DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 201280/S-003 and S-004

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 Applications (sNDA) dated and received on October 14 and 31, 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 November 16 (S-003 and S-004), 2011 and January 10 (S-003), January 31 (S-004), February 24 (S-003), March 5 (S-004), March 30 (S-004), May 14 (S-003), May 31 (S-003 and S-004), June 5 (S-003), June 15 (S-003 and S-004), June 21 (S-004), July 6 (S-004), July 13 (S-004), July 16 (S-004), and July 19 (S-004), 2012. We also acknowledge receipt of your email dated August 09, 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 **RECENT MAJOR CHANGES, INDICATIONS AND USAGE, and ADVERSE REACTIONS** sections of the Highlights of Prescribing Information and changes to the **INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, WARNINGS AND PRECAUTIONS, ADVERSE REACTIONS, AND CLINICAL STUDIES** sections of the Full Prescribing Information of the Tradjenta package insert (PI).

The changes for S-003 are based on the safety and efficacy results from trial 1218.43, entitled "*A phase 3, randomised, double-blind, placebo-controlled, parallel group, safety and efficacy study of BI 1356 (5 mg), compared to placebo as add on to pre-existing antidiabetic therapy (insulin or any combination with insulin; sulphonylurea or glinides as monotherapy; pioglitazone or any other antidiabetics, excluding only DPP-4 inhibitors other than BI 1356) over 52 weeks in type 2 diabetic patients with severe chronic renal impairment*." The changes for S-004 are based on the safety and efficacy results from trial 1218.36, entitled "*A phase 3, randomized, double-blind, placebo-controlled, parallel-group, efficacy and safety study of linagliptin (5 mg), administered daily for at least 52 weeks in type 2 diabetic patients in combination with basal insulin therapy*."

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.

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/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. 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.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

We request that for a period of two years, you submit all cases of hypersensitivity reactions (including angioedema, anaphylaxis, and Stevens-Johnson Syndrome) reported with Tradjenta (linagliptin) as 15-day alert reports, and that you provide detailed analyses of clinical trial and post-marketing reports of hypersensitivity reactions (including angioedema, anaphylaxis, and Stevens-Johnson Syndrome) as adverse events of special interest in your periodic safety update reports (PSURs). These analyses should show cumulative data relative to the date of approval of Tradjenta (linagliptin) as well as relative to the prior PSUR. Medical literature reviews for case reports/case series of serious hypersensitivity reactions with Tradjenta (linagliptin) should also be provided in the PSURs.

If you have any questions, call Raymond Chiang, Regulatory Project Manager, at (301) 796-1940.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURES:
Package Insert (PI)
Patient Package Insert (PPI)

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
08/13/2012