



TRANSMITTED BY FACSIMILE

Mr. Robert Clark
Vice President, US Regulatory Affairs
Pfizer Inc.
235 East 42nd St
New York, NY 10017

**RE: NDA #021928
CHANTIX[®] (varenicline) Tablets
NDA #021540
CADUET[®] (amlodipine besylate/atorvastatin calcium) Tablets
NDA #019787
NORVASC[®] (amlodipine besylate) Tablets
MA # 2071**

Dear Mr. Clark,

The Division of Drug Marketing, Advertising, and Communications (DDMAC) of the U.S. Food and Drug Administration (FDA) has reviewed the "Online Resources" webpage (or webpage)¹ of the Pfizer, Inc. (Pfizer) website for LIPITOR[®] (atorvastatin calcium) Tablets (Lipitor). The webpage was submitted as a complaint to the DDMAC Bad Ad Program. The webpage cited in this letter is misleading because it makes representations and/or suggestions about the efficacy of CADUET[®] (amlodipine besylate/atorvastatin calcium) Tablets (Caduet), CHANTIX[®] (varenicline) Tablets (Chantix), and NORVASC[®] (amlodipine besylate) Tablets (Norvasc), but fails to communicate **any** risk information associated with the use of these drugs. Thus, the webpage misbrands the drugs in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 352(a) & (n); 321(n). See 21 CFR 202.1(e)(5).

Background²

Below are the indications (in pertinent part) and summary of the most serious and most common risks associated with the use of Norvasc. According to its FDA-approved product labeling (PI):

NORVASC[®] is indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agents. . . .

¹ Lipitor "Online Resources" webpage, at <http://www.lipitor.com/toolsResources/onlineResources.aspx> (last accessed on August 29, 2011).

² This information is for background purposes only and does not necessarily represent the indication or risk information that should be included in the promotional piece cited in this letter.

NORVASC is indicated for the symptomatic treatment of chronic stable angina. NORVASC may be used alone or in combination with other antianginal agents. . . .

NORVASC is indicated for the treatment of . . . vasospastic angina [Prinzmetal's or variant angina]. . . .

In patients with recently documented CAD [coronary artery disease] by angiography and without heart failure or an ejection fraction <40%, NORVASC is indicated to reduce the risk of hospitalization due to angina and to reduce the risk of a coronary revascularization procedure.

The PI for Norvasc contains a Contraindication regarding known hypersensitivity to amlodipine. The PI for Norvasc also contains Warnings and Precautions regarding hypotension, increased angina or myocardial infarction, beta-blocker withdrawal, and use in patients with hepatic failure. In addition, the most commonly reported adverse reactions for Norvasc were headache, fatigue, nausea, abdominal pain, and somnolence.

Below is the summary of the indications (in pertinent part) and the most serious and most common risks associated with the use of Caduet. According to its FDA-approved PI (emphasis in original):

CADUET . . . is indicated in patients for whom treatment with both amlodipine and atorvastatin is appropriate.

Amlodipine

1. Hypertension: Amlodipine is indicated for the treatment of hypertension

2. Coronary Artery Disease (CAD):

Chronic Stable Angina: Amlodipine is indicated for the treatment of chronic stable angina. . . .

Vasospastic Angina (Prinzmetal's or Variant Angina): Amlodipine is indicated for the treatment of confirmed or suspected vasospastic angina. . . .

Angiographically Documented CAD: In patients with recently documented CAD by angiography and without heart failure or an ejection fraction <40%, amlodipine is indicated to reduce the risk of hospitalization due to angina and to reduce the risk of a coronary revascularization procedure.

AND

Atorvastatin

Therapy with lipid-altering agents should be only one component of multiple risk factor intervention in individuals at significantly increased risk for atherosclerotic vascular disease due to hypercholesterolemia. Drug therapy is recommended as an adjunct to diet when the response to diet restricted in saturated fat and cholesterol and other nonpharmacologic measures alone has been inadequate. In patients with CHD [coronary heart disease] or multiple risk factors for CHD, the atorvastatin component of CADUET can be started simultaneously with diet restriction.

1. Prevention of Cardiovascular Disease:

In adult patients without clinically evident coronary heart disease, but with multiple risk factors for coronary heart disease . . . atorvastatin is indicated to:

- Reduce the risk of myocardial infarction
- Reduce the risk of stroke
- Reduce the risk for revascularization procedures and angina

In patients with type 2 diabetes, and without clinically evident coronary heart disease, but with multiple risk factors for coronary heart disease . . . LIPITOR is indicated to:

- Reduce the risk of myocardial infarction
- Reduce the risk of stroke;

In patients with clinically evident coronary heart disease, LIPITOR is indicated to:

- Reduce the risk of non-fatal myocardial infarction
- Reduce the risk of fatal and non-fatal stroke
- Reduce the risk for revascularization procedures
- Reduce the risk of hospitalization for CHF [congestive heart failure]
- Reduce the risk of angina

2. Heterozygous Familial and Nonfamilial Hyperlipidemia . . .

3. Elevated Serum TG Levels . . .

4. Primary Dysbetalipoproteinemia . . .

5. Homozygous Familial Hypercholesterolemia . . .

6. Pediatric Patients: Atorvastatin is indicated as an adjunct to diet . . . in boys and postmenarchal girls, 10 to 17 years of age

The PI for Caduet contains Contraindications regarding active liver disease, known hypersensitivity to any component of the medication, and use in pregnant and nursing women. The PI for Caduet also contains Warnings and Precautions regarding skeletal muscle effects (e.g., myopathy and rhabdomyolysis), liver dysfunction, increased angina and/or myocardial infarction, hypotension, beta-blocker withdrawal, endocrine function, CNS [central nervous system] toxicity, and use in patients with recent stroke or TIA [transient ischemic attack]. In addition, the PI indicates that the adverse experiences for Caduet are similar in terms of nature, severity, and frequency to those reported previously with amlodipine and atorvastatin. The most commonly reported adverse reactions for atorvastatin were nasopharyngitis, arthralgia, diarrhea, pain in extremity, and urinary tract infection, and the most commonly reported adverse reactions for amlodipine were headache and edema.

Below is the indication and summary of the most serious and most common risks associated with the use of Chantix. According to its FDA-approved PI:

CHANTIX is indicated for use as an aid to smoking cessation treatment.

The PI for Chantix contains a Boxed Warning regarding serious neuropsychiatric events. The PI also contains Contraindications regarding known history of serious hypersensitivity reactions or skin reactions to this drug. The PI for Chantix also contains Warnings and

Precautions regarding neuropsychiatric symptoms and suicidality, angioedema and hypersensitivity reactions, serious skin reactions, accidental injury, and nausea. In addition, the most commonly reported adverse reactions associated with Chantix were nausea, abnormal (e.g., vivid, unusual, or strange) dreams, constipation, flatulence, and vomiting.

Prior Communications

On March 26, 2009, DDMAC sent Pfizer an Untitled Letter regarding sponsored links on internet search engines for several of its products, including Caduet and Chantix. The sponsored links cited in the Untitled Letter were misleading because they made representations and/or suggestions about the efficacy of the products, but failed to communicate **any** risk information associated with the use of these drugs. DDMAC is concerned that Pfizer is continuing to promote its products in a similarly violative manner.

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 webpage presents the following claims (emphasis in original):

- “CADUET® (amlodipine besylate/atorvastatin calcium)
Learn about a treatment for high blood pressure and high cholesterol in a single pill.”
- “CHANTIX® (varenicline)
Learn about a prescription drug to help people quit smoking”
- “NORVASC® (amlodipine besylate)
Learn about a treatment for high blood pressure and the chest pain of angina”

Accordingly, the webpage makes representations and/or suggestions about the efficacy of Caduet, Chantix, and Norvasc, but fails to communicate **any** risk information. This omission of risk information is particularly concerning as one of these products, Chantix, has a Boxed Warning. By omitting the most serious and frequently occurring risks associated with Caduet, Chantix, and Norvasc, the webpage misleadingly suggests that these drugs are safer than have been demonstrated. We note that for each of these drugs, the webpage contains a link that leads to a webpage about Lipitor which contains a “Click to Continue” link. This link takes the user to the individual product website for Caduet and Chantix and to the PI for Norvasc. However, this is insufficient to mitigate the misleading omission of risk information from the “Online Resources” webpage.

Conclusion and Requested Action

For the reasons discussed above, the webpage misbrands Caduet, Chantix, and Norvasc, in violation of the FD&C Act, 21 U.S.C. 352(a) & (n); 321(n). See 21 CFR 202.1(e)(5).

DDMAC requests that Pfizer immediately cease the dissemination of violative promotional materials for Caduet, Chantix, and Norvasc, such as those described above. Please submit a written response to this letter on or before September 14, 2011, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Caduet, Chantix, and Norvasc that contain violations such as those described above, and explaining your plan for discontinuing use of such violative materials. Please direct your response to me 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 20705-1266, facsimile at 301-847-8444. DDMAC recently migrated to a different tracking system. Therefore, DDMAC letters will now refer to MA numbers instead of MACMIS numbers. In all future correspondence regarding this matter, please refer to MA # 2071 in addition to the NDA numbers. 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 Caduet, Chantix, and Norvasc comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Zarna Patel, PharmD
Regulatory Review Officer
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/

ZARNA PATEL
08/31/2011