (if appropriate, attached):
Addendum to review (if necessary):
Appendix/attachments: