DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020908/S-017

SUPPLEMENT APPROVAL

Novo Nordisk Inc.
Attention: Anne Phillips, M.D.
Corporate Vice President
Clinical, Medical, and Regulatory Affairs
100 College Road West
Princeton, NJ 08540

Dear Dr. Phillips:

Please refer to your Supplemental New Drug Application (sNDA) dated and received April 15, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Vagifem® (estradiol vaginal tablets).

We acknowledge receipt of your amendments dated August 18 and September 30, 2011.

This "Changes Being Effected" supplemental new drug application provides for revisions in the Physician Insert (PI), *Section 17.4, Instructions for Use of Applicator, Step 5* and revisions in the Patient Package Insert (PPI), *How Should I use Vagifem?, step 5*. This supplemental application, as amended, also provides for the addition of a new CONTRAINDICATION of thrombophilic disorders, a new CONTRAINDICATION of anaphylactic reaction or angioedema, a new WARNINGS AND PRECAUTIONS of hereditary angioedema, and revisions to the labeling based on current recommended estrogen-class labeling for hormone therapy products.

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

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

/s/

CHRISTINE P NGUYEN
04/11/2012