NDA 20-375/S-014

Berlex Laboratories, Inc.
Attention: Geoffrey Millington
Manager, Drug Regulatory Affairs
340 Changebridge Road
P.O. Box 1000
Montville, NJ 07450-1000

04 APR 2001

Dear Mr. Millington

Please refer to your supplemental new drug application dated January 28, 1999, received January 28, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Climara® (Estradiol transdermal System) 0.025, 0.05, 0.075, 0.1 mg/day.

We acknowledge receipt of your submissions dated February 9 and 10, 1999; and February 7, and March 15, and April 2, 2001.

This supplemental new drug application provides for revisions to the **Black Box WARNING, CLINICAL PHARMACOLOGY**, **INDICATIONS AND USAGE**, **CONTRAINDICATIONS**, **WARNINGS**, **PRECAUTIONS**, **ADVERSE REACTIONS**, and **DOSAGE AND ADMINISTRATION** sections of the physican insert. It also provides revisions to the **INTRODUCTION** section of the patient package insert, and adds carton and immediate container labeling for the 0.025 mg /day transdermal system.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the attached labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted April 2, 2001, patient package insert submitted February 9, 1999, and immediate container and carton labels submitted February 9, 1999).

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-375/S-014." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Diane Moore, BS, Regulatory Project Manager, at (301) 827-4260.

Sincerely,

Susan Allen, M.D.
Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research