CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-375/S-016

CLINICAL PHARMACOLOGY BIOPHARMACEUTICS REVIEW

Supplemental New Drug Application - Review
Office of Clinical Pharmacology and Biopharmaceutics

NDA:	20-375 SE1-016
Type of Submission:	Efficacy Supplement
Brand Name:	Climara™
Generic Name:	Estradiol Adhesive Transdermal System
Formulation(s); **Strength(s);** **Nominal Delivery Rate;** **Route**	Adhesive Transdermal System 6.5 cm^2 0.025 mg/day Transdermal
Sponsor:	Berlex Laboratories, Inc.
Submission Date:	June 2, 2000
Reviewer:	Ronald Evan Kavanagh, B.S. Pharm., Pharm.D., Ph.D.

SYNOPSIS:

Climara™ is an approved controlled release transdermal product containing estradiol.

This efficacy supplement provides for the indication, *'treatment of moderate to severe vasomotor symptoms associated with menopause'*, for the lowest strength of 6.5 cm^2 (0.025 mg/day). This strength has previously been approved for treatment of osteoporosis.

The pharmacokinetics and biopharmaceutics for this strength were submitted in an earlier supplemental NDA (sNDA 20-994 SE-011) filed with the Division of Endocrine and Metabolic Drug Products (submission date May 1, 1998). That submission was reviewed by this reviewer.

No new human pharmacology or biopharmaceutic data was included in the present submission.

The formulation used in studies reported in the present efficacy supplement is currently approved and is not the proposed new formulation, as outlined in chemistry supplemen ——— Consequently, no additional clinical pharmacology, pharmacokinetic, or bioavailability studies are required.

LABELING:

The pharmacokinetics of the 6.5 cm^2 (0.025 mg/day) strength is currently described in the label and there are no changes proposed.

A section on adhesion is included in the clinical pharmacology section. The proposed labeling for this section appears to have been submitted with NDA 20-375 labeling supplement, SLR-014. The cover letter for supplement SLR-014 refers to an open label adhesion study, and indicates that the final study report will be submitted to IND 40,928. The final study report for the adhesion study (Berlex report no. 99001 Jan 26, 1999) was found in IND 40,928 N-054 IM letter date 2/4/99, date received 2/9/99. An amendment to SLR-014 containing the final study report has been requested and the adhesion labeling will be reviewed under supplement SLR-014.

RECOMMENDATIONS:

The Office of Clinical Pharmacology and Biopharmaceutics/Division of Pharmaceutical Evaluation II (HFD-870) (OCPB/DPEII) has evaluated NDA 20-375 SE1-016 dated June 2, 2000. Based on this review, the Division has determined that this application is acceptable to OCPB/DPEII.

The sponsor has been requested to submit an amendment to NDA supplement 20-375 SLR-014, containing the final study report for the adhesion study (Berlex report no. 99001 Jan 26, 1999). The labeling regarding adhesion will be updated under supplement SLR-014 upon review of this data.

COMMENTS FOR THE SPONSOR:

None.

LABELING COMMENTS FOR THE SPONSOR:

SIGNATURES

Ronald Evan Kavanagh, B.S. Pharm., Pharm.D., Ph.D. — Date

Division of Pharmaceutical Evaluation II
Office of Clinical Pharmacology and Biopharmaceutics

Ameeta Parekh, Ph.D. — Date

Team Leader
Division of Pharmaceutical Evaluation II
Office of Clinical Pharmacology and Biopharmaceutics

OCPB Briefing Meeting: Not Applicable.

CC:

NDA #30-375	**SE-016**
	SLR-014 (orig., 1 copy)
HFD-580	**(AllenS, Slaughter, Price, Moore)**
HFD-870	**(Parekh, Kavanagh, Malinowski)**
CDR	**(Barbara Murphy)**

/s/

Ron Kavanagh
2/23/01 10:34:47 AM
BIOPHARMACEUTICS

Ameeta Parekh
2/26/01 04:25:35 PM
BIOPHARMACEUTICS
I concur.