DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020496/S-027

SUPPLEMENT APPROVAL

Sanofi-aventis U.S. LLC
Attention: Payal Patel, Pharm.D.
Manager, U.S. Regulatory Affairs Marketed Products
55 Corporate Drive, Mailstop: 55C-205A
Bridgewater, NJ 08807

Dear Dr. Patel:

Please refer to your Supplemental New Drug Application (sNDA) dated and received May 2, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Amaryl (glimepiride) tablets, 1 mg, 2 mg, and 4 mg.

We acknowledge receipt of your amendments dated June 26 and August 14, 2013.

We also refer to our Prior Approval Supplement Request letter dated March 7, 2013, requesting revisions to the label for Amaryl (glimepiride).

Supplemental new drug application, S-027, provides for the following revisions to the labeling for Amaryl. Additions are noted by underline.

Highlights page, under Drug Interactions:

DRUG INTERACTIONS

- Colesevelam: Coadministration may reduce glimepiride absorption. AMARYL should be administered at least 4 hours prior to colesevelam. (2.1, 7.4)

FULL PRESCRIBING INFORMATION: CONTENTS*

7 DRUG INTERACTIONS

7.4 Concomitant Administration of Colesevelam

Under **DOSAGE AND ADMINISTRATION**, **2.1 Recommended Dosing**:

When colesevelam is coadministered with glimepiride, maximum plasma concentration and total exposure to glimepiride is reduced. Therefore, AMARYL should be administered at least 4 hours prior to colesevelam.

Under **DRUG INTERACTIONS**:

7.4 Concomitant Administration of Colesevelam
Colesevelam can reduce the maximum plasma concentration and total exposure of glimepiride when the two are coadministered. However, absorption is not reduced when glimepiride is administered 4 hours prior to colesevelam**.** Therefore, AMARYL should be administered at least 4 hours prior to colesevelam.

Under **Clinical Pharmacology**, **Pharmacokinetics**, *Drug Interactions*, after the paragraph on Aspirin:

Colesevelam: Concomitant administration of colesevelam and glimepiride resulted in reductions in glimepiride $AUC_{0-\infty}$ and C_{max} of 18% and 8%, respectively. When glimepiride was administered 4 hours prior to colesevelam, there was no significant change in glimepiride $AUC_{0-\infty}$ or C_{max}, -6% and 3%, respectively. [see Dosage and Administration 2.1 and Drug Interactions 7.4]

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.

Revised: ~~xx~~10/2013

Revised ~~Month~~ October 2013

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), 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.

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 Raymond Chiang, Regulatory Project Manager, at (301) 796-1940.

Sincerely,

{See appended electronic signature page}

Amy G. Egan, 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

ENCLOSURE:
Package Insert

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

/s/

AMY G EGAN
10/15/2013