



NDA 20-839/S-038

Sanofi-aventis U.S., LLC
Attention: Matthew R. Boyd, R.Ph., M.B.A.
Director, US Regulatory Affairs, Marketed Product
55 Corporate Drive
PO Box 5925
Bridgewater, NJ 08807-5925

Dear Mr. Boyd:

Please refer to your supplemental new drug application dated May 21, 2007, received May 22, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Plavix (clopidogrel bisulfate) 75 mg Tablets.

We also acknowledge your submission dated September 10, 2007.

This supplemental new drug application provides for a new 300 mg loading dose.

We have completed our review of this supplemental new drug application. It is approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on May 21, 2007; however, please note the following:

- Clopidogrel's inactive metabolite (SR26334) was used to demonstrate bioequivalence between the two dosage strengths. The Agency does not usually consider this an acceptable method to test for bioequivalence between the two formulations since prior pharmacokinetic studies conducted assessed the pharmacodynamics and the pharmacokinetics of Plavix due to the metabolite being inactive; however, utilizing the inactive metabolite in this study seems acceptable since:
 - the new strength tablet given is the same strength given previously clinically as the four 75 mg tablets, and
 - the change in rate of absorption will not make a significant difference as this will be administered as a one-time dose for the indication of acute coronary syndrome to be administered with aspirin followed by a daily 75 mg dose of Plavix and aspirin.
- Establishment of bioequivalence between the new dosage strength of 300 mg and four 75 mg tablets of Plavix has been made; however, this method of establishing bioequivalence will not be acceptable under any other setting. In the future, bioequivalence will be based on the parent drug due to analytical methods now being able to measure the parent drug, unlike when Plavix was initially approved when only the inactive metabolite was measurable.

Please note that a two (2) year expiry period is granted for the new 300 mg strength of Plavix (clopidogrel bisulfate) when stored at 25°C (77°F) in the approved container closure system.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Cardiovascular and Renal Products and two copies of both the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you issue a letter communicating important information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call:

Ms. Meg Pease-Fye, M.S.
Regulatory Project Manager
(301) 796-1130

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

Attached:
Approved 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/

Norman Stockbridge
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