



NDA 20839/S-057

SUPPLEMENT APPROVAL

sanofi aventis
Attention: Cristina Di Ramio, PharmD
Manager US Regulatory Affairs
55 Corporate Drive
Mail Stop: 55C-205A
Bridgewater, NJ 08807

Dear Dr. Di Ramio:

Please refer to your Supplemental New Drug Application (sNDA) dated January 31, 2013, received January 31, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Plavix (clopidogrel bisulfate) 75 mg Tablets.

This Prior Approval supplemental new drug application provides for a new warning concerning allergic cross-reactivity in those patients with a history of hypersensitivity to other thienopyridines as well as new allergic reactions listed in Section 6.2, Postmarketing Experience.

The agreed upon changes to the labeling and Medication Guide are as follows:

FULL PRESCRIBING INFORMATION (FPI) CHANGES

- In Section 5, **WARNINGS AND PRECAUTIONS**, a new subsection was added:
5.6 Allergic Cross-Reactivity
Patients should be evaluated for history of hypersensitivity to another thienopyridine (such as ticlopidine, prasugrel) since allergic cross-reactivity among thienopyridines has been reported.
- In the following Section 6.2 subsections, a few reactions were added:
 - Respiratory, thoracic and mediastinal disorders: eosinophilic pneumonia
 - Skin and subcutaneous tissue disorders: drug-induced hypersensitivity syndrome, drug rash with eosinophilia and systemic symptoms (DRESS),
- The **HIGHLIGHTS** and Table of Contents of the label were amended to reflect the above changes. Further edits were made to **HIGHLIGHTS** to limit them to one-half page.

MEDICATION GUIDE CHANGES

Due to the changes detailed above, the following changes were made to the Medication Guide:

- In the section, “**What should I tell my doctor before taking Plavix?**”, the below sentence was added:

“have had an allergy or reaction to any medicine used to treat your disease.”

- Under the section, “**What are the possible side effects of Plavix?**”, the following verbiage was added:

“Tell your doctor if you develop an allergic reaction while taking Plavix.”

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.

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 and Medication Guide) with the addition of any labeling changes in pending “Changes Being Effectuated” (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 via 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 with the revisions listed 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).

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

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:

Alison Blaus, RAC
Regulatory Project Manager
(301) 796-1138

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, PharmD
Deputy Director for Safety
Division of Cardiovascular & Renal Products
Office of Drug Evaluation I
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
09/12/2013