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APPLICATION NUMBER:

20-839/S-051

OTHER ACTION LETTER(s)

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 20839/S-051

COMPLETE RESPONSE

sanofi-aventis U.S. LLC
Attention: Nancy Barone Kribbs, Ph.D.
Senior Director, Global Regulatory Affairs
9 Great Valley Parkway
PO Box 3026
Malvern, PA 19355

Dear Dr. Kribbs:

Please refer to your Supplemental New Drug Application (sNDA) dated July 15, 2010, received July 15, 2010, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Plavix (clopidogrel bisulfate) 75 mg Tablets.

We acknowledge receipt of your amendments dated August 26, September 8, 9, 15, 23, 27, and 30, October 1, and December 17 and 23, 2010.

Your supplemental new drug application responds to the October 15, 2001 Pediatric Written Request, as amended August 24, 2007. The pivotal trial submitted to support your sNDA was CLARINET, a trial of administering clopidogrel to patients with cyanotic congenital heart disease palliated with a systemic-to-pulmonary arterial shunt. In the sNDA and in subsequent discussions with us, you have made various proposals for language to be included in the package insert (PI) for Plavix describing the results of CLARINET.

We have completed the review of your application, as amended, and have determined that we cannot approve this application in its present form. We do not agree with any of your proposals for describing the results of CLARINET in the PI. Our final proposal for the language to be used is as follows:

> **8.4 Pediatric Use**
> Safety and effectiveness in pediatric populations have not been established.
>
> A randomized, placebo-controlled trial (CLARINET) did not demonstrate clinical benefit in neonates and infants with cyanotic congenital heart disease palliated with a systemic-to-pulmonary arterial shunt. The trial, however, used a relatively low dose of Plavix and randomized patients a mean of 20 days post-procedure, so that it did not adequately test for effectiveness.

LABELING

Please submit revised labeling per our proposal above.

Your response must include updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. When responding to this letter, submit labeling that includes all previous revisions, as reflected in the most recently approved package insert. 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 also include annotations with the supplement number for previously-approved labeling changes.

OTHER

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the supplemental application. A resubmission must fully address all the deficiencies listed. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

Under 21 CFR 314.102(d), you may request a meeting or telephone conference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the FDA's "Guidance for Industry - Formal Meetings Between the FDA and Sponsors or Applicants", May 2009 at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM153222.pdf.

If you have any questions, please call:

Alison Blaus
Regulatory Health Project Manager
301-796-1138

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

/s/

NORMAN L STOCKBRIDGE
01/14/2011