

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20375/S012

CHEMISTRY REVIEW(S)

ORIGINAL

JUN 10 1998

**DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG
PRODUCTS**

**REVIEW OF CHEMISTRY MANUFACTURING AND CONTROLS
CHEMIST'S REVIEW**

1. NDA NUMBER: 20-375

2. NAME AND ADDRESS OF APPLICANT

Berlex Laboratories, Inc.
340 Changebridge Road
P.O Box 1000
Montville, NJ 07045-1000

3. SUPPLEMENT NUMBER/DATE/DATE ASSIGNED

SCS-012/5-27-98/5-28-98

4. NAME OF THE DRUG: Climara[®] (estradiol transdermal system)

5. NONPROPRIETARY NAME: Estradiol Transdermal System

6. SUPPLEMENT PROVIDES FOR: Change in the expiration date from 24 to 36 months

7. AMENDMENTS/REPORTS/ DATE: None

8. PHARMACOLOGICAL CATEGORY

Estrogen

9. HOW DISPENSED

Prescription

10. RELATED IND/NDA/DMF/SUPPLEMENT

DMF

11. DOSAGE FORM : Transdermal

12. POTENCY

0.05 , 0.075 and 0.1 mg/day

13. CHEMICAL NAME AND STRUCTURE

$C_{18}H_{24}O_2 \cdot \frac{1}{2} H_2O$

MW = 281.4

Estra-1,3,5(10)-triene-3,17 β -diol, hemi hydrate

14. COMMENTS

NDA 20-375 was approved for marketing 12.5 , 18.75, and 25 Cm² patches of estradiol. The drug product is manufactured under DMF. The supplement was submitted for requesting extension of expiration date from 24 to 36 months for all three strengths. During a Teleconference with the sponsor on 6-9-98, the following agreements were made.

1. An extension of shelf life from 2 to 3 years for 0.05 mg/day strength can be granted based on facsimile information to be submitted to the DMF.
2. The shelf life for 0.075 mg/day strength would remain at two years until satisfactory stability data under ICH conditions is available to support the 3 years shelf life.
3. Thirty six months stability data for the third lot of 0.1 mg/day strength would be available by the end of June. If the stability data is satisfactory, the data can be reported in the annual report with the extension of shelf life to 36 months.

The following changes were made:

Change in shelf life from 2 to 3 years was requested.

1. **15. CONCLUSIONS AND RECOMMENDATIONS:** The supplement can be approved with the following stipulation. The expiration date of 0.05 and 0.075 mg/day strengths would be 36 months and 24 months respectively. Thirty six months stability data for the third lot of 0.1 mg/day strength would be available by the end of June. If the stability data is satisfactory, the data can be reported in the annual report with the extension of shelf life to 36 months.

IS/

Reviewed By: Amit K. Mitra, Ph.D. 6-10-98

R/D INIT BY: Moo-Jhong Rhee, Ph.D.

IS/ 6/10/98

CC: A. K. MITRA/HFD-580
M.J.RHEE/HFD-580
D. Moore/HFD-580
NDA 20-375