**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-355

Berlex, Inc.
Attention: Michael Doroshuk
Manager, Drug Regulatory Affairs
340 Changebridge Road
Montville, NJ 07045-1000

Dear Mr. Doroshuk:

Please refer to your new drug application (NDA) dated December 14, 2001, received December 17, 2001, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Angeliq™ (drospirenone/17ß-estradiol) tablets.

We acknowledge receipt of your submissions dated December 14, 2001, January 10, 14, 16, 21, February 1, 8, 15, March 7, 13, April 1, 11, May 1, 8, 13, June 10, 14, 19, July 3, 10, 11, 16, 17, 22, 26, August 8, 13, 15, 19, September 5, 10, 16, 30, October 8, 16, 2002, March 18, April 16(2), 19, 23, 26(3), 28(2), July 16, 19, August 4, 23, 25, September 3, 7, 13, 2004, March 31, May 6, July 15, 22, September 8, 16, 22, 23, and 28, 2005.

The March 31, 2005 submission constituted a complete response to our September 14, 2004 action letter.

This new drug application provides for the use of Angeliq™ for the following indications:

1) Treatment of moderate to severe vasomotor symptoms associated with the menopause
2) Treatment of moderate to severe symptoms of vulvar and vaginal atrophy associated with the menopause. When prescribing solely for the treatment of symptoms of vulvar and vaginal atrophy, topical vaginal products should be considered.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. 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. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-355**." 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.

We remind you of your postmarketing study commitment in your submission dated September 22, 2005. This commitment is listed below.

> To conduct a study to determine the lowest effective dose of Angeliq™ for the relief of moderate to severe vasomotor symptoms and vulvar and vaginal atrophy.
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> | | |
> |---|---|
> | Protocol Submission: | Within 6 months of the date of this letter |
> | Study Start: | Within 6 months of reaching protocol agreement with the Division of Reproductive and urologic Products |
> | Final Report Submission: | Within 6 months of the study completion |

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

We also acknowledge your agreement to submit the interim results and the Final Report of the EURAS-HRT study in a timely manner, and to submit the EURAS-OC interim results and final report to the Angeliq™ 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).

If you have any questions, call Kassandra Sherrod, R.Ph., Regulatory Project Manager, at (301) 796-2130.

Sincerely,

*{See appended electronic signature page}*

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

Enclosure

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

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/s/
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Daniel A. Shames
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