

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-166

PHARMACOLOGY REVIEW

REVIEW AND EVALUATION OF PHARMACOLOGY/TOXICOLOGY DATA

KEY WORDS: ERT, estrogen
Reviewer Name: Alex Jordan
Division Name: DRUDP
HFD#: 580
Review Completion Date: 4/25/00

Electronic file number:
IND/NDA number: 21-166
Serial number/date/type of submission: 00; 8/13/99; Original NDA
Information to sponsor: Yes () No (X)
Sponsor (or agent): Unimed
Manufacturer (if different) for drug substance: _____

Drug:

Code Name:
Generic Name: Estradiol 17 β
Trade Name: Estrojel
Chemical Name: Estra-1,3,5(10)-triene-3,17 β -diol
CAS Registry Number (if provided by sponsor): 50-28-2
Molecular Formula/ Molecular Weight: 272
Structure:

Relevant INDs/NDAs/DMFs: IND 29,020; unapproved NDA _____ DMF's _____

Drug Class: steroid, estrogen

Indication: Treatment of moderate to severe vasomotor symptoms associated with menopause, the treatment of vulval and vaginal atrophy,

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Clinical formulation: Hydroalcoholic gel containing estradiol (0.06%), water, alcohol, triethanolamine and carbomer 934P.

Route of administration: Topical

Studies reviewed within this submission: Skin irritation studies GBL 41590 and GBL 41531; Pig sensitization studies GBL 41907 and GBL 41908.

Studies not reviewed within this submission: None

PHARMACOLOGY

The pharmacology of estradiol is well known and is not reviewed here.

TOXICOLOGY

General Comments: All inactive ingredients are in previously approved products and are USP or NF. Carbomer 934P is in approved topical creams, gels, emulsions and lotions and in a vaginal gel. The only toxicology studies performed were dermal irritation and sensitization studies by _____ under GLP's. Estrogel was not a primary irritant to New Zealand White rabbits with intact and abraded skin (report no. 41590 and 41531) and did not produce allergic contact dermatitis in Harley guinea pigs (report no. 41907 and 41908).

OVERALL SUMMARY AND EVALUATION

Introduction: Because the drug product is estradiol, no toxicology studies were needed. The formulation is not irritating and does not produce an allergic contact dermatitis.

Safety Evaluation: No safety concerns

Clinical Relevance of Safety Issues: None

Other Clinically Relevant Issues: None

Conclusions: No pharm/tox safety issues.

Communication Review:

- Labeling Review (NDA): Labeling conforms to estrogen class labeling and is satisfactory.

RECOMMENDATIONS

Internal comments: Pharmacology recommends approval of estrogel for menopausal symptoms.

External Recommendations (to sponsor): None

Draft letter Content for Sponsor: None

Future development or NDA issues: None

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

cc: list NDA 21-166; HFD-580; DSpell-LeSane; AJordan

APPEARS THIS WAY
ON ORIGINAL