CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 201280/S-002

Trade Name: **TRADJENTA**

Generic Name: **Linagliptin**

Sponsor: **Boehringer Ingelheim Pharmaceuticals, Inc.**

Approval Date: 05/22/2012

Indications: TRADJENTA is a dipeptidyl peptidase-4 (DPP-4) inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus

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APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 201280/S-002

SUPPLEMENT APPROVAL

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Chung Lee-Sogaard, Ph.D.
Associate Director, Drug Regulatory Affairs
900 Ridgebury Road, P.O. Box 368
Ridgefield, CT 06877

Dear Dr. Lee-Sogaard:

Please refer to your Supplemental New Drug Application (sNDA) dated and received on July 22, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tradjenta (linagliptin) tablets, 5 mg.

We acknowledge receipt of your amendments dated September 21, and 22, and November 16, 2011, and March 9, and April 19, 2012. We also acknowledge receipt of your email dated May 21, 2012, that includes the agreed-upon labeling.

This "Prior Approval" supplemental new drug application provides for modifications to the Patient Package Insert (PPI), changes to the **ADVERSE REACTIONS** section of the Highlights of Prescribing Information section and changes to the **ADVERSE REACTIONS, USE IN SPECIFIC POPULATIONS, OVERDOSAGE, CLINICAL PHARMACOLOGY, AND CLINICAL STUDIES** of the Full Prescribing Information sections of the Tradjenta package insert (PI).

These changes are based on the safety and efficacy results from trial 1218.46, entitled "A Phase 3, randomized, double-blind, placebo-controlled parallel group study to compare the efficacy and safety of twice daily administration of the free combination of linagliptin 2.5 mg + metformin 500 mg or of linagliptin 2.5 mg + metformin 1000 mg, with the individual components of metformin (500 mg or 1000 mg, twice daily) and linagliptin (5 mg, once daily) over 24 weeks in drug naive or previously treated (4 weeks washout and 2 weeks placebo run-in) type 2 diabetic patients with insufficient glycemic control." The efficacy and safety of trial 1218.46 was fully reviewed under the Jentadueto (linagliptin/metformin fixed-dose combination) NDA (201281).

We have completed our review of the 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 and 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.

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