



TRANSMITTED BY FACSIMILE

Christopher Graham
Associate Vice President, US Regulatory Affairs
sanofi-aventis U.S. LLC
55 Corporate Drive, P.O. Box 5925
Bridgewater, NJ 08807

**RE: NDA #20-839
PLAVIX[®] (clopidogrel bisulfate) Tablets
MACMIS ID # 17325**

Dear Mr. Graham:

As part of its routine monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) of the U.S. Food and Drug Administration (FDA) has reviewed three sponsored links [US.CLO.08.02.035 (BMS#264US08PM115), US.CLO.08.02.036 (BMS#264US08PM116), US.CLO.08.02.037 (BMS#264US08PM117)] for PLAVIX (clopidogrel bisulfate) Tablets (Plavix) submitted by sanofi-aventis U.S. LLC (Sanofi) under cover of Form FDA- 2253. The sponsored links cited in this letter are misleading because they make representations and/or suggestions about the efficacy of PLAVIX, but fail to communicate **any** risk information associated with the use of this drug. The links also fail to use the required established name. Thus, the sponsored links misbrand the drug in violation of the Federal Food, Drug, and Cosmetic Act (the Act) and FDA implementing regulations. See 21 U.S.C. 352(a) & (n), 321(n); 21 CFR 201.10(g)(1), 202.1(b)(1), (e)(3)(i) & (e)(6)(i).

Background

The Indications and Usage section of the approved product labeling (PI) for PLAVIX states the following (in pertinent part):

PLAVIX (clopidogrel bisulfate) is indicated for the reduction of atherothrombotic events as follows:

- **Recent MI, Recent Stroke, or Established Peripheral Arterial Disease**
For patients with a history of recent myocardial infarction (MI), recent stroke, or established peripheral arterial disease, PLAVIX has been shown to reduce the rate of a combined endpoint of new ischemic stroke (fatal or not), new MI (fatal or not), and other vascular death. [emphasis original]

PLAVIX is also associated with a number of risks as reflected in the Contraindications, Warnings, Precautions, and Adverse Reactions sections of its PI.

Omission of Risk Information

Promotional materials, other than reminder pieces, which include the name of the drug product but do not include indications or other representations or suggestions relative to the drug product (see 21 CFR 200.200, 201.100(f), 202.1(e)(2)(i)), are required to disclose risk and other information about the drug. Such materials are misleading if they fail to reveal facts that are material in light of the representations made by the materials or with respect to consequences that may result from the use of the drug as recommended or suggested by the materials. The sponsored links present the following claims (emphasis in original):

- **PLAVIX Medication Lowers Risks of Future Heart Attack or Stroke from PAD**
See how prescription PLAVIX medication may help patients with recent heart attack, recent stroke, or established P.A.D. at PADfacts.com....
- **Plavix: Help P.A.D. Patients Lower Future Heart Attack And Stroke Risk...**
Discover the benefits of the prescription drug, PLAVIX. A medication that has been shown to help lower risk of future heart attack or stroke....
- **An Antiplatelet Medication for Patients with P.A.D... | PADFacts.com**
For those with established P.A.D., learn to help lower the risk of heart attack and stroke with Plavix. Learn more at PADFacts.com....

These sponsored links make representations and/or suggestions about the efficacy of PLAVIX, but fail to communicate **any** risk information. For promotional materials to be truthful and non-misleading, they must contain risk information in each part as necessary to qualify any claims made about the drug.

By omitting the most serious and frequently occurring risks associated with PLAVIX, the sponsored links misleadingly suggest that PLAVIX is safer than has been demonstrated.

Failure to Use Required Established Name

The sponsored links fail to present the full established name for PLAVIX, despite the requirement to do so. See 21 CFR 201.10(g)(1) & 202.1(b)(1).

Conclusions and Requested Action

For the reasons discussed above, the sponsored links misbrand PLAVIX, in violation of the Act and FDA regulations. See 21 U.S.C. 352(a) & (n), 321(n); 21 CFR 201.10(g)(1), 202.1(b)(1), (e)(3)(i) & (e)(6)(i).

DDMAC requests that Sanofi immediately cease the dissemination of violative promotional materials for PLAVIX, such as those described above. Please submit a written response to this letter on or before April 9, 2009, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) in use for PLAVIX as of the date of this letter, identifying which of these materials contain violations such as those described above, and explaining your plan for discontinuing use of such materials.

Finally, we encourage you to review your promotional materials for the other prescription drug products that Sanofi promotes in the United States and to discontinue or revise any materials with the same or similar violations, and request that your response address this issue as well.

Please direct your response to the undersigned at the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications, 5901-B Ammendale Road, Beltsville, MD, facsimile at 301-847-8444. In all future correspondence regarding this matter, please refer to MACMIS # 17325 in addition to the NDA number. We remind you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for PLAVIX comply with each applicable requirement of the Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Sangeeta Vaswani, Pharm.D.
Acting Group Leader
Division of Drug Marketing,
Advertising and Communications

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

/s/

Sangeeta Vaswani
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