DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-674

Berlex Laboratories Inc.
Attention: Geoffrey Millington
Manager, Drug Regulatory Affairs
340 Changebridge Road; P.O. Box 1000
Montville, NJ 07045-1000

Dear Mr. Millington:

Please refer to your new drug application (NDA) dated August 7, 2003, received August 8, 2003, submitted under section 505b of the Federal Food, Drug, and Cosmetic Act for Menostar (estradiol transdermal system).

We acknowledge receipt of your submissions dated October 7, November 14, December 17, 2003 and March 15, May 4, 12, 14, and June 2, and 8 (2 submissions), 2004.

This new drug application provides for the use of Menostar (estradiol transdermal system) for prevention of postmenopausal osteoporosis.

We have completed our review of this application and it is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial changes to the foil pouches, containers and cartons listed below. The changes to the foil pouches must be implemented before manufacture of batch (b)(4)-

General Revisions to foil pouches, containers and cartons:

1. Relocate the graphic that covers the beginning letter 'M' of the proprietary name so that it does not interfere with the readability of the proprietary name.

2. Increase the prominence of the established name and strength, so that they are at least one-half the size of the proprietary name.

3. Eliminate the terminal zeros listed throughout the container labels and carton labeling since they could be misinterpreted (e.g., 1.0 as 10).

Specific Revision to the foil pouches (sample and trade):

1. Include the route of administration on the principal display panel (e.g., For Transdermal Use).

Specific Revisions to Menostar Carton Labeling (4 systems, 6 x 4 systems, sample card):

1. Increase the prominence of the route of administration statement on the principal display panel.

2. Revise the net quantity statement to read '4 Transdermal Systems', '6 Patient Packs each containing '4 Transdermal Systems' or '1 Transdermal System', as appropriate.

The final printed labeling (FPL) must be identical to the enclosed labeling for the package insert and the patient package insert and include the minor editorial revisions to the submitted labeling (foil pouch, containers and cartons, submitted May 14, 2004). We remind you of your agreement to make the labeling changes to the foil pouches before production of batch (b)(4) These changes can be submitted as a CBE-0 labeling supplement, which must contain final printed labeling.

These revisions are terms of the NDA approval. Marketing the product before making the revisions, exactly as stated, in the product's labeling may render the product misbranded and an unapproved new drug.

The electronic labeling rule published December 11, 2003, (68 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidances for industry regarding electronic submissions: *Providing Regulatory Submissions in Electronic Format – NDAs* (January, 1999) and draft guidance *Providing Regulatory Submissions in Electronic Format – Content of Labeling* ((February 2004). The guidances specify labeling to be submitted in *pdf* format. To assist in our review, we request that labeling also be submitted in MS Word format. If formatted copies of all labeling pieces (i.e., package insert, patient package insert, container labels, and carton labels) are submitted electronically, labeling does not need to be submitted in paper. For administrative purposes, designate this submission "**FPL for approved NDA 21-674**." Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for this application.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

All 15-day alert reports, periodic (including quarterly) adverse drug experience reports, field alerts, annual reports, supplements, and other submissions should be addressed to the original NDA 20-375 for this drug product, not to this NDA. In the future, do not make submissions to this NDA except for the final printed labeling requested above.

If you have any questions, call Pat Madara, Regulatory Project Manager, at (301) 827-6416.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure: package insert
patient package insert

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

David Orloff

6/8/04 06:08:27 PM