DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021925/S-015

SUPPLEMENT APPROVAL

Takeda Pharmaceutical U.S.A., Inc.
Attention: Esha Desai, MS, RAC (US, EU)
Manager, Global Regulatory Affairs Development
One Takeda Parkway
Deerfield, IL 60015

Dear Ms. Desai:

Please refer to your Supplemental New Drug Application (sNDA) dated and received September 22, 2014, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Duetact (pioglitazone hydrochloride and glimepiride) tablets.

This "Prior Approval" supplemental new drug application, submitted in response to our supplement request letter dated August 22, 2014, provides for the following changes:

Under Section 4 **CONTRAINDICATIONS**, added the following:

Reported hypersensitivity reactions with glimepiride include cutaneous eruptions with or without pruritus as well as more serious reactions (e.g., anaphylaxis, angioedema, Stevens-Johnsons Syndrome, dyspnea)

Under Section 6 **ADVERSE REACTIONS**, sub-section 6.2 **Post-Marketing Experience**, **Glimepride**, added the following:

Thrombocytopenia (including severe cases with platelet count less than 10,000/μL) and thrombocytopenic purpura.

Under Section 7 **DRUG INTERACTIONS**, sub-section 7.3 **Drugs Affecting Glucose Metabolism: Glimepiride**, text was added.

Under Section 12 **CLINICAL PHARMACOLOGY**, sub-section 12.3 **Pharmacokinetics**, text was revised.

In addition, changes were made to the Highlights and **USE IN SPECIFIC POPULATIONS** sections for consistency with the currently approved labeling for Amaryl (glimepiride) tablets, and minor editorial changes were made to the package insert and Medication Guide.

APPROVAL & LABELING

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 and with the minor editorial revisions listed below and reflected in the enclosed labeling.

- Revision date changed to "3/2015" to reflect the date of approval for this supplement
- Restored the space in the heading in section 5 **WARNINGS AND PRECAUTIOUS**, subsection 5.4 **Potential Increased Risk of Cardiovascular Mortality with Sulfonylureas**

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 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 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).

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/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 Elizabeth Chen, Regulatory Project Manager, at (240) 402-3729.

Sincerely,

{See appended electronic signature page}

Jennifer R. 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:
Content of Labeling
Package Insert
Medication Guide

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

/s/

JENNIFER R PIPPINS
03/16/2015