DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022341/S-004

SUPPLEMENT APPROVAL
REMOVE REMS ELEMENT

Novo Nordisk, Inc.
Attention: Anne Phillips, M.D.
Corporate Vice President, CMR
100 College Road West
Princeton, NJ 08540

Dear Dr. Phillips:

Please refer to your Supplemental New Drug Application (sNDA) dated November 19, 2010, received November 19, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for VICTOZA (liraglutide [rDNA origin]) Injection.

We acknowledge receipt of your amendments dated December 22, 2010, January 5, April 28, and May 10 (2), and 17, 2011; and your risk evaluation and mitigation strategy (REMS) assessment dated January 25, 2011.

We also refer to our letter dated May 6, 2011, which required revisions to the communication plan of your REMS. These revisions were required because your January 25, 2011, REMS assessment showed that the REMS was not meeting its goal of educating health care providers about the potential risks associated with the use of VICTOZA (liraglutide [rDNA origin]). We acknowledge receipt of your revised REMS dated May 10 and 17, 2011.

This supplemental NDA provides for the addition of information regarding postmarketing reports of worsening renal function, including acute renal failure, to the package insert and corresponding text in the Medication Guide, and proposed modifications to the approved REMS.

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.

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 (Physician Insert and Medication Guide)

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).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for VICTOZA (liraglutide [rDNA origin]) was originally approved on January 25, 2010. The REMS consisted of a Medication Guide, a communication plan, and a timetable for submission of assessments of the REMS.

Your proposed modification to the REMS consists of a request to eliminate the Medication Guide as an element of the approved REMS, and modifications to the communication plan to include a modified reminder *Dear Healthcare Provider* letter to be sent to the primary care physician audience within 60 days of approval of the REMS modification, and a revised *Direct Mail* letter to be sent to all prescribers of VICTOZA (liraglutide [rDNA origin]) on an annual basis for a total of 3 years following approval of this REMS modification.

We have determined that maintaining the Medication Guide as part of the approved labeling is adequate to address the serious and significant public health concern and meets the standard in 21 CFR 208.1 and, therefore, it is no longer necessary to include the Medication Guide as an element of the approved REMS to ensure that the benefits of the drug outweigh the risks.

Therefore, we agree with your proposal, and a Medication Guide is no longer required as part of the REMS for VICTOZA (liraglutide [rDNA origin]). We remind you that the Medication Guide will continue to be part of the approved labeling for VICTOZA (liraglutide [rDNA origin]) in accordance with 21 CFR 208.

Your proposed modified REMS, submitted on May 10 and 17, 2011, and appended to this letter, is approved. The modified REMS consists of a communication plan and a timetable for submission of assessments of the REMS.

The timetable for submission of assessments of the REMS will remain the same as that approved on January 25, 2010.

The revised REMS assessment plan should include, but is not limited to, the following:

1. Evaluation of healthcare providers' understanding of the serious risks of VICTOZA (liraglutide [rDNA origin])

2. An assessment of healthcare providers' awareness of:

    a. appropriate patient population characteristics, and
    b. the potential risk for medullary thyroid carcinoma
    c. the need for prompt evaluation of patients who develop symptoms suggestive of pancreatitis

3. Evaluation of healthcare providers' identification and treatment of:

    a. medullary thyroid carcinoma after initiation of VICTOZA (liraglutide [rDNA origin])
    b. acute pancreatitis after initiation of VICTOZA (liraglutide [rDNA origin])

4. Evaluation of the extent to which the communication plan is meeting the goals of the REMS and whether modifications to the elements or goals are needed

5. An assessment of the number of VICTOZA (liraglutide [rDNA origin]) prescribers identified to receive the *Dear Health Care Provider* (DHCP) letter and the number of DHCP letters mailed

6. An assessment of the percentage of targeted physicians who are presented with the Highlighted Information for Prescribers via Sales Specialists, the website, or medical information department

7. As required under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o)(3) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

If you currently distribute or plan to distribute an authorized generic product under this NDA, you must submit a complete proposed REMS that relates only to the authorized generic product. Submit a proposed REMS, REMS supporting document, and any required appended documents as a prior approval supplement. Approval of the proposed REMS is required before you may market your authorized generic product.

Prominently identify the submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA 022341 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 022341
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 022341
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

REPORTING REQUIREMENTS

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, please call Pooja Dharia, Pharm.D., Regulatory Project Manager, at (301) 796-5332.

Sincerely,

{See appended electronic signature page}

Mary Parks, M.D.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURES:
Package Insert
Medication Guide
REMS

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

/s/

MARY H PARKS
05/18/2011