DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 206321

NDA APPROVAL

Novo Nordisk, Inc.
Attention: Michelle Thompson
Senior Director, Regulatory Affairs
P.O. Box 846
800 Scudders Mill Road
Plainsboro, NJ 08536

Dear Ms. Thompson:

Please refer to your New Drug Application (NDA) dated and received December 20, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Saxenda (liraglutide [rDNA origin] injection), 3 mg.

We acknowledge receipt of your amendments dated January 10, February 6, 13, and 14, March 4 and 21, April 2(3), 11, 15, 18, and 29, May 1, 2(2), 23, and 27, June 6, 16, 18, and 26, July 1, 3, 8, 9, 11, 14, and 15(2), August 14(2), 20, 28, and 29, September 24, 26, and 29(2), October 1(2), 2, 3(2), 6, 7, 9, 15, 17(2), 18, 20 and 24, November 10(2), 18, and December 12,16, 17, 18, and 2014.

This new drug application provides for the use of Saxenda (liraglutide [rDNA] injection), as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of 30 kg/m2 or greater (obese), or 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia).

We have completed our review of this 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 (text for the package insert, medication guide, and instructions for use). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*,

available at
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

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

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008).* Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 206321**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the products with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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 indications(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric studies requirement for ages 0 to 6 years (inclusive) because necessary studies are impossible or highly impracticable. This is because weight maintenance, not weight loss, is the clinical goal for obese children 2 to 6 years of age. Weight loss is not recommended in children less than 2 years of age because of the requirement for adequate growth and development and optimal deposition of lipids in the developing nervous system.

We are deferring submission of your pediatric studies for ages 7 to 17 years (inclusive) for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. These required studies are listed below.

2802-1 A juvenile rat toxicity study with liraglutide treatment from pre-puberty through reproductive maturity.

Final Report Submission: December 2014

2802-2 A clinical pharmacology study (Trial NN8022-3967) to assess pharmacokinetic and pharmacodynamic parameters of Saxenda in obese pediatric patients ages 12 to 17 years (inclusive).

Final Report Submission: December 2014

2802-3 A 56-week randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of Saxenda for the treatment of obesity in pediatric patients ages 12 to 17 (inclusive).

Final Protocol Submission August 2015
Study Completion: August 2019
Final Report Submission: August 2020

2802-4 A clinical pharmacology study to assess pharmacokinetic and pharmacodynamics parameters of Saxenda in obese pediatric patients ages 7 to 11 years (inclusive).

Final Protocol Submission September 2015
Study Completion: August 2017
Final Report Submission: February 2018

2802-5 A 56-week randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of Saxenda for the treatment of obesity in pediatric patients ages 7 to 11 (inclusive). The trial may not be initiated until results from the Saxenda adolescent safety and efficacy trial have been submitted to and reviewed by the Agency.

Final Protocol Submission April 2020
Study Completion: October 2023
Final Report Submission: August 2024

Submit the protocols to your IND 073206, with a cross-reference letter to this NDA.

Reports of these required pediatric postmarketing studies must be submitted as an NDA or as a supplement to your approved NDA with the proposed labeling changes you believe are

warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess a signal of a serious risk of medullary thyroid carcinoma associated with Saxenda (liraglutide [rDNA origin] injection).

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

2802-6 A medullary thyroid carcinoma registry-based case series of at least 15 years duration to systematically monitor the annual incidence of medullary thyroid carcinoma in the United States and to identify any increase related to the introduction of Saxenda (liraglutide [rDNA origin] injection) into the marketplace. This study will also establish a registry of incident cases of medullary thyroid carcinoma and characterize their medical histories related to diabetes and use of Saxenda (liraglutide [rDNA origin] injection).

The timetable you submitted on December 16, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	June 2015
Study Completion:	September 2030
Final Report Submission:	September 2031

Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to assess a signal of a serious risk of breast cancer associated with Saxenda (liraglutide [rDNA origin] injection).

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

2802-7 To assess the risk of breast cancer associated with liraglutide in the LEADER (Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular

Outcome Results) cardiovascular outcomes trial. To assess this risk, collect information on baseline cancer risk and potential confounders for all identified cases of breast cancer in the trial, including (but not limited to) prior history of breast cancer, family history of breast cancer, BRCA1/BRCA2 status, age at menopause, history of radiation to the chest, age at menarche, and current/prior use of hormonal therapy.

The timetable you submitted on December 16, 2014, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	January 2015
Trial Completion:	September 2015
Final Report Submission:	April 2016

2802-8 To assess the risk of breast cancer associated with liraglutide in Trial 1839. To assess this risk, collect information on baseline cancer risk and potential confounders for all identified cases of breast cancer in the trial, including (but not limited to) prior history of breast cancer, family history of breast cancer, BRCA1/BRCA2 status, age at menopause, history of radiation to the chest, age at menarche, and current/prior use of hormonal therapy.

The timetable you submitted on December 16, 2014, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	January 2015
Trial Completion:	March 2015
Final Report Submission:	August 2015

Submit the protocols to your IND 073206, with a cross-reference letter to this NDA. Submit all final reports to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **"Required Postmarketing Protocol Under 505(o)", "Required Postmarketing Final Report Under 505(o)", "Required Postmarketing Correspondence Under 505(o)"**.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR

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