DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020758/S-072

SUPPLEMENT APPROVAL

Sanofi-aventis U.S. LLC
c/o: Sanofi US Services, Inc.
Attention: John Cook
Senior Director, Global Regulatory Affairs
55 Corporate Drive
Mailstop 55C-205A
Bridgewater, NJ 08807

Dear Mr. Cook:

Please refer to your Supplemental New Drug Application (sNDA) dated and received March 13, 2017, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Avalide® (irbesartan and hydrochlorothiazide) 150/12.5mg and 300/12.5mg Tablets.

This supplemental new drug application provides for the following revisions to the approved labeling (additions are marked with underlined text and deletions are marked with ~~strikethrough~~ text):

1. Under **ADVERSE REACTIONS/Post-marketing Experience**, the following text was added/deleted:

6.2 Post-Marketing Experience

The following adverse reactions have been identified during post-approval use of AVALIDE. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Decisions to include these reactions in labeling are typically based on one or more of the following factors: (1) seriousness of the reaction, (2) frequency of reporting, or (3) strength of causal connection to AVALIDE.

(b) (4)

The following have been reported with irbesartan and with hydrochlorothiazide monotherapies: urticaria, jaundice, hepatitis, thrombocytopenia, impaired renal function including renal failure.

The following have been reported with irbesartan monotherapy: tinnitus, hyperkalemia, angioedema (involving swelling of the face, lips, pharynx, and/or tongue), increased CPK

The following have been reported with hydrochlorothiazide monotherapy: secondary acute angle closure glaucoma and/or acute myopia.

~~Very rare cases of jaundice have been reported with irbesartan.~~

~~Impaired renal function, including cases of renal failure in patients at risk, has been reported with irbesartan and AVALIDE.~~

~~Cases of increased CPK have been reported in patients receiving angiotensin II receptor blockers.~~

(b) (4)

2. The revision date and version number were updated.

APPROVAL & LABELING

We have completed our review of this supplemental application and 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), 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 include 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).

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, please call:

Lori Anne Wachter, RN, BSN, RAC
Regulatory Project Manager for Safety
at (301) 796-3975

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, PharmD.
Deputy Director for Safety
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

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

/s/

MARY R SOUTHWORTH
07/10/2017