DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020757/S-056

SUPPLEMENT APPROVAL

Sanofi-Aventis c/o Bristol-Myers Squib Company
Attention: Charles D. Wolleben, Ph.D.
Groups Director, Global Regulatory Sciences
5 Research Parkway
Wallingford, CT 06492

Dear Dr. Wollenben:

Please refer to your Supplemental New Drug Application (sNDA) dated and received July 19, 2011, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Avapro (irbesartan) 75 mg, 150 mg, and 300 mg Tablets.

We acknowledge receipt of your amendment dated November 10, 2011.

This "Changes Being Effected" supplemental new drug application provides for labeling revised as follows:

1. Under **PRECAUTIONS, Drug Interactions,** the following text was added as the fourth paragraph:

   Concomitant use of potassium-sparing diuretics, potassium supplements, or salt substitutes containing potassium may lead to increases in serum potassium.

2. Under **ADVERSE REACTIONS, Post-Marketing Experience**, the section was revised from:

   The following have been very rarely reported in post-marketing experience: urticaria; angioedema (involving swelling of the face, lips, pharynx, and/or tongue); increased liver function tests; jaundice; and hepatitis; Hyperkalemia has been rarely reported.

   Rare cases of rhabdomyolysis have been reported in patients receiving angiotensin II receptor blockers.

To:

   The following adverse reactions have been identified during post-approval use of AVAPRO. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate reliably their frequency or to 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 AVAPRO.

The following have been reported: urticaria; angioedema (involving swelling of the face, lips, pharynx, and/or tongue); increased liver function tests; jaundice; hepatitis; hyperkalemia; and thrombocytopenia.

Impaired renal function, including cases of renal failure, has been reported.

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

3. The revision date and version number were updated.

There are no other changes from the last approved package insert.

We have completed our review of this supplemental application, as amended, 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 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
Regulatory Project Manager for Safety
(301) 796-3975

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, Pharm.D.
Deputy Director for Safety
Division of Cardiovascular and Renal Products
Office of Drug Evaluation 1
Center for Drug Evaluation and Research

ENCLOSURE:
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
12/08/2011