



NDA 021813/S-003

## SUPPLEMENT APPROVAL

Azur Pharma International II, Limited  
c/o Beckloff Associates, Inc.  
Attention: Gary D. Hindman, Ph.D., M.B.A.  
7400 W. 110th Street, Suite 300  
Overland Park, KS 66210

Dear Dr. Hindman:

Please refer to your Supplemental New Drug Application (sNDA) dated June 30, 2010, received July 2, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Elestrin™ (estradiol gel).

We acknowledge receipt of your amendments dated February 4, May 25, and September 22, 2011.

This supplemental new drug application provides for conversion of the labeling to Physician Labeling Rule (PLR) format.

In addition, this labeling, as amended, also provides for the following new information:

- Addition of two new CONTRAINDICATIONS of known anaphylactic reaction or angioedema and known protein C, protein S, or antithrombin deficiency, or other known thrombophilic disorders
- Addition of a new WARNINGS AND PRECAUTIONS of hereditary angioedema

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

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

## **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the package insert, text for the patient package insert), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As” at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

## **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

## **REPORTING REQUIREMENT**

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 Kim Shiley, R.N., B.S.N., Regulatory Health Project Manager, at (301) 796-2117

Sincerely,

*{See appended electronic signature page}*

Christine Nguyen, M.D.  
Acting Deputy Director for Safety  
Division of Reproductive and Urologic Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

ENCLOSURE:  
Content of Labeling

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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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CHRISTINE P NGUYEN  
02/24/2012