



NDA 021536/S-031 and S-051

**SUPPLEMENT APPROVAL**

Novo Nordisk, Inc.  
Attention: Robert B. Clark  
VP Regulatory Affairs  
800 Scudders Mill Road, P.O. Box 846  
Plainsboro, NJ 08536

Dear Mr. Clark:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received July 17, 2009 (S-031) and August 15, 2014 (S-051), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Levemir (insulin detemir [rDNA origin] injection), 100 Units/mL.

We acknowledge receipt of your amendments dated:

Supplement S-031: August 20, 2009, May 14, 2010, March 27 and April 19, 2013, and  
February 20, 2015

Supplement S-051: November 10 and December 22, 2014, and January 12 and February 3, 2015

The "Changes Being Effected" supplemental new drug application (S-031) proposes to revise the labeling for Levemir to include a warning against the sharing of pens between patients.

We also refer to our letter dated July 17, 2014, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for products indicated for diabetes mellitus that have multi-dose pen presentations. This information pertains to the risk of transmission of bloodborne pathogens resulting from pen devices and pen cartridges that are intended for single patient use only, being shared among numerous patients.

The "Prior Approval" supplemental new drug application (S-051) provides for revisions to the labeling for Levemir consistent with our July 17, 2014, letter.

In our July 17, 2014, letter, we also required you to submit a plan for how you would modify the pen device to include a statement warning against the sharing of pens, on the body of the pen. In your submission dated August 15, 2014, you provided a rationale for why you believe that adding the warning statement to the body of the pen is not necessary and/or feasible. We have reviewed this rationale and found it acceptable that the warning not be placed on the body of the pen at this time.

Further, in our July 17, 2014 letter, we required you to modify the labeling for the Levemir FlexPen to include the warning against the sharing of pens. However, we acknowledge that the Levemir FlexPen was discontinued as of August 1, 2014, and therefore you are no longer required to modify the labeling for it. If you re-introduce Levemir FlexPen into the market, please update the labeling to match that for your other pens.

### **APPROVAL & LABELING**

We have completed our review of these supplemental applications, as amended. They are 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 (text for the package insert, patient package insert and Instructions for Use), with the addition of any labeling changes in pending “Changes Being Effectuated” (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 that includes labeling changes 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).

### **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  
Office of Prescription Drug Promotion (OPDP)  
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/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>.

Information and Instructions for completing the form can be found at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For

more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), 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, call Callie Cappel-Lynch, Regulatory Project Manager, at (301) 796-8436.

Sincerely,

*{See appended electronic signature page}*

Jennifer Rodriguez Pippins, M.D., M.P.H.  
Deputy Director for Safety  
Division of Metabolism and Endocrinology Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

### **ENCLOSURES:**

Levemir Package Insert  
Levemir Patient Package Insert  
Levemir FlexTouch Pen Instructions for Use  
Levemir Carton and Container labels

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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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JENNIFER R PIPPINS  
02/25/2015